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Synthesis of Fluorine-Containing Molecular Rotors and Their Assembly on Gold Nanoparticles

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A series of eight rotors containing thiol groups for attachment to gold surfaces and fluorine atoms for solid-state ^{19}F NMR spectroscopy have been prepared through linear, multistep synthesis. The common rotating part of the rotors (rotator), consisting of a 2,6-difluorobenzene moiety, is introduced into the rotor structure through an unusual regioselective Sonogashira coupling with 2,6-difluoro-1,4-diiodobenzene. Rotors with different bulky trityl headgroups were prepared, along with their linear, less hindered analogues. These molecular rotors were assembled on gold nanoparticles (AuNPs) and preliminary characterization was performed on these AuNPs in order to study the effects of the sizes of the molecules on the packing behaviour on the AuNP surfaces. As expected, we found that linear molecules adopt more closely packed structures on the surfaces than their bulky analogues. This offers a very promising opportunity to study rotation dynamics at the molecular level by solid-state NMR spectroscopy.

Introduction

Synthetic molecular machines, or nanomachines, mimicking the functions of those found in nature, have attracted lot of attention in the past fifteen years.[1–4] Their preparation, but most importantly their characterization and their use in real devices, is one of the biggest challenges facing researchers involved in nanoscience. The inherent difficulties in predicting the dynamic behaviour of such tiny machines arises from the non-deterministic nature of quantum mechanics, which governs motion at the molecular level. Nonetheless, researchers have developed very powerful tools to study the dynamics of motions in both simple and complex molecules. Among others, NMR spectroscopy has proved to be a very useful and versatile tool to study rapid molecular motions, especially rotation and translation, both in solution[5–8] and in the solid state.[9–12]

The characterization of molecular motions on surfaces and at interfaces is much more difficult, however, because NMR spectroscopy is not suitable for the study of molecules on flat surfaces, because of the low concentrations of the active molecules per surface unit. More sophisticated techniques such as scanning tunnelling microscopy (STM) have thus been used extensively to obtain information on molecular dynamics on surfaces.[13–17] Although very helpful, STM analysis suffers from time-consuming sample preparation, which makes the investigation of large numbers of rotors very tedious. Investigation of several molecules is necessary, however, for identification of the parameters that influence the rotation dynamics at the molecule level and for the eventual development of faster and more efficient rotors. Two different strategies through which to increase the analytical capability can hence be employed: 1) the development of a more versatile and rapid characterization technique, or 2) adaptation of an already existing useful technique to allow studies of motions on surfaces. Because the second strategy is much more realistic and easy to undertake, we envisaged the use of solid-state NMR spectroscopy to study the rotation dynamics of molecular rotors mounted on gold nanoparticles (AuNPs). AuNPs could be very useful because they offer higher surface contact and organic content than flat surfaces, thus providing enough signals in solid-state NMR spectroscopy to allow dynamic study on surfaces to be carried out. The first steps towards the validation of our strategy are to prepare a variety of rotors that exhibit structural variation, to assemble them on AuNPs and to characterize the resulting AuNPs in order to assess whether or not they are suitable and reliable test beds for further rotor investigation.

As the first step of this long-term project, here we report the detailed synthesis of fluorine-containing rotors featuring structural differences with regard to the stator and the anchoring groups used for attachment on AuNPs. An idealized schematic representation of the rotors attached to the surface of a gold nanoparticle is presented in Figure 1. The primary goal of this study was to find efficient and versatile synthetic pathways for the preparation of a series of thiol-containing rotors that can be assembled on gold nanoparticles. The synthesis and characterization of AuNPs by ther-

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mogravimetric analysis (TGA) and transmission electron microscopy (TEM) are also presented. The preliminary characterization of AuNPs was undertaken in order to determine the influence of the size of the stator on the footprint of the molecular rotor on an AuNP surface in the context of the creation of free volume inside the monolayer. It also helps evaluation of the quality of AuNPs obtained when bulky molecules are used as surface ligands during the synthesis. It should be noted that the thorough characterization of the nanoparticles and their solid-state ^{19}F NMR analysis will be presented in forthcoming articles.

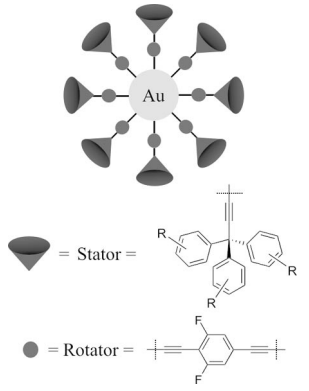


Figure 1. Idealized schematic representation of a molecular rotor on an AuNP surface.

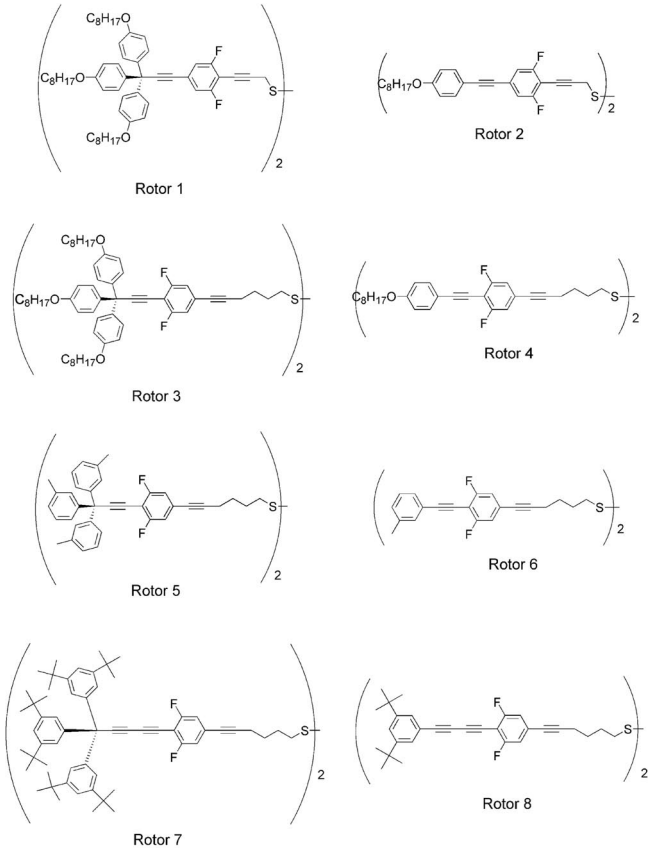


Figure 2. Structures of rotors **1**–**8**.

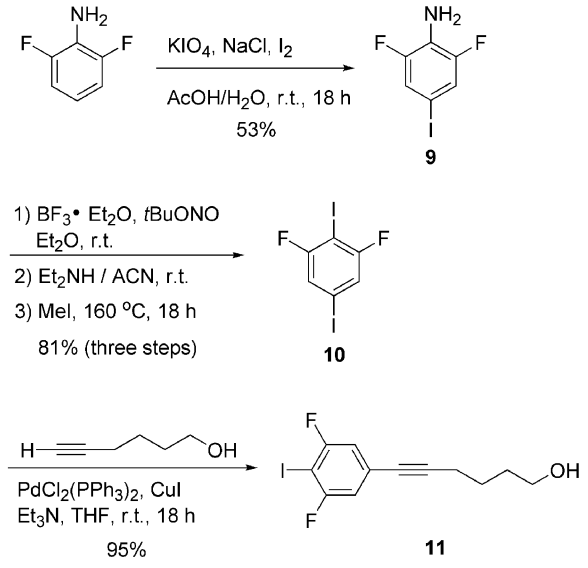
Results and Discussion

The structural characteristics of the rotors were especially designed to maximize speeds of rotation and to provide clear and strong NMR signals. Firstly, the rotator part, containing fluorine atoms, is attached to two ethynyl groups in a *para* relationship, because the rotation of a phenyl group around an alkyne is almost barrierless in the gas phase, allowing fast rotation at room temperature.[18] Secondly, fluorine atoms were introduced on the rotator of each rotor because ^{19}F is one of the most sensitive nuclei in NMR spectroscopy, thus providing strong signals even when the molar percentage of fluorine in a molecule is low.[19] Thirdly, trityl derivatives were used as the stators because they provide good protecting pockets around the rotators by creating free volume around them.[9–12] The creation of free volume near the rotator is of particular importance for ensuring fast rotation of the rotator, as has been shown several times by the Garcia–Garibay group in crystalline state rotors.[20–22] Additionally, the presence of trityl groups at the top of the monolayer is expected to protect the rotator from intermolecular contacts (AuNP–AuNP) in the solid state and interdigitation of the long alkyl chains used to solubilize AuNPs. Finally, a thiol group was introduced onto each rotor to allow attachment to AuNPs. It is worth mentioning that different spacers between the rotator and the thiol have been used in order to study the influence of the F–Au distance on solid-state ^{19}F NMR spectra in further experiments. The structures of all the rotors prepared for this study are presented in Figure 2.

For the purpose of our study, we decided to evaluate three different trityl derivatives – the 4-octyloxy derivative **15** (Scheme 2, below), the 3-methyl derivative **16** and the 3,5-di-*tert*-butyl derivative **17** – as stators. These groups are expected to provide different packing behaviour patterns on the AuNP surfaces. It is also well known that the endgroups of molecules attached to AuNPs can change their solubilities and aggregation properties.[23] For purposes of comparison in the context of free volume creation on AuNP surfaces, linear, less hindered analogues of all the bulky rotors were also synthesized.

The syntheses of the rotors are shown in Scheme 1 to Scheme 9. Firstly, the rotator (compound **10**, Scheme 1), the central building block of all the rotors, was synthesized in two steps starting from 2,6-difluoroaniline, on which we performed an iodination by a procedure published by Emmanuvel et al.[24] to obtain compound **9** in modest yields (53%). Some other iodination methods including the use of benzyltrimethylammonium dichloroiodate,[25] molecular iodine with HgO[26] and iodine with Ag_2SO_4[27] gave poorer yields or no reaction at all. The conversion yield of 2,6-difluoroaniline into **9** in our hands is as good as that reported in the literature with molecular iodine and $AgNO_3$.[28] The amino group was then transformed into a diazonium salt by treatment with $BF_3{\cdot}Et_2O$ and *t*BuONO. Interestingly, the use of KI to afford compound **10** directly from the diazonium salt intermediate was unsuccessful and a large amount of the protonated intermediate was reco-

vered. To overcome this problem, diethylamine was added to the diazonium salt in order to provide a triazene intermediate, which after filtration through silica gel was heated at 160 °C in iodomethane under argon in a pressurized vessel. Compound **10** was then obtained in good yield (81%) from the aniline **9**. The reaction time and the temperature needed to convert the triazene intermediate into its iodo derivative (compound **10**) were much higher than usually required in examples reported in the literature for different substrates.[29] In fact, we observed that the reactivity at the 1-position in 2,6-difluorobenzene derivatives is much lower than we had expected and so we exploited the low reactivity of compound **10** at its 1-position to perform a regioselective Sonogashira coupling with hex-5-yn-1-ol to provide solely compound **11**, in 95% yield and with no sign of reaction at the site between the two fluorine atoms.

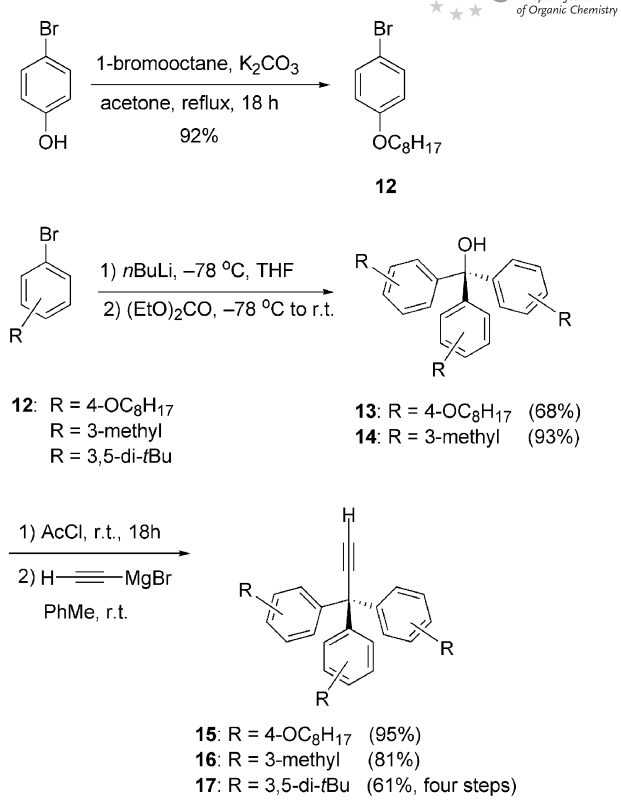


Scheme 1. Synthesis of fluorine-containing building block.

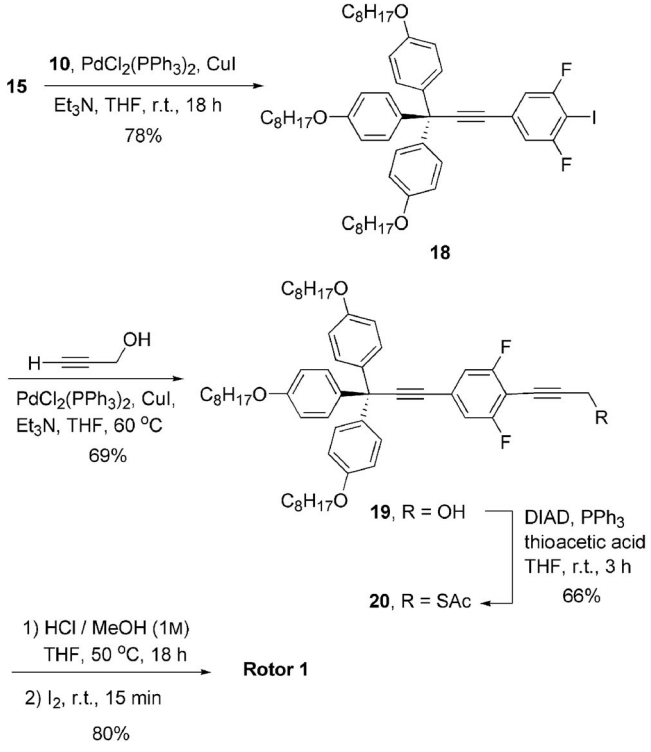
The synthesis of the rotor **1** is shown in Scheme 2 and Scheme 3. For this model we chose to introduce octyl chains to improve the solubility of the nanoparticles. Nucleophilic substitution of 4-bromophenol on 1-bromooctane afforded compound **12** in very good yield (92%). This bromoaryl was then converted into compound **13** by treatment with *n*BuLi and diethylcarbonate in 68% yield. The alcohol was efficiently converted into an alkyne by treatment with acetyl chloride and subsequently with ethynylmagnesium bromide, providing compound **15** in an excellent yield (95%).

This compound was then coupled to compound **10** to afford compound **18** in 78% yield (Scheme 3). Because compounds **15** and **18** have similar polarities, an excess of compound **10** was required to ensure complete conversion of compound **15**.

For the same reasons as mentioned above, Sonogashira coupling between compound **18** and propargyl alcohol was difficult to achieve. Indeed, 1.5 equiv. of propargyl alcohol, 4 mol-% of palladium catalyst and 4 mol-% of CuI in THF at 60 °C for several hours were needed to perform the synthesis of compound **19** in a satisfactory yield of 69%. This lower reactivity of the iodine atom between the two fluorine atoms is consistent with what we had observed in the syn-



Scheme 2. Synthesis of the trityl stators.



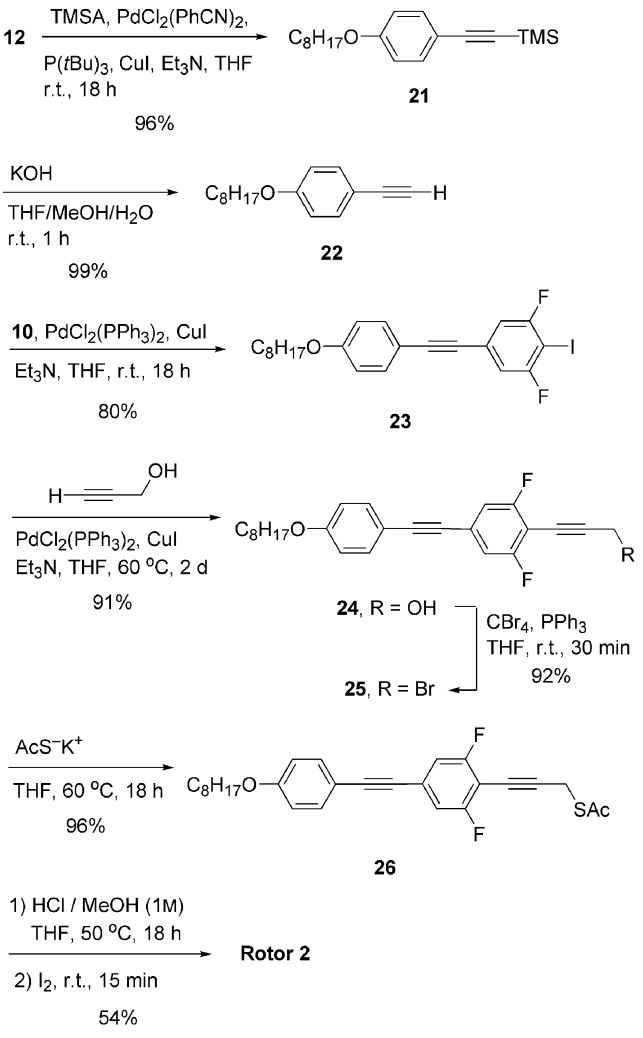
Scheme 3. Synthesis of rotor **1**.

thesis of compound **11**. Similar low reactivity (15–30% yields) has recently been reported for Sonogashira coupling under harsh conditions with 1,4-dibromo-2,3,5,6-tetrafluorobenzene as substrate.[30]

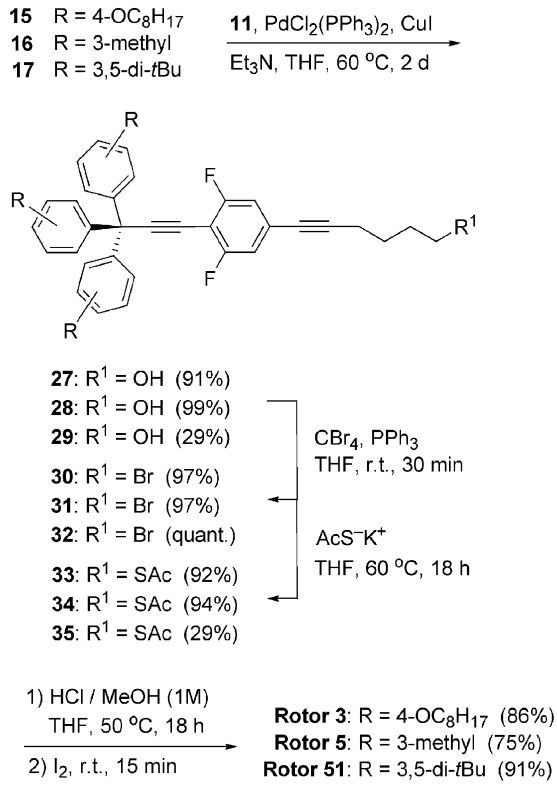
The alcohol function of compound **19** was replaced by a thioacetate by treatment with thioacetic acid under Mitsunobu conditions to afford compound **20** in good yield (66%). Finally, the thioacetate **20** was converted into the rotor **1** in 80% yield by acidic hydrolysis followed by a mild oxidation with molecular iodine.[31,32]

Our comparative model for the rotor **1** was the linear, less hindered rotor **2** (Figure 2), and the synthetic pathway used to prepare this is shown in Scheme 4. Initially, compound **12** was converted in excellent yield (96%) into compound **21** under Buchwald conditions for Sonogashira coupling of unactivated aryl bromides.[33] It is worth mentioning that, in our hands, standard Sonogashira conditions failed to provide compound **21** in reasonable yield. The alkyne was then deprotected and compound **22** was coupled with compound **10** under Sonogashira coupling conditions to provide compound **23** in good yield (80%). As in the synthesis of compound **15** discussed above, an excess of compound **10** was necessary to achieve complete conversion of compound **22** into compound **23** and to enable purification. The synthesis of compound **24** was achieved in a 91% yield by Sonogashira coupling between compound **23** and propargyl alcohol under the more severe conditions described previously for the synthesis of compound **19**. The alcohol was then replaced by a bromine atom (PPh_3/CBr_4) to afford **25** in excellent yield (92%). Compound **25** was converted into compound **26** in 96% yield by treatment with potassium thioacetate. This method was used instead of the Mitsunobu reaction – as in the case of compound **20** – because the latter method leads to a significant amount of side products, which makes purification difficult. Finally, the rotor **2** was obtained from compound **26** in modest yield (54%) by the same pathway as shown in Scheme 3 for the rotor **1**.

The synthesis of the rotor **3** (Figure 2) is shown in Scheme 5 and was similar to the synthesis described above. Compound **11** was coupled with compound **15** under the improved Sonogashira conditions described above to afford compound **27** in 91% yield. Addition of propargyl alcohol at the end of the reaction as a "workup" technique is necessary to destroy any residual compound **11** left and, consequently, to enable purification of **27** by column chromatography. The yield obtained for this reaction is quite high in view of the very low reactivity of compound **11** observed previously in Sonogashira coupling at room temperature. To obtain such a yield however, the reactions have to be run for two days at 60 °C with twice the amount of catalyst



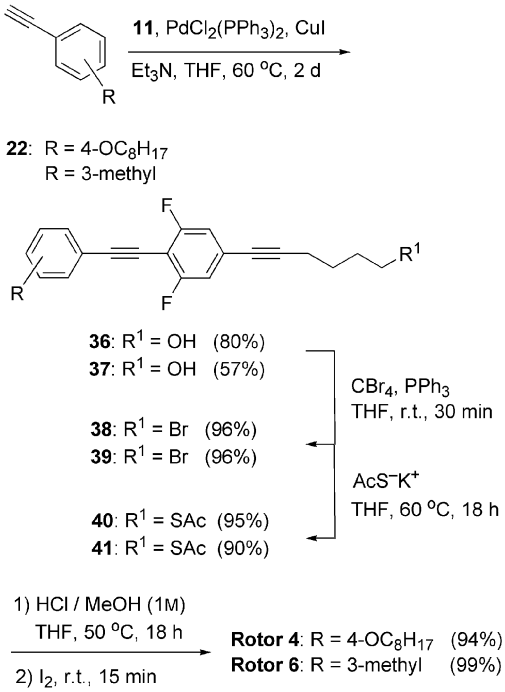
Scheme 4. Synthesis of rotor **2**.



Scheme 5. Synthesis of rotors **3**, **5**, and **51**.

and copper(I), thus providing further evidence of the low reactivities of the 1-positions in 2,6-difluorobenzene derivatives. The further synthetic steps used were the same as those described previously, with compounds **30** and **33** and the rotor **3** being obtained in 97%, 92% and 86% yields, respectively.

The rotor **4** (Figure 2), the less hindered analogue of the rotor **3**, was synthesized as shown in Scheme 6. Sonogashira coupling between compounds **22** and **11** afforded compound **36** in 80% yield. As in the case of compound **27**, addition of propargyl alcohol to destroy any residual compound **11** was necessary during the synthesis of **36**. This compound was further transformed into compounds **38** and **40** and the rotor **4** in 96%, 95% and 94% yields, respectively, under the usual reaction conditions.



Scheme 6. Synthesis of rotors **4** and **6**.

In many cases the chromatographic purification of the low-polarity synthetic intermediates described so far was difficult because of similarities in the polarities of impurities and of the desired compounds. Moreover, co-elution phenomena that we attributed to the presence of long, fatty octyl chains were also observed. This serious drawback prompted us to design another class of compounds, because we were expecting difficulties in the purification of the corresponding nanoparticles, which mostly relies on solubility and polarity differences. We therefore decided to synthesize the rotors **5** and **6** by the same pathway as we had used for the rotors **3** and **4**. As shown in Scheme 2, 3-bromotoluene was converted into compound **14** in 93% yield by treatment with *n*BuLi and diethylcarbonate. This alcohol was efficiently converted into compound **16** in good yield (81%) by successive treatment with acetyl chloride and ethynylmagnesium bromide. The synthesis of the rotor **5** was then performed as shown in Scheme 5. A Sonogashira coupling between compound **16** and compound **11** was performed under the improved conditions to afford compound **28** in 99% yield. This compound was then converted into compounds **31** and **34** and the rotor **5** in 97%, 94% and 75% yields, respectively.

The rotor **6** (Figure 2), the less hindered analogue of the rotor **5**, was synthesized as shown in Scheme 6. A Sonogashira coupling between 3-ethynyltoluene and compound **11** afforded compound **37** in 57% yield, and this was further transformed into compounds **39** and **41** and the rotor **6** in 96%, 90% and 99% yields.

In order to simplify the synthesis of the rotors, we attempted to assemble them through Sonogashira reactions either with the thioacetate derivative of **11** (**I**, Figure 3) or with the disulfide derivative (**II**).[34] This would have given us the opportunity to perform fewer reactions once the stator (trityl) group was attached to the rotor. In a first attempt we used compound **15** and, surprisingly, no reaction occurred. The reaction was also unsuccessful even with a simpler alkyne such as propargylic alcohol. We believe that catalyst poisoning with these intermediates is responsible for the failure of this reaction. Poisoning by sulfur is a well known undesired event in palladium-catalysed systems.[35,36] This inconvenience led us to use Sonogashira coupling with **11** instead of **I** or **II**, resulting in a three-steps-longer process for each rotor.

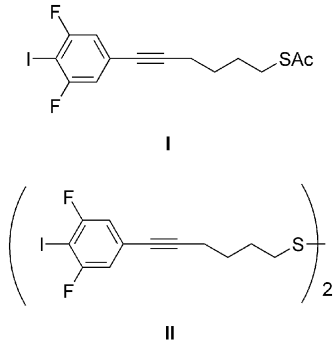
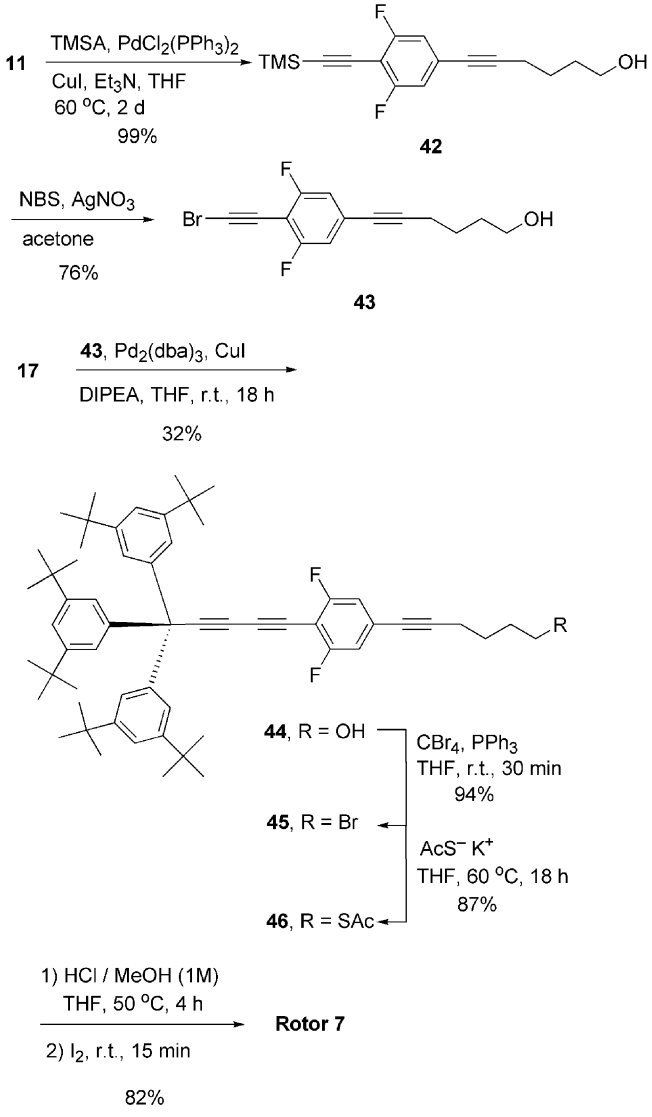
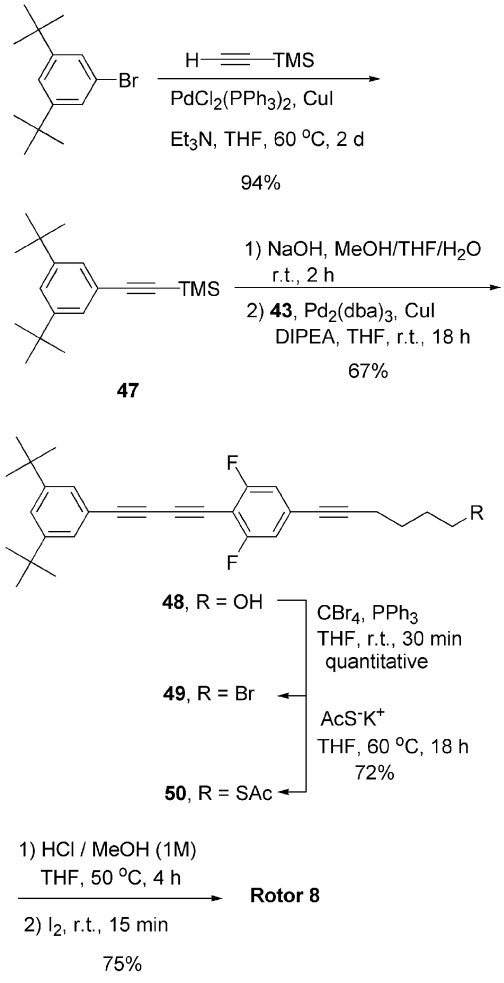


Figure 3. Sulfur-containing iodoarene.

To complete our study we needed a very bulky and hindered model, so we designed the rotor **7** (Figure 2) as shown in Scheme 7 and the less hindered analogue rotor **8** (Figure 2) as shown in Scheme 8. Use of a diyne unit was chosen in order to overcome van der Waals contacts between the fluorine atoms and the *tert*-butyl groups. A Cadiot–Chodkiewicz cross-coupling reaction, the most commonly used method to prepare unsymmetrical diynes,[37,38] was used for the synthesis of our models. Compound **42** was therefore prepared from compound **11** and TMSA in 99% yield under the improved Sonogashira conditions. Desilylation and bromination of **42** with $AgNO_3$ and NBS afforded compound **43** in 74% yield. To avoid degradation, this compound has to be stored under argon in a dark place if not used immediately.



Scheme 7. Synthesis of rotor **7**.



Scheme 8. Synthesis of rotor **8**.

The bulky compound **17** (Scheme 2), synthesized by the same strategy as presented for other trityl derivatives (61% yield over four steps), was then coupled to compound **43** in a palladium-catalysed Cadiot–Chodkiewicz reaction[38] to give compound **44** in a low 32% yield (Scheme 7). It is noteworthy that palladium-catalysed coupling with $Pd_2(dba)_3$·$CHCl_3$ was used rather than the classical Cadiot–Chodkiewicz conditions (CuCl, $HONH_2$·HCl, $EtNH_2$, MeOH)[37] because it is much more conveniently applied to large hydrophobic molecules. In an attempt to improve the yield of our reaction we performed the same reaction at 60 °C but only a poor 6% yield was obtained, indicating that these conditions are not amenable to heating. We also attempted to increase the efficiency of the coupling through the use of $PdCl_2(PPh_3)_2$ under conventional Sonogashira conditions, but the homocoupling by-product of **43** and **17** were the only products recovered, whereas the use of $Pd(dba)_2$ in place of $Pd_2(dba)_3$·$CHCl_3$ gives a slightly lower yield. Poor solubility of the cuprate intermediate of **17** was suspected, so we attempted the reaction in the presence of TMEDA, but this approach also failed. We also attempted the palladium-catalysed cross-coupling reaction in pyrrolidine with $PdCl_2(PPh_3)_2$ and CuI, by Alami's procedure,[39] with the commercially available dodec-1-yne rather than compound **17** in order to prevent the waste of synthetic product. Unfortunately, the reaction simply failed, even when $Pd_2(dba)_3$·$CHCl_3$ was used. Lei et al. recently reported a new hindered and electron-rich ligand designed to accelerate the reductive elimination process and, consequently, to improve the yields of palladium-catalysed Cadiot–Chodkiewicz reactions.[40] In fact, competitive homocoupling of both alkynes and bromoalkynes is a major problem, which decreases cross-coupling yields considerably. We synthesized this ligand by Lei's procedure[41] and used it in the diyne synthesis under the optimized conditions described above, but no improvement was observed.

An alternative approach, used by Zhao et al.,[42] to obtain the desired diyne was to synthesize a TMS-protected diyne through a statistical Glaser reaction between **17** and TMSA, followed by deprotection of the terminal diyne and Sonogashira coupling with compound **11**. Surprisingly, no reaction occurred, even after several attempts to optimize this reaction. We suspect the terminal diyne is unstable in

solution, because the solution rapidly turned dark before its addition to the reaction mixture. In final attempts, classical Cadiot–Chodkiewicz cross-coupling was performed by Gung's[43] and Negishi's[44] procedures, but both reactions failed. The low reactivity of compound **17** at room temperature is likely attributable to the steric hindrance caused by the multiple *tert*-butyl groups on the trityl moieties. Heating the reaction mixture in an attempt to accelerate the reaction also failed, with production of several unknown side products.

The rotor **7** (Figure 2) was obtained in the same way as used for the other rotors (Scheme 7). Compound **44** was further transformed into compound **45**, compound **46** and rotor **7** in 94%, 87% and 82% yields, respectively, under the usual conditions.

The rotor **8** (Figure 2), the linear analogue of the rotor **7**, was synthesized in a similar manner as the other compounds (Scheme 8). 1-Bromo-3,5-di-*tert*-butylbenzene was coupled to TMSA by Sonogashira coupling and the TMS group was removed by basic hydrolysis. Palladium-catalysed Cadiot–Chodkiewicz coupling of compounds **47** and **43** under the best conditions described above provided compound **48** in a good 67% yield, again indicating that the low reactivity of **17** with **43** was responsible for the poor 32% yield obtained for compound **44**. Finally, the rotor **8** was obtained by the same approach as described for the other rotors: compound **48** was converted into compounds **49** and **50** and rotor **8** in 99%, 72% and 75% yields, respectively.

In order to assess whether or not the diyne linker is long enough to overcome the steric hindrance between the *tert*-butyl groups and the fluoroaryl rotator, the monoyne analogue, the rotor **51** (Scheme 5), was synthesized by the same procedures as used for the rotors **3** and **5**. However, the synthesis of compound **29** under standard Sonogashira coupling conditions with trityl **17** once more gave a poor yield, which is again attributable to the steric hindrance caused by the six *tert*-butyl groups. It should be noted that rotor **51** was not assembled on AuNPs in the course of this study, because we do not expect significant differences in the assembly behaviour of this molecule on AuNPs in relation to rotor **7**. Rotor **51** will be further assembled on AuNPs and studied by solid-state NMR to assess the importance of the length of the alkyne spacer on the rotation rate.

With rotors **1**–**8** in hand we proceeded to the synthesis of the AuNPs. In attempts to obtain high-quality AuNPs, different synthetic methods were tried with varying degrees of success. As a first try, the synthesis of nanoparticles capped with 4-dimethylaminopyridine (DMAP) as ligand according to Lennox's procedure was attempted.[45] However, the reaction failed, with the recovery of a black precipitate in a milky solution. We also attempted the synthesis of Schmid's cluster,[46] a phosphane-capped cluster $[Au_{55}(PPh_3)_{12}Cl_6]$, by the improved procedure developed by Hutchison.[47] This procedure is essentially the same as the Brust approach but with triphenylphosphane as ligand. Unfortunately, the AuNPs obtained in this case were too soluble in common organic solvents to allow purification by precipitation. The best results were obtained by Brust's method,[48] which enables the preparation of AuNPs of specific dimensions (1–5 nm) with use of Murray's modification.[23] Indeed, the traditional Brust procedure consists of the reduction of a gold salt ($HAuCl_4$) with $NaBH_4$ in the presence of the desired thiol in a biphasic toluene/water mixture with tetrabutylammonium bromide (TBAB) as phase transfer agent. In Murray's procedure, control of the core size is achieved by varying the temperature and addition rate of the reducing agent, but also, more importantly, the $HAuCl_4$/disulfide molar ratio. An increase in this molar ratio results in an increase in the nanoparticles' diameters. Subsequent reduction of $HAuCl_4$ with $NaBH_4$ in the presence of TBAB and the desired disulfide afforded **NP1**–**NP8** (**NP1** corresponds to AuNP functionalized with the rotor **1**, and so on) in good quantities. The reaction conditions were carefully chosen to provide AuNPs with diameters of about 2.0 nm. All AuNPs were purified by successive precipitation and size exclusion chromatography. As expected, the nature of the ligands dictates the solubilities of the AuNPs; detailed purification procedures for all the AuNPs are presented in the Experimental Section. Unfortunately, it was not possible to obtain **NP1** and **NP2** in pure form despite all the purification steps performed. Similarly, **NP3** and **NP4** were found to contain small amounts (<5%) of unlinked ligand molecules. It is noteworthy that after a few precipitation cycles the AuNPs become cleaner and successive attempts to precipitate them failed. The presence of small amounts of unlinked materials can be attributed to van der Waals interactions between octyl chains of free and attached ligands when precipitated in an unsuitable solvent. Furthermore, size exclusion chromatography with Biobeads© S-X1 was not suitable for removing the unlinked materials completely from **NP1**–**NP4**. **NP1** and **NP2** were therefore discarded for TGA analysis, although **NP3** and **NP4** were analysed despite the presence of very small amounts of unlinked materials.

The **NP1**–**NP8** diameter measurements were conducted by transmission electron microscopy (TEM; see the Supporting Information for all the images obtained). Examples of images obtained for **NP5** and **NP6** are shown in Figure 4. The AuNP diameters were calculated with the aid of ImageJ 1.41o software by conventional treatments such as baseline correction, threshold adjustment and exclusion of poorly spherical shapes. Averages over hundreds of particles afforded values with standard deviations similar to those reported in the literature. The average AuNP sizes are shown in Table 1. As predicted, the AuNP diameters range from 1.8 to 2.3 nm with a standard deviation of ca. 25%, which is consistent with other AuNPs prepared by the Murray-modified Brust method.[23] As shown in Figure 3, the AuNPs appears as individual particles of similar size and no aggregation is observed. This behaviour has been observed for all AuNPs synthesized in this study. This indicates that the AuNPs synthesized in this study do not display specific interaction that could lead to formation of aggregates in the solid state.

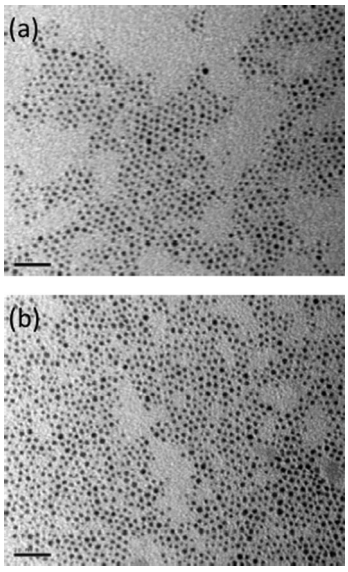


Figure 4. Transmission electron micrographs of a) **NP5** and b) **NP6**. Scale bar = 20 nm.

Table 1. Sizes and compositions of **NP3** – **NP8**.

AuNP	Diameters [nm]	Mass loss [%]	γ	Organic/Au surface [mol/mol]
NP3	1.8 ± 0.6	35.7	0.22	0.21
NP4	2.0 ± 0.5	28.2	0.33	0.32
NP5	1.9 ± 0.5	26.0	0.24	0.23
NP6	2.0 ± 0.5	23.2	0.33	0.32
NP7	2.2 ± 0.6	29.6	0.20	0.20
NP8	2.3 ± 0.7	20.9	0.24	0.24

In order to confirm the creation of free volume by the trityl moieties on AuNPs, thermogravimetric analysis (TGA) was performed to measure the numbers of rotors per surface unit on the AuNPs. By comparison of the bulky rotors with their linear analogues we wanted to assess whether or not trityl groups were more efficient than single phenyl groups for isolation of the rotator. The TGA results are shown in Table 1. Values for **NP1** and **NP2** are not represented; these were discarded from our study because we had not been able to obtain materials of satisfactory purity (as discussed above and as shown by ^{19}F NMR). We then focused our analysis on **NP3**–**NP8**, which were much easier to purify.

The organic loadings (or coverages) at the surfaces of **NP3**–**NP8** were calculated by the Equation (1):[49]

$$\chi_{organic} = \frac{4\pi(R_{Core} - R_{Au})^2 \rho_{HCP}(MW_{thiol})\gamma}{4\pi(R_{Core} - R_{Au})^2 \rho_{HCP}(MW_{thiol})\gamma + \frac{4}{3}\pi R^3_{Core}(\rho_{Au})(AW_{Au})} \quad (1)$$

where $\chi_{organic}$ is the mass fraction of alkanethiolate in the cluster, R_{Au} is the crystallographic radius of a gold atom (0.145 nm), ρ_{HCP} is the number density of surface gold atoms (13.89 atoms nm^{-2}, assuming hexagonal close packing), MW_{thiol} is the alkanethiol molecular weight in mass per molecule, γ is the coverage (ratio of thiolates to surface Au atoms), ρ_{Au} is the atom density of bulk gold (58.01 atoms nm^{-3}) and AW_{Au} is the atomic weight of Au in mass per atom. The γ values for **NP3**–**NP8** are shown in Table 1. These γ values are well below the 0.66 value (i.e., approx. two thiolates per three surface gold atoms) calculated for thioalkanes as ligands of AuNPs[23] because **NP3**–**NP8** do not benefit from the strong van der Waals interactions of alkanethiolates, which favour close packing on the surface.[49]

The organic loadings of AuNPs were also calculated as molar ratios of organic ligands on surface gold atoms. These calculations were performed through the use of the number of surface gold atoms per total gold atoms as a function of AuNP size.[23] All data and graphs for the calculation of this molar ratio are available in the Supporting Information. Briefly, the organic loss during TGA measurement was converted into moles of organic materials and the areas of nanoparticles were obtained by assumption of a spherical shape, because this approximation has proved to be very consistent with the true shape of AuNPs.[49] Two plots were then made with values reported by Hostetler: 1) the number of total gold atoms as a function of AuNP radius and 2) the number of surface gold atoms as a function of total gold atoms of AuNPs. From the first graph we obtained the total number of gold atoms from the radii of **NP3**–**NP8**. These values were used in the second graph to provide the corresponding number of surface gold atoms from the radii of **NP3**–**NP8**. A simple ratio of the surface gold atoms to total gold atoms afforded a surface coefficient, which was multiplied by the number of remaining moles of gold after TGA measurements. This provides the number of moles of gold atoms on the surface for **NP3**–**NP8**. Finally, the ratio of moles of organic to moles of surface gold atoms afforded the values reported in Table 1.

The ratio values shown in Table 1 correlated surprisingly well with the γ values calculated previously. These results are in agreement with our hypothesis that sterically hindered rotors provide lower surface loadings than their less hindered analogues. In fact, **NP3**, **NP5** and **NP7** show molar ratios of 0.21, 0.23 and 0.20 and γ values of 0.22, 0.24 and 0.20, respectively, which means that about one molecule is linked to about five surface gold atoms. In comparison, both **NP4** and **NP6** show a molar ratio of 0.32 and a γ value of 0.33, suggesting about one molecule per three surface gold atoms. The lower molar ratio and γ value of **NP8**, 0.24 in both methods, could be explained by the more significant van der Waals radius of the 3,5-di-*tert*-butylphenyl unit, leading to poorer packing than in the cases of **NP4** and **NP6**. Nonetheless, the molar ratio of the trityl analogue is below 0.24 with a value of 0.20. In light of these results, one can agree that the use of a trityl group to create free volume in AuNP monolayers is efficient, as expected, but that solvent molecules are likely to be intercalated inside the monolayer. This assumption will be tested shortly by solid-state NMR and XPS spectroscopy.

Conclusions

We report the synthesis of molecular rotors containing fluorine atoms. Both trityl and linear derivatives of those rotors were assembled on AuNPs by the Murray-modified Brust method. AuNPs with diameters of about 2 nm were synthesized and TGA analysis showed that the footprints of trityl-containing rotors are higher than those measured for the linear analogues. This supports the idea that a more sterically hindered stator should create more free volume in the monolayer, thus increasing the chances of fast rotation of the rotator. From these results, one can assume that AuNPs represent a promising test-bed for kinetic studies on surface-bound molecular rotors. This will be tested soon by study of these AuNPs by variable-temperature solid-state ^{19}F NMR experiments.

Experimental Section

General Methods: Ethynylmagnesium bromide in THF (0.5 M) and butyllithium in hexanes (2.5 M) were purchased from Sigma–Aldrich Co., Canada. Others chemical reagents were purchased from Sigma–Aldrich Co., Canada, Alfa Aesar Co., TCI America Co. or Oakwood Products Inc. and were used as received. Solvents used for organic synthesis were obtained from Fisher Scientific (except THF, from Sigma–Aldrich Co. Canada) and purified with a Solvent Purifier System (SPS) (Vacuum Atmosphere Co., Hawthorne, USA). Other solvents were obtained from Fisher Scientific and were used as received. Tetrahydrofuran (THF) and triethylamine (Et_3N) used for Sonogashira reactions were degassed 30 min prior to use. All anhydrous and air-sensitive reactions were performed in oven-dried glassware under positive argon pressure. Analytical thin-layer chromatography was performed with pre-coated TLC plates (silica gel 60 F_{254}, 0.25 mm, Silicycle, Québec, Canada). Compounds were visualized with the aid of 254 nm and/or 365 nm UV and/or aqueous sulfuric acid solution of ammonium heptamolybdate tetrahydrate (10 g/100 mL H_2SO_4 + 900 mL H_2O). Preparative thin-layer chromatography was performed with pre-coated TLC plates (silica gel 60 F_{254}, 1.00 mm, Silicycle, Québec, Canada). Flash column chromatography was performed on silica gel (230–400 mesh, R10030B, Silicycle, Québec, Canada). Nuclear magnetic resonance (NMR) spectra were recorded with a Varian Inova AS400 spectrometer (Varian, Palo Alto, USA) at 400 MHz (^1H), 376 MHz (^{19}F) or 100 MHz (^{13}C). Signals are reported as m (multiplet), s (singlet), d (doublet), dd (doublet of doublet), br s (broad singlet) and ar (aromatic) and coupling constants are reported in Hertz (Hz). The chemical shifts are reported in ppm (δ) relative to residual solvent peak. High-resolution mass spectra (HRMS) were recorded with an Agilent 6210 Time-of-Flight (TOF) LC-MS apparatus with an ESI or APPI ion source (Agilent Technologies, Toronto, Canada). Thermogravimetric analysis (TGA) measurements were performed with a Mettler-Toledo Model TGA SDTA 851e apparatus (Mettler–Toledo, Schwerzenbach, Switzerland) from 50 °C to 800 °C at a heating rate of 20 °C min^{-1} under nitrogen. TEM observations were performed as follows: gold nanoparticles were dissolved in toluene and 5 μL was deposited on a nickel grid recovered with formvar. After drying, the grid was observed with a JEOL JEM-1230 TEM (JEOL, Tokyo, Japan) at 80 kV. Diameters of nanoparticles were calculated with the aid of ImageJ 1.41o software.

Compound 9: 2,6-Difluoroaniline (8.34 mL, 77.5 mmol) was dissolved in a mixture of acetic acid/H_2O (230:25 mL) at room temperature. KIO_4 (19.6 g, 85.2 mmol) was added, followed by NaCl (9.96 g, 170 mmol) and I_2 (10.8 g, 42.6 mmol). The mixture was stirred overnight and diluted in water (1 L), and the acetic acid was carefully neutralized with KOH in an ice-bath until pH 8–9 was reached. The mixture was washed three times with CH_2Cl_2 and the combined organic layers were washed with saturated aqueous Na_2SO_3 until the disappearance of the dark colouration. The organic phase was dried with Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified by filtration through silica gel with pure hexanes, followed by EtOAc/hexanes (3%) as eluents to provide the title compound **9** (10.5 g, 53% yield) as an orange solid. ^1H NMR ($CDCl_3$): δ = 7.13 (d, J = 7.2 Hz, 2 H ar.), 3.76 (br s, NH_2) ppm. ^{13}C NMR ($CDCl_3$): δ = 151.8 (dd, J = 243.4, J = 8.0 Hz, 2 C), 124.3 (t, J = 16.0 Hz), 120.3 (m*, 2 C), 74.3 (t, J = 9.9 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ = –131.2 (d, J = 7.5 Hz) ppm. HRMS: calcd. for $[C_6H_4F_2IN]^{*+}$ 254.9351 $[M]^{*+}$; found 254.9355. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 10: Compound **9** (4.85 g, 19.0 mmol) was dissolved in Et_2O (60 mL) and the solution was cooled to –20 °C under argon, after which $BF_3{\cdot}Et_2O$ (7.16 mL, 57.0 mmol) was added. The resulting mixture was stirred for 20 min and *t*BuONO (4.51 mL, 38.0 mmol) was added. The resulting mixture was stirred for one hour at –20 °C. A solution of Et_2NH (9.87 mL, 95.0 mmol) in acetonitrile (24 mL) was then added and the temperature was raised to room temperature for two hours. Water was added and the mixture was extracted three times with CH_2Cl_2. The combined organic layers were dried with Na_2SO_4 and the solvents were removed under reduced pressure to provide the crude triazene. Filtration on silica gel with EtOAc/hexanes (2%) as eluent provide the triazene compound, which was pure enough to use in the next step without further purification. The triazene was dissolved in CH_3I (40 mL) in a pressurized vessel and heated at 150 °C for 8 h. *Note: Adequate shielding is necessary to avoid risks of injuries!* The crude compound was next purified by flash chromatography on silica gel with EtOAc/hexanes (0.5%) as eluent to provide the title compound **10**(5.62 g, 81% yield over two steps from **7**) as a white solid. ^1H NMR ($CDCl_3$): δ = 7.23 (d, J = 7.0 Hz, 2 H ar.) ppm. ^{13}C NMR ($CDCl_3$): δ = 162.3 (d, J = 334.0, J = 7.5 Hz, 2 C), 121.0 (m*, 2 C), 92.2 (t, J = 12.7 Hz), 71.4 (t, J = 38.9 Hz) ppm. ^{19}F NMR ($CDCl_3$): δ = –91.3 (d, J = 5.4 Hz) ppm. HRMS: calcd. for $[C_6H_2F_2I_2]^{*+}$ 365.8208 $[M]^{*+}$; found 365.8205. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 11: Hex-5-yn-1-ol (1.77 mL, 16.4 mmol) and compound **10** (5.44 g, 14.9 mmol) were dissolved in THF (75 mL) at room temperature under argon. Et_3N (8.30 mL, 59.5 mmol) was added, followed by $PdCl_2(PPh_3)_2$ (209 mg, 0.30 mmol) and CuI (57 mg, 0.30 mmol), and the resulting solution was stirred overnight. The mixture was then diluted in CH_2Cl_2 and washed with saturated aqueous NH_4Cl, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude product was purified by flash chromatography on silica gel with EtOAc/hexanes (25%) as eluent to provide the title compound **11** (4.75 g, 95% yield) as a pale orange and gummy oil. ^1H NMR ($CDCl_3$): δ = 6.87 (d, J = 6.7 Hz, 2 H ar.), 3.68 (t, J = 5.8 Hz, CH_2–O), 2.87 (br s, OH), 2.43 (t, J = 6.4 Hz, CH_2–C≡C), 1.69 (m, 4 H alkyl) ppm. ^{13}C NMR ($CDCl_3$): δ = 162.7 (dd, J = 246.6, J = 6.8 Hz, 2 C), 126.7 (t, J = 11.4 Hz), 114.3 (m*, 2 C), 93.6, 78.6 (t, J = 3.7 Hz), 70.7 (t, J = 29.4 Hz), 62.0, 31.7, 24.7, 19.2 ppm. ^{19}F NMR ($CDCl_3$): δ = –93.0 (d, J = 6.7 Hz) ppm. HRMS: calcd. for $C_{12}H_{12}F_2IO$ 336.9901 $[M + H]^+$; found 336.9893. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 12: 4-Bromophenol (5.00 g, 28.9 mmol) and 1-bromooctane (8.37 g, 43.4 mmol) were dissolved in acetone (100 mL), followed by addition of K_2CO_3 (9.98 g, 72.3 mmol). The mixture was stirred overnight at reflux, after which it was allowed to cool to room temperature. The white precipitate was removed by filtration and washed with acetone. The filtrate was then concentrated to dryness under reduced pressure. The crude product was purified by flash chromatography on silica gel with pure hexanes as eluent to provide the title compound **12**(7.61 g, 92% yield) as a clear oil. ^{1}H NMR ($CDCl_3$): δ = 7.32 (d, J = 8.7 Hz, 2 H ar.), 6.73 (d, J = 8.7 Hz, 2 H ar.), 3.86 (t, J = 6.5 Hz, CH_2–O), 1.74 (m, 2 H alkyl), 1.40 (m, 2 H alkyl), 1.29 (m, 8 H alkyl), 0.88 (t, J = 6.5 Hz, CH_3–C) ppm. ^{13}C NMR ($CDCl_3$): δ = 158.2, 132.1 (2×), 116.2 (2×), 112.5, 68.2, 31.8, 29.4, 29.3, 29.2, 26.0, 22.7, 14.1 ppm. HRMS: calcd. for $[C_{14}H_{21}BrO]^{*+}$ 284.0770 $[M]^{*+}$; found 284.0768).

Compound 13: *n*BuLi (44.2 mmol) was added at –78 °C to a solution of compound **12** (12.0 g, 42.1 mmol) in THF (100 mL) and the solution was stirred for 30 min. Diethylcarbonate (1.68 mL, 13.9 mmol) was added dropwise and the resulting mixture was allowed to warm to room temperature and stirred for an additional 3 h. The solution was then diluted with water and extracted three times with CH_2Cl_2. The combined organic layers were dried with Na_2SO_4, and the solvents were removed under reduced pressure. The crude product was purified by flash chromatography on silica gel with EtOAc/hexanes (3%) as eluent to provide the title compound **13** (6.13 g, 68% yield) as a clear oil. ^{1}H NMR ($CDCl_3$): δ = 7.14 (d, J = 8.8 Hz, 6 H ar.), 6.80 (d, J = 8.8 Hz, 6 H ar.), 3.93 (t, J = 6.5 Hz, 3 × CH_2–O), 2.70 (s, OH), 1.76 (m, 6 H alkyl), 1.44 (m, 6 H alkyl), 1.25 (m, 24 H alkyl), 0.88 (t, J = 6.7 Hz, 3 × CH_3–C) ppm. ^{13}C NMR ($CDCl_3$): δ = 158.1 (3×), 139.5 (3×), 129.0 (6×), 113.6 (6×), 81.2, 67.9 (3×), 31.8 (3×), 29.4 (3×), 29.3 (6×), 26.1 (3×), 22.7 (3×), 14.1 (3×) ppm. HRMS: calcd. for $C_{43}H_{63}O_3$ 627.4772 $[M – OH]^+$; found 627.4789.

Compound 14: *n*BuLi (71.59 mmol) was added at –78 °C to a solution of 3-bromotoluene (11.66 g, 68.18 mmol) in THF (120 mL) and the solution was stirred for 30 min. Diethylcarbonate (2.75 mL, 22.73 mmol) was added dropwise and the resulting mixture was allowed to warm to room temperature and stirred for an additional 3 h. The solution was then diluted with water and extracted three times with CH_2Cl_2. The combined organic layers were dried with Na_2SO_4, and the solvents were removed under reduced pressure. The crude product was purified by flash chromatography on silica gel with EtOAc/hexanes (1%to 2%) as eluents to provide the title compound **14** (6.42 g, 93% yield) as a clear and gummy oil. ^{1}H NMR ($CDCl_3$): δ = 7.36, (m, 6 H ar.), 7.23 (m, 6 H ar.), 2.47 (s, 3 × CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 147.1 (3×), 137.4 (3×), 128.5 (3×), 127.9 (3×), 127.7 (3×), 125.3 (3×), 82.0, 21.6 (3×) ppm. HRMS: calcd. for $C_{22}H_{20}$ 285.1643 $[M – OH]^{*+}$; found 285.1647.

Compound 15: Compound **13** (6.04 g, 9.36 mmol) was dissolved in acetyl chloride (100 mL) at room temperature under argon and stirred overnight. The excess acetyl chloride was removed under reduced pressure and the crude product was dried under high vacuum for two hours. The gummy oil was dissolved in toluene at room temperature, ethynylmagnesium bromide (28.1 mmol) was added under argon, and the solution was stirred overnight. Water was added and the mixture was extracted three times with CH_2Cl_2. Combined organic layers were dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel with EtOAc/petroleum ether (1%) as eluent to provide the title compound **15**(5.80 g, 95% yield) as a yellow and gummy oil. ^{1}H NMR ($CDCl_3$): δ = 7.14 (d, J = 8.8 Hz, 6 H ar.), 6.79 (d, J = 8.8 Hz, 6 H ar.), 3.92 (t, J = 6.5 Hz, 3 × CH_2–O), 2.64 (s, HC≡C), 1.78 (m, 6 H alkyl), 1.44 (m, 6 H alkyl), 1.29 (m, 24 H alkyl), 0.88 (t, J = 6.8 Hz, 3 × CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 157.7 (3×), 137.3 (3×), 130.0 (6×), 113.7 (6×), 90.5, 72.6, 67.9 (3×), 53.4, 31.8 (3×), 29.4 (3×), 29.3 (6×), 26.1 (3×), 22.7 (3×), 14.1 (3×) ppm. HRMS: calcd. for $C_{45}H_{65}O_3$ 653.4928 $[M + H]^+$; found 653.4932.

Compound 16: Compound **14** (3.83 g, 12.67 mmol) was dissolved in acetyl chloride (115 mL) at room temperature under argon and stirred overnight. The excess acetyl chloride was removed under reduced pressure and the crude product was dried under high vacuum for two hours. The gummy oil was dissolved in toluene at room temperature, ethynylmagnesium bromide (63.3 mmol) was added under argon, and the solution was stirred overnight. Water was then added and the mixture was extracted three times with CH_2Cl_2. Combined organic layers were dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel with CH_2Cl_2/hexanes (2%) as eluent to provide the title compound **16**(3.17 g, 81% yield) as a pale yellow and sticky gum, which became a pale yellow solid after long-term vacuum. ^{1}H NMR ($CDCl_3$): δ = 7.28 (m, 6 H ar.), 7.14 (m, 6 H ar.), 2.80 (s, HC≡C), 2.42 (s, 3 × CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 145.0 (3×), 137.7 (3×), 129.9 (3×), 127.9 (3×), 127.7 (3×), 126.4 (3×), 90.2, 73.4, 55.4, 21.7 (3×) ppm. HRMS: calcd. for $C_{24}H_{23}$ 311.1794 $[M + H]^+$; found 311.1790).

Compound 17: *n*BuLi (8.13 mL, 19.5 mmol) was slowly added at –78 °C to a solution of 3,5-di-*tert*-butylbromobenzene (5.00 g, 18.6 mmol) in THF (90 mL) and the solution was stirred for 30 min. Diethylcarbonate (0.72 mL, 5.94 mmol) was added dropwise and the resulting mixture was allowed to warm to room temperature and stirred for an additional 3 h. The solution was then diluted with water and extracted three times with CH_2Cl_2. The combined organic layers were dried with Na_2SO_4 and the solvents were removed under reduced pressure. Filtration on silica gel with EtOAc/hexanes (2%) as eluent provided the crude product (3.55 g), which was used in the next step without further purification. The crude product was then dissolved in acetyl chloride (90 mL) at room temperature under argon and stirred for 4 h. The acetyl chloride was then removed under reduced pressure and the crude compound was dried under high vacuum for two hours. The gummy oil was dissolved in THF at room temperature, ethynylmagnesium bromide (29.8 mmol) was added under argon, and the solution was stirred overnight. Water was then added and the mixture was extracted three times with CH_2Cl_2. Combined organic layers were dried with Na_2SO_4 and the solvents were removed under reduced pressure. The crude product was purified by flash chromatography on silica gel with pure hexanes in order to remove impurities, followed by EtOAc/hexanes (1%) as eluents to provide the title compound **17** (2.18 g, 61% yield) as a white solid. ^{1}H NMR ($CDCl_3$): δ = 7.25 (s, 3 H ar.), 7.00 (s, 6 H ar.), 2.61 (s, HC≡C), 1.20 (brs, 18 × CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 149.6 (6×), 144.6 (3×), 123.8 (6×), 119.8 (3×), 90.7, 71.6, 34.8 (3×), 31.5 (18×) ppm. HRMS: calcd. for $C_{45}H_{65}$ 605.5081 $[M + H]^+$; found 605.5076.

Compound 18: Compound **10** (108 mg, 0.29 mmol) and compound **15** (160 mg, 0.25 mmol) were dissolved in THF (1.5 mL) and Et_3N (137 μL, 0.98 mmol) was added, followed by $PdCl_2(PPh_3)_2$ (3 mg, 0.005 mmol) and CuI (1 mg, 0.005 mmol). The resulting solution was stirred at room temperature overnight under argon. The mixture was then diluted in CH_2Cl_2 and washed with saturated aqueous NH_4Cl, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude product was purified by preparative TLC on silica gel with EtOAc/hex-

anes (1%) as eluent to provide the title compound **18** (171 mg, 78% yield) as a pale yellow oil. ^{1}H NMR ($CDCl_3$): δ = 7.14 (d, J = 8.8 Hz, 6 H ar.), 6.98 (d, J = 6.5 Hz, 2×HC–CF), 6.81 (d, J = 8.8 Hz, 6 H ar.), 3.93 (t, J = 6.5 Hz, 3×CH_2–O), 1.77 (m, 6 H alkyl), 1.44 (m, 6 H alkyl), 1.29 (m, 24 H alkyl), 0.88 (t, J = 6.7 Hz, 3×CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 162.3 (dd, J = 245.7, J = 6.9 Hz, 2 C), 158.0 (3×), 137.1 (3×), 130.0 (6×), 126.5 (t, J = 11.4 Hz), 114.4 (m*, 2 C), 113.9 (6×), 99.7, 81.8 (t, J = 3.5 Hz), 71.0 (t, J = 29.4 Hz), 68.0 (3×), 54.1, 31.8 (3×), 29.4 (3×), 29.3 (6×), 26.1 (3×), 22.7 (3×), 114.1 (3×) ppm. ^{19}F NMR ($CDCl_3$): δ = –92.9 (d, J = 6.6 Hz) ppm. HRMS: calcd. for $C_{51}H_{66}F_2IO_3$ 891.4019 [M + H]$^+$; found 891.4000. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 19: Compound **18** (1.64 g, 1.84 mmol) was dissolved in THF (10 mL) and Et_3N (1.03 mL, 7.36 mmol) was added, followed by $PdCl_2(PPh_3)_2$ (26 mg, 0.04 mmol), CuI (7 mg, 0.04 mmol) and propargyl alcohol (0.16 mL, 2.76 mmol). The resulting solution was stirred overnight at 60 °C under argon. After the reaction mixture had been allowed to cool to room temperature, it was diluted in CH_2Cl_2 and washed with saturated aqueous NH_4Cl, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude product was purified by flash chromatography on silica gel with EtOAc/hexanes (20%) as eluent to provide the title compound **19** (1.04 g, 69% yield) as a clear oil. ^{1}H NMR ($CDCl_3$): δ = 7.15 (d, J = 8.7 Hz, 6 H ar.), 6.99 (d, J = 7.2 Hz, 2×HC–CF), 6.81 (d, J = 8.7 Hz, 6 H ar.), 4.49 (s, C≡C–CH_2–O), 3.92 (t, J = 6.4 Hz, 3×CH_2–O), 2.59 (br s, OH), 1.75 (m, 6 H alkyl), 1.43 (m, 6 H alkyl), 1.28 (m, 24 H alkyl), 0.88 (t, J = 6.5 Hz, 3×CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 162.7 (dd, J = 253.3, 6.9 Hz, 2 C), 157.9 (3×), 137.1 (3×), 129.9 (6×), 125.6 (t, J = 12.2 Hz), 114.3 (m*, 2 C), 113.8 (6×), 101.6 (t, J = 19.1 Hz), 100.5, 98.7 (t, J = 3.1 Hz), 82.2 (t, J = 3.8 Hz), 72.2, 67.9 (3×), 54.1, 51.4, 31.8 (3×), 29.3 (3×), 29.2 (6×), 26.0 (3×), 22.6 (3×), 14.1 (3×) ppm. ^{19}F NMR ($CDCl_3$): δ = –108.2 (d, J = 7.2 Hz) ppm. HRMS: calcd. for $C_{54}H_{69}F_2O_4$ 819.5158 [M + H]$^+$; found 819.5150. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 20: A solution of PPh_3 (1.00 g, 3.81 mmol) and DIAD (0.64 mL, 3.81 mmol) in THF (12 mL) was stirred at 0 °C for 30 min. A solution of compound **19** (1.04 g, 1.27 mmol) and thioacetic acid (0.27 mL, 3.81 mmol) in THF (8 mL) was added to this solution and the mixture was allowed to warm to room temperature and stirred for 3 h. After addition of water, the mixture was extracted three times with CH_2Cl_2 and the organic layers were dried with Na_2SO_4. The solvents were removed under reduced pressure to provide the crude thioacetate. Purification by preparative TLC on silica gel with EtOAc/hexanes (2%) as eluent afforded the title compound **20**(730 mg, 66% yield) as a pale yellow oil. ^{1}H NMR ($CDCl_3$): δ = 7.14 (d, J = 8.5 Hz, 6 H ar.), 6.98 (d, J = 7.2 Hz, 2×HC–CF), 6.81 (d, J = 8.5 Hz, 6 H ar.), 3.94 (s, CH_2–S), 3.93 (t, J = 6.8 Hz, 3×CH_2–O), 2.37 (s, CH_3–C=O), 1.75 (m, 6 H alkyl), 1.44 (m, 6 H alkyl), 1.28 (m, 24 H alkyl), 0.88 (m, 3×CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 193.6, 162.8 (d, J = 251.8, J = 6.9 Hz, 2 C), 158.0 (3×), 137.1 (3×), 129.9 (6×), 125.4 (t, J = 11.8 Hz), 114.3 (m*, 2 C), 113.9 (6×), 101.8 (t, J = 19.8 Hz), 100.5, 95.6 (t, J = 3.1 Hz), 82.2 (t, J = 3.8 Hz), 69.7, 68.0 (3×), 54.1, 31.8 (3×), 30.1, 29.4 (3×), 29.3 (6×), 26.1 (3×), 22.7 (3×), 18.6, 14.1 (3×) ppm. ^{19}F NMR ($CDCl_3$): δ = –108.4 (d, J = 7.2 Hz) ppm. HRMS: calcd. for $C_{56}H_{71}F_2O_4S$ 877.5036 [M + H]$^+$; found 877.5032. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 1: Compound **20** (314 mg, 0.36 mmol) was dissolved in a solution of HCl/MeOH (1 M, 6 mL) with THF (6 mL) and the resulting mixture was stirred overnight at 50 °C. A saturated solution of I_2 in CH_2Cl_2 was added to this solution until persistence of the brown colouration. The mixture was stirred for 15 min, diluted in CH_2Cl_2 and washed with saturated aqueous $Na_2S_2O_3$ until the disappearance of the brown colouration. The organic layer was dried with Na_2SO_4 and the solvents were removed under reduced pressure. The crude product was purified by preparative TLC on silica gel with EtOAc/hexanes (4%) as eluent to provide the title compound **1** (240 mg, 80% yield) as a yellow oil. ^{1}H NMR ($CDCl_3$): δ = 7.14 (d, J = 8.7 Hz, 12 H ar.), 7.00 (d, J = 7.3 Hz, 4×HC–CF), 6.81 (d, J = 8.7 Hz, 12 H ar.), 3.93 (s, 2×CH_2–S), 3.93 (t, J = 6.5 Hz, 6×CH_2–O), 1.76 (m, 12 H alkyl), 1.44 (m, 12 H alkyl), 1.29 (m, 48 H alkyl), 0.88 (t, J = 6.6 Hz, 6×CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 162.8 (dd, J = 251.8, J = 6.9 Hz, 4 C), 158.0 (6×), 137.1 (6×), 129.9 (12×), 125.5 (t, J = 11.8 Hz, 2 C), 114.4 (m*, 4 C), 113.8 (12×), 101.8 (t, J = 19.8 Hz, 2 C), 100.5 (2×), 96.5 (t, J = 3.1 Hz, 2 C), 82.2 (t, J = 3.5 Hz, 2 C), 71.4 (2×), 67.9 (6×), 54.1 (2×), 31.8 (6×), 29.4 (6×), 29.3 (6×), 29.2 (6×), 28.9 (2×), 26.1 (6×), 22.7 (6×), 14.1 (6×) ppm. ^{19}F NMR ($CDCl_3$): δ = –108.3 (d, J = 7.3 Hz) ppm. HRMS: calcd. for $C_{108}H_{135}F_4O_6S_2$ 1667.9636 [M + H]$^+$; found 1667.9642. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 21: Compound **12** (3.00 g, 10.5 mmol) was dissolved in THF (30 mL) at room temperature under argon. Et_3N (4.26 mL, 42.1 mmol) was added, followed by $PdCl_2(PhCN)_2$ (121 mg, 0.32 mmol), CuI (40 mg, 0.21 mmol), P(tBu)$_3$ (0.63 mmol) and TMSA (2.91 mL, 21.0 mmol). The resulting solution was stirred overnight. The mixture was then diluted in CH_2Cl_2 and washed with saturated aqueous NH_4Cl, and the organic layers were dried with Na_2SO_4. The solvent was removed under reduced pressure. The crude product was purified by flash chromatography on silica gel with hexanes to EtOAc/hexanes (1%) as eluents to provide the title compound **21** (3.07 g, 96% yield) as a deep orange oil. ^{1}H NMR ($CDCl_3$): δ = 7.38 (d, J = 8.7 Hz, 2 H ar.), 6.79 (d, J = 8.7 Hz, 2 H ar.), 3.93 (t, J = 6.6 Hz, CH_2–O), 1.76 (m, 2 H alkyl), 1.44 (m, 2 H alkyl), 1.29 (m, 8 H alkyl), 0.89 (t, J = 6.7 Hz, CH_3), 0.23 (s, TMS-C) ppm. ^{13}C NMR ($CDCl_3$): δ = 159.3, 133.4 (2×), 115.0, 114.3 (2×), 105.3, 92.2, 68.0, 31.8, 29.4, 29.2 (2×), 26.0, 22.7, 14.1 ppm. HRMS: calcd. for $C_{19}H_{31}OSi$ 303.2144 [M + H]$^+$; found 303.2143.

Compound 22: Compound **21** (1.44 g, 4.76 mmol) was dissolved in a THF/MeOH/H_2O mixture (10:10:2 mL) at room temperature. KOH (1.60 g, 28.6 mmol) was then added and the resulting solution was stirred for 4 h, after which additional water was added. The mixture was extracted three times with CH_2Cl_2. The combined organic layers were dried with Na_2SO_4 and solvents were removed under reduced pressure. The crude product was purified by flash chromatography on silica gel with EtOAc/hexanes (1%) as eluent to provide the title compound **22** (1.08 g, 99% yield) as an orange oil. ^{1}H NMR ($CDCl_3$): δ = 7.41 (d, J = 8.7 Hz, 2 H ar.), 6.82 (d, J = 8.7 Hz, 2 H ar.), 3.93 (t, J = 6.6 Hz, CH_2–O), 2.98 (s, HC≡C), 1.77 (m, 2 H alkyl), 1.43 (m, 2 H alkyl), 1.30 (m, 8 H alkyl), 0.88 (t, J = 6.7 Hz, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 159.5, 133.5 (2×), 114.4 (2×), 113.8, 83.8, 75.6, 68.0, 31.8, 29.3, 29.2 (2×), 26.0, 22.7, 14.1 ppm. HRMS: calcd. for $C_{16}H_{23}O$ 231.1749 [M + H]$^+$; found 231.1741.

Compound 23: Compound **10** (2.41 g, 6.59 mmol) and compound **22** (1.38 g, 5.99 mmol) were dissolved in THF (15 mL) and Et_3N (3.34 mL, 24.0 mmol) was added, followed by $PdCl_2(PPh_3)_2$ (84 mg, 0.12 mmol) and CuI (23 mg, 0.12 mmol). The resulting solution was stirred overnight at room temperature. The mixture

was then diluted in CH_2Cl_2 and washed with saturated aqueous NH_4Cl, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure. The crude product was purified by flash chromatography on silica gel with CH_2Cl_2/hexanes (5%) as eluent to provide the title compound **23** (2.25 g, 80% yield) as a yellow solid. ^1H NMR ($CDCl_3$): δ = 7.37 (d, J = 8.6 Hz, 2 H ar.), 6.90 (d, J = 6.7 Hz, 2 × HC–CF), 6.78 (d, J = 8.6 Hz, 2 H ar.), 3.85 (t, J = 6.5 Hz, CH_2–O), 1.73 (m, 2 H alkyl), 1.39 (m, 2 H alkyl), 1.27 (m, 8 H alkyl), 0.88 (t, J = 6.6 Hz, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 163.1 (dd, J = 247.1, J = 7.1 Hz, 2 C), 159.8, 133.2 (2 ×), 126.5 (t, J = 11.5 Hz), 114.5 (2 ×), 113.9 (m*, 2 C), 113.7, 92.9, 85.5 (t, J = 3.8 Hz), 70.8 (t, J = 29.4 Hz), 68.0, 31.9, 29.4, 29.3, 29.2, 26.1, 22.7, 14.2 ppm. ^{19}F NMR ($CDCl_3$): δ = –92.5 (d, J = 6.2 Hz) ppm. HRMS: calcd. for $[C_{22}H_{23}OF_2I]^{*+}$ 468.0756 $[M]^{*+}$; found 468.0754. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 24: Compound **23** (2.20 g, 4.69 mmol) was dissolved in THF (15 mL) and Et_3N (2.61 mL, 18.7 mmol) was added, followed by $PdCl_2(PPh_3)_2$ (132 mg, 0.19 mmol), CuI (18 mg, 0.09 mmol) and propargyl alcohol (0.55 mL, 9.37 mmol). The resulting solution was stirred overnight at 60 °C for 2 d. The mixture was then diluted in CH_2Cl_2 and washed with saturated aqueous NH_4Cl, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure. The crude product was purified by flash chromatography on silica gel with CH_2Cl_2 in hexanes (50% to 60%) as eluents to provide the title compound **24** (1.69 g, 91% yield) as a white solid. ^1H NMR ($CDCl_3$): δ = 7.41 (d, J = 8.8 Hz, 2 H ar.), 6.99 (d, J = 7.3 Hz, 2 × HC–CF), 6.85 (d, J = 8.8 Hz, 2 H ar.), 4.56 (d, J = 5.7 Hz, C≡C–CH_2–O), 3.94 (t, J = 6.5 Hz, CH_2–O), 2.39 (m, OH), 1.77 (m, 2 H alkyl), 1.44 (m, 2 H alkyl), 1.29 (m, 8 H alkyl), 0.89 (t, J = 6.6 Hz, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 162.7 (dd, J = 253.4, J = 6.7 Hz, 2 C), 159.9, 133.3 (2 ×), 125.7 (t, J = 11.9 Hz), 114.7 (2 ×), 114.1 (m*, 2 C), 113.8, 101.4 (t, J = 20.0 Hz), 98.6 (t, J = 3.1 Hz), 93.6, 85.9 (t, J = 3.8 Hz), 72.6, 68.2, 51.6, 31.8, 29.4, 29.3, 29.2, 26.0, 22.7, 14.1 ppm. ^{19}F NMR ($CDCl_3$): δ = –108.4 (d, J = 7.6 Hz) ppm. HRMS: calcd. for $C_{25}H_{27}F_2O_2$ 397.1974 $[M + H]^+$; found 397.1979. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 25: CBr_4 (3.47 g, 10.5 mmol) and PPh_3 (2.75 g, 10.5 mmol) were added at room temperature to a solution of the compound **24** (1.66 g, 4.19 mmol) in THF (25 mL) and the resulting mixture was stirred for 30 min. The solution was then diluted in CH_2Cl_2 and washed with water, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude product was filtered through silica gel with EtOAc/hexanes (2%)as eluent to provide the title compound **25** (1.77 g, 92% yield) as a yellow solid. ^1H NMR ($CDCl_3$): δ = 7.43 (d, J = 8.7 Hz, 2 H ar.), 7.01 (d, J = 7.4 Hz, 2 × HC–CF), 6.86 (d, J = 8.7 Hz, 2 H ar.), 4.19 (s, CH_2–Br), 3.95 (t, J = 6.5 Hz, CH_2–O), 1.78 (m, 2 H alkyl), 1.44 (m, 2 H alkyl), 1.31 (m, 8 H alkyl), 0.89 (t, J = 6.5 Hz, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 162.8 (dd, J = 253.8, J = 6.8 Hz, 2 C), 160.0, 133.4 (2 ×), 126.2 (t, J = 12.1 Hz), 114.7 (2 ×), 114.1 (m*, 2 C), 133.7, 101.1 (t, J = 19.9 Hz), 95.1 (t, J = 3.0 Hz), 93.9, 85.9 (t, J = 3.8 Hz), 73.6, 68.1, 31.8, 29.4, 29.2 (2 ×), 26.0, 22.7, 14.3, 14.1 ppm. ^{19}F NMR ($CDCl_3$): δ = –107.9 (d, J = 7.0 Hz) ppm. HRMS: calcd. for $[C_{25}H_{25}OBrF_2]^{*+}$ 458.1051 $[M]^{*+}$; found 458.1049. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 26: Compound **25** (1.63 g, 3.55 mmol) and potassium thioacetate (811 mg, 7.10 mmol) were dissolved in THF (14 mL) and the resulting mixture was heated at 60 °C overnight. The mixture was then diluted in CH_2Cl_2 and washed with water. The organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude compound was purified by flash chromatography on silica gel with EtOAc/hexanes (2%) as eluent to provide the thioacetate **26** (1.55 g, 96% yield) as an orange solid. ^1H NMR ($CDCl_3$): δ = 7.40 (d, J = 8.4 Hz, 2 H ar.), 6.95 (d, J = 7.4 Hz, 2 × HC–CF), 6.83 (d, J = 8.4 Hz, 2 H ar.), 3.94 (s, CH_2–S), 3.90 (t, J = 6.4 Hz, CH_2–O), 2.35 (s, CH_3–C=O), 1.75 (m, 2 H alkyl), 1.42 (m, 2 H alkyl), 1.28 (m, 8 H alkyl), 0.88 (t, J = 6.5 Hz, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 193.5, 162.8 (dd, J = 253.5, J = 6.7 Hz, 2 C), 159.9, 133.3 (2 ×), 125.5 (t, J = 11.9 Hz), 114.7 (2 ×), 114.0 (m*, 2 C), 113.8, 101.6 (t, J = 20.0 Hz), 95.7 (t, J = 2.8 Hz), 93.6, 86.0 (t, J = 3.7 Hz), 69.8, 68.1, 31.9, 30.0, 29.4, 29.3, 29.2, 26.1, 22.7, 18.7, 14.1 ppm. ^{19}F NMR ($CDCl_3$): δ = –108.3 (d, J = 7.1 Hz) ppm. HRMS: calcd. for $[C_{27}H_{28}O_2SF_2]^{*+}$ 455.1855 $[M]^{*+}$; found 455.1851. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 2: Compound **26** (1.48 g, 3.26 mmol) was dissolved in a solution of HCl/MeOH (1 M, 10 mL) with THF (10 mL) and stirred overnight at 50 °C. A saturated solution of I_2 in CH_2Cl_2 was added to this solution until persistence of a brown colouration. The mixture was stirred for 15 min, diluted in CH_2Cl_2 and washed with saturated aqueous $Na_2S_2O_3$ until the disappearance of the brown colour. The organic layer was dried with Na_2SO_4 and the solvents were removed under reduced pressure. The crude product was purified by flash chromatography on silica gel with CH_2Cl_2/hexanes (20%) as eluent to provide the title compound **2** (727 mg, 54% yield) as a yellow solid, together with the corresponding thiol (253 mg, 19% yield). ^1H NMR ($CDCl_3$): δ = 7.41 (d, J = 8.6 Hz, 4 H ar.), 6.98 (d, J = 7.3 Hz, 4 × HC–CF), 6.84 (d, J = 8.6 Hz, 4 H ar.), 3.92 (m, 2 × CH_2–S and 2 × CH_2–O), 1.76 (m, 4 H alkyl), 1.43 (m, 4 H alkyl), 1.29 (m, 16 H alkyl), 0.89 (t, J = 6.4 Hz, 2 × CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 162.8 (dd, J = 246.7, J = 6.7 Hz, 4 C), 159.9 (2 ×), 133.3 (4 ×), 125.5 (t, J = 11.9 Hz, 2 C), 114.6 (4 ×), 114.0 (m*, 4 C), 113.8 (2 ×), 101.7 (t, J = 20.0 Hz, 2 C), 96.5 (t, J = 2.9 Hz, 2 C), 93.5 (2 ×), 86.0 (t, J = 3.6 Hz, 2 C), 71.5 (2 ×), 68.1 (2 ×), 31.8 (2 ×), 29.4 (2 ×), 29.3 (2 ×), 29.2 (2 ×), 29.0 (2 ×), 26.0 (2 ×), 22.7 (2 ×), 14.1 (2 ×) ppm. ^{19}F NMR ($CDCl_3$): δ = –108.2 (d, J = 7.2 Hz) ppm. HRMS: calcd. for $C_{50}H_{51}O_2S_2F_4$ 823.3261 $[M + H]^+$; found 823.3250. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 27: Compound **11** (750 mg, 2.23 mmol) and compound **15** (1.73 g, 2.68 mmol) were dissolved in THF (8 mL) and Et_3N (1.24 mL, 8.93 mmol) was added, followed by $PdCl_2(PPh_3)_2$ (63 mg, 0.09 mmol) and CuI (17 mg, 0.09 mmol). The resulting solution was stirred at 60 °C under argon for 2 d. Propargyl alcohol (1 mL) was then added (to remove the unreacted compound **11**) and the mixture was stirred for another day at 60 °C. The mixture was then diluted in CH_2Cl_2 and washed with saturated aqueous NH_4Cl, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure. The crude product was purified by flash chromatography on silica gel with EtOAc/hexanes (20%)as eluent to provide the title compound **27** (1.75 g, 91% yield) as a pale yellow oil. ^1H NMR ($CDCl_3$): δ = 7.22 (d, J = 8.7 Hz, 6 H ar.), 6.89 (d, J = 7.2 Hz, 2 × HC–CF), 6.80 (d, J = 8.7 Hz, 6 H ar.), 3.90 (t, J = 6.4 Hz, 3 × CH_2–O), 3.62 (t, J = 6.0 Hz, CH_2–O), 2.39 (t, J = 6.4 Hz, C≡C–CH_2), 2.13 (s, OH), 1.74 (m, 6 H alkyl), 1.65 (m, 4 H alkyl), 1.43 (m, 6 H alkyl), 1.28 (m, 26 H alkyl), 0.87 (t, J = 6.5 Hz, 3 × CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 162.8 (dd, J = 252.9, J = 7.0 Hz, 2 C), 157.9 (3 ×), 137.2 (3 ×), 130.0 (6 ×), 125.1 (t, J = 11.8 Hz), 114.2 (m*, 2 C), 113.8 (6 ×), 107.8 (t, J = 3.1 Hz), 102.5 (t, J = 19.8 Hz), 93.6, 79.1 (t, J = 3.5 Hz), 71.7, 67.9 (3 ×), 62.1, 54.7, 31.9 (3 ×), 31.8, 29.4 (3 ×), 29.3 (6 ×), 26.1 (3 ×), 25.3, 22.7 (3 ×), 19.2, 14.1 (3 ×) ppm. ^{19}F

NMR ($CDCl_3$): δ = –108.3 (d, J = 7.2 Hz) ppm. HRMS: calcd. for $C_{57}H_{75}F_2O_4$ 861.5633 $[M + H]^+$; found 861.5628. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 28: Compound **11** (300 mg, 0.89 mmol) and compound **16** (416 mg, 1.34 mmol) were dissolved in THF (3 mL) and Et_3N (0.50 mL, 3.57 mmol) was added, followed by $PdCl_2(PPh_3)_2$ (25 mg, 0.04 mmol) and CuI (7 mg, 0.04 mmol). The resulting solution was stirred at 60 °C under argon for 2 d. Propargyl alcohol (1 mL) was then added (to remove the unreacted compound **11**) and the mixture was stirred for another day at 60 °C. The mixture was then diluted in CH_2Cl_2 and washed with saturated aqueous NH_4Cl, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude product was purified by flash chromatography on silica gel with CH_2Cl_2/hexanes (60%) as eluent to provide the title compound **28** (457 mg, 99% yield) as a pale yellow oil. ^1H NMR ($CDCl_3$): δ = 7.27 (br s, 3 H ar.), 7.15 (m, 3 H ar.), 7.04 (m, 6 H ar.), 6.90 (d, J = 7.2 Hz, 2 × HC–CF), 3.61 (t, J = 5.8 Hz, CH_2–O), 2.39 (t, J = 6.4 Hz, C≡C–CH_2), 2.28 (s, 3 × CH_3), 1.64 (m,4 H alkyl) ppm. ^{13}C NMR ($CDCl_3$): δ = 162.9 (dd, J = 252.9, J = 7.2 Hz, 2 C), 144.7 (3 ×), 137.6 (3 ×), 129.9 (3 ×), 127.8 (3 ×), 127.7 (3 ×), 126.3 (3 ×), 125.1 (t, J = 11.7 Hz), 114.3 (m*, 2 C), 107.4 (t, J = 3.1 Hz), 102.5 (t, J = 20.2 Hz), 94.0, 79.1 (t, J = 3.6 Hz), 72.3, 62.1, 56.5, 31.7, 24.7, 21.5 (3 ×), 19.2 ppm. ^{19}F NMR ($CDCl_3$): δ = –108.1 (d, J = 7.6 Hz) ppm. HRMS: calcd. for $C_{36}H_{33}F_2O$ 519.2494 $[M + H]^+$; found 519.2487. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 29: Compound **11** (0.500 mg, 1.49 mmol) and compound **17** (1.00 g, 1.65 mmol) were dissolved in THF (7 mL) and Et_3N (0.92 mL, 6.61 mmol) was added, followed by $PdCl_2(PPh_3)_2$ (46 mg, 0.07 mmol) and CuI (13 mg, 0.07 mmol). The resulting solution was stirred at 60 °C under argon for 2 d. The mixture was then diluted in CH_2Cl_2 and washed with saturated aqueous NH_4Cl, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude product was purified by flash chromatography on silica gel with EtOAc/hexanes (20%)as eluent to provide the title compound **29** (348 mg, 29% yield) as a white solid, together with compound **11**(309 mg, 62% recovery). ^1H NMR ($CDCl_3$): δ = 7.29 (s, 3 H ar.), 7.11 (br s, 6 H ar.), 6.93 (d, J = 7.0 Hz, 2 × HC–CF), 3.64 (t, J = 5.7 Hz, CH_2–O), 2.41 (t, J = 6.1 Hz, C≡C-CH_2), 1.67 (m, 4 H alkyl), 1.24 (br s, 18 × CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 163.0 (dd, J = 252.4, J = 7.0 Hz, 2 C), 149.8 (6 ×), 144.6 (3 ×), 124.7 (t, J = 11.7 Hz), 123.9 (6 ×), 119.8 (3 ×), 114.2 (m*, 2 C), 108.3 (t, J = 2.9 Hz), 102.9 (t, J = 20.3 Hz), 93.6, 79.2 (t, J = 3.6 Hz), 70.9, 62.0, 57.3, 34.8 (6 ×), 31.7, 31.4 (18 ×), 24.7, 19.1 ppm. ^{19}F NMR ($CDCl_3$): δ = –108.5 (d, J = 7.1 Hz) ppm. HRMS: calcd. for $C_{57}H_{75}F_2O$ $[M + H]^+$ 813.5780; found 813.5788. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 30: CBr_4 (1.68 g, 5.08 mmol) and PPh_3 (1.33 g, 5.08 mmol) were added at room temperature to a solution of the compound **27** (1.75 g, 2.03 mmol) in THF (14 mL) and the resulting mixture was stirred for 30 min. The solution was then diluted in CH_2Cl_2 and washed with water, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude product was filtered through silica gel with EtOAc/hexanes (2%) as eluent to provide compound **30** (1.81 g, 97% yield) as a yellow oil. ^1H NMR ($CDCl_3$): δ = 7.21 (d, J = 8.6 Hz, 6 H ar.), 6.89 (d, J = 7.0 Hz, 2 × HC–CF), 6.80 (d, J = 8.6 Hz, 6 H ar.), 3.91 (t, J = 6.4 Hz, 3 × CH_2–O), 3.39 (t, J = 6.6 Hz, CH_2–Br), 2.39 (t, J = 6.8 Hz, C≡C–CH_2), 1.96 (m, 2 H alkyl), 1.73 (m, 8 H alkyl), 1.43 (m, 6 H alkyl), 1.28 (m, 24 H alkyl), 0.87 (t, J = 6.4 Hz, 3 × CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 162.9 (dd, J = 252.6, J = 6.8 Hz, 2 C), 157.9 (3 ×), 137.2 (3 ×), 130.0 (6 ×), 124.8 (t, J = 11.4 Hz), 114.3 (m*, 2 C), 113.8 (6 ×), 107.8 (t, J = 3.1 Hz), 102.6 (t, J = 19.8 Hz), 93.2, 79.4 (t, J = 3.8 Hz), 71.6, 67.9 (3 ×), 54.7, 32.9, 31.8 (3 ×), 31.7, 29.4 (3 ×), 29.3 (6 ×), 26.8, 26.1 (3 ×), 22.7 (3 ×), 18.6, 14.1 (3 ×) ppm. ^{19}F NMR ($CDCl_3$): δ = –108.2 (d, J = 7.1 Hz) ppm. HRMS: calcd. for $C_{57}H_{74}BrF_2O_3$ 923.4784 $[M + H]^+$; found 923.4797. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 31: CBr_4 (711 mg, 2.15 mmol) and PPh_3 (563 mg, 2.15 mmol) were added at room temperature to a solution of the compound **28** (445 mg, 0.86 mmol) in THF (4 mL) and the resulting mixture was stirred for 30 min. The solution was then diluted with CH_2Cl_2 and washed with water, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude product was filtered through silica gel with EtOAc/hexanes (4%) as eluent to provide the title compound **31** (486 mg, 97% yield) as a yellow oil. ^1H NMR ($CDCl_3$): δ = 7.26 (br s, 3 H ar.), 7.16 (m, 3 H ar.), 7.05 (m, 6 H ar.), 6.90 (d, J = 7.2 Hz, 2 × HC–CF), 3.37 (t, J = 6.6 Hz, CH_2–Br), 2.38 (t, J = 7.0 Hz, C≡C–CH_2), 2.28 (s, 3 × CH_3), 1.94 (m, 2 H alkyl), 1.69 (m, 2 H alkyl) ppm. ^{13}C NMR ($CDCl_3$): δ = 162.9 (dd, J = 252.5, J = 7.0 Hz, 2 C), 144.6 (3 ×), 137.6 (3 ×), 129.9 (3 ×), 127.8 (3 ×), 127.7 (3 ×), 126.3 (3 ×), 124.9 (t, J = 11.9 Hz), 114.3 (m*, 2 C), 107.4 (t, J = 3.1 Hz), 102.6 (t, J = 20.2 Hz), 93.3, 79.3 (t, J = 3.7 Hz), 72.2, 56.5, 32.9, 31.7, 26.7, 21.5 (3 ×), 18.6 ppm. ^{19}F NMR ($CDCl_3$): δ = –108.0 (d, J = 7.2 Hz) ppm. HRMS: calcd. for $[C_{36}H_{31}BrF_2]^{*+}$ 580.1572 $[M]^{*+}$; found 580.1561. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 32: CBr_4 (306 mg, 0.92 mmol) and PPh_3 (242 mg, 0.92 mmol) were added at room temperature to a solution of the compound **29** (300 mg, 0.37 mmol) in THF (4 mL) and the resulting mixture was stirred for 30 min. The solution was then diluted in CH_2Cl_2 and washed with water, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude product was filtered through silica gel with EtOAc/hexanes (1%) as eluent to provide the title compound **32** in quantitative yield as a pale yellow solid. ^1H NMR ($CDCl_3$): δ = 7.28 (s, 3 H ar.), 7.08 (br s, 6 H ar.), 6.92 (d, J = 7.1 Hz, 2 × HC–CF), 3.43 (t, J = 6.6 Hz, CH_2–Br), 2.43 (t, J = 6.9 Hz, C≡C–CH_2), 2.00 (m, 2 H alkyl), 1.74 (m, 2 H alkyl), 1.23 (br s, 18 × CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 162.9 (dd, J = 252.7, J = 7.0 Hz, 2 C), 149.8 (6 ×), 144.6 (3 ×), 124.4 (t, J = 11.7 Hz), 123.9 (6 ×), 119.9 (3 ×), 114.2 (m*, 2 C), 108.4 (t, J = 3.1 Hz), 103.1 (t, J = 20.2 Hz), 92.8, 79.4 (t, J = 3.5 Hz), 70.8, 57.3, 34.8 (6 ×), 32.9, 31.6, 31.4 (18 ×), 26.8, 18.6 ppm. ^{19}F NMR ($CDCl_3$): δ = –108.4 (d, J = 7.3 Hz) ppm. HRMS: calcd. for $C_{57}H_{74}BrF_2$ 875.4936$[M + H]^+$; found 875.4953. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 33: Compound **30** (1.81 g, 1.96 mmol) and potassium thioacetate (448 mg, 3.92 mmol) in THF (10 mL) were heated at 60 °C overnight. The mixture was diluted in CH_2Cl_2 and washed with water, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude product was purified by flash chromatography on silica gel with EtOAc/hexanes (2%) as eluent to provide the title compound **33** (1.65 g, 92% yield) as a yellow oil. ^1H NMR ($CDCl_3$): δ = 7.21 (d, J = 8.7 Hz, 6 H ar.), 6.89 (d, J = 7.1 Hz, 2 × HC–CF), 6.79 (d, J = 8.7 Hz, 6 H ar.), 3.90 (t, J = 6.3 Hz, 3 × CH_2–O), 2.87 (t, J = 6.9 Hz, CH_2–S), 2.37 (t, J = 6.6 Hz, C≡C–CH_2), 2.28 (s, CH_3–C=O), 1.74 (m, 8 H alkyl), 1.62 (m, 2 H alkyl), 1.42 (m, 6 H alkyl), 1.28 (m, 24 H alkyl), 0.87 (t, J = 6.9 Hz, 3 × CH_3) ppm. ^{13}C NMR

($CDCl_3$): δ = 195.3, 163.1 (dd, J = 252.9, J = 7.0 Hz, 2 C), 158.0 (3×), 137.2 (3×), 130.1 (6×), 125.0 (t, J = 11.9 Hz), 114.6 (m*, 2 C), 113.8 (6×), 108.7 (t, J = 2.9 Hz), 102.6 (t, J = 20.3 Hz), 93.5, 79.3 (t, J = 3.5 Hz), 71.7, 67.8 (3×), 54.7, 31.9 (3×), 30.5, 29.4 (3×), 29.3 (6×), 28.8, 28.5, 27.3, 26.1 (3×), 22.7 (3×), 19.0, 14.1 (3×) ppm. ^{19}F NMR ($CDCl_3$): δ = –108.3 (d, J = 7.2 Hz) ppm. HRMS: calcd. for $C_{59}H_{77}F_2O_4S$ 919.5511 $[M + H]^+$; found 919.5494. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 34: Compound **31** (440 mg, 0.76 mmol) and potassium thioacetate (173 mg, 1.51 mmol) in THF (4 mL) were heated at 60 °C overnight. The mixture was diluted in CH_2Cl_2 and washed with water, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude product was purified by flash chromatography on silica gel with EtOAc/hexanes (5%)as eluent to provide the title compound **34** (411 mg, 94% yield) as a yellow oil. ^1H NMR ($CDCl_3$): δ = 7.25 (br s, 3 H ar.), 7.16 (m, 3 H ar.), 7.05 (m, 6 H ar.), 6.91 (d, J = 7.2 Hz, 2×HC–CF), 2.89 (t, J = 6.9 Hz, CH_2–S), 2.39 (t, J = 6.6 Hz, C≡C–CH_2), 2.29 (s, 3×CH_3 and CH_3–C=O), 1.70 (m, 2 H alkyl), 1.64 (m, 2 H alkyl) ppm. ^{13}C NMR ($CDCl_3$): δ = 195.6, 162.9 (dd, J = 252.8, J = 6.7 Hz, 2 C), 144.7 (3×), 137.6 (3×), 129.9 (3×), 127.8 (3×), 127.7 (3×), 126.3 (3×), 125.0 (t, J = 11.8 Hz), 114.3 (m*, 2 C), 107.3 (t, J = 3.1 Hz), 102.5 (t, J = 20.1 Hz), 93.5, 79.2 (t, J = 3.7 Hz), 72.3, 56.5, 30.6, 28.7, 28.5, 27.3, 26.1 (3×), 19.0 ppm. ^{19}F NMR ($CDCl_3$): δ = –108.3 (d, J = 7.4 Hz) ppm. HRMS: calcd. for $[C_{38}H_{34}F_2OS]^{*+}$ 576.2293 $[M]^{*+}$; found 576.2305. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 35: Compound **32** (310 mg, 0.35 mmol) and potassium thioacetate (121 mg, 1.06 mmol) were heated at 60 °C in THF (5 mL) overnight. The mixture was diluted in CH_2Cl_2 and washed with water, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude product was purified by preparative TLC on silica gel with EtOAc/hexanes (2%) as eluent to provide the title compound **35** (260 mg, 85% yield) as a yellow solid. ^1H NMR ($CDCl_3$): δ = 7.29 (s, 3 H ar.), 7.09 (br s, 6 H ar.), 6.93 (d, J = 7.0 Hz, 2×HC–CF), 2.90 (t, J = 6.9 Hz, CH_2–S), 2.41 (t, J = 6.5 Hz, C≡C–CH_2), 2.29 (s, CH_3–C=O), 1.73 (m, 2 H alkyl), 1.66 (m, 2 H alkyl), 1.23 (br s, 18×CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 195.4, 162.9 (dd, J = 252.6, J = 6.9 Hz, 2 C), 149.8 (6×), 144.6 (3×), 124.6 (t, J = 11.6 Hz), 123.9 (6×), 119.9 (3×), 114.2 (m*, 2 C), 108.3 (t, J = 3.1 Hz), 103.0 (t, J = 20.3 Hz), 93.2, 79.4 (t, J = 3.6 Hz), 70.9, 57.3, 34.8 (6×), 31.4 (18×), 30.5, 28.8, 28.5, 27.3, 18.9 ppm. ^{19}F NMR ($CDCl_3$): δ = –108.6 (d, J = 7.1 Hz) ppm. HRMS: calcd. for $C_{59}H_{77}F_2OS$ 871.5658 $[M + H]^+$; found 871.5677. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 3: Compound **33** (1.60 g, 1.74 mmol) was dissolved in a solution of HCl/MeOH (1 M, 7 mL) with THF (7 mL) and stirred overnight at 50 °C. A saturated solution of I_2 in CH_2Cl_2 was added to this solution until persistence of the brown colouration. The mixture was stirred for 15 min, diluted in CH_2Cl_2 and washed with saturated aqueous $Na_2S_2O_3$ until the disappearance of the brown colour. The organic layer was dried with Na_2SO_4 and the solvents were removed under reduced pressure. The crude product was purified by flash chromatography on silica gel with EtOAc/hexanes (1%) as eluent to provide the title compound **3** (1.31 g, 86% yield) as an orange oil. ^1H NMR ($CDCl_3$): δ = 7.21 (d, J = 8.7 Hz, 12 H ar.), 6.89 (d, J = 7.2 Hz, 4×HC–CF), 6.80 (d, J = 8.7 Hz, 12 H ar.), 3.90 (t, J = 6.3 Hz, 6×CH_2–O), 2.68 (t, J = 7.1 Hz, 2×CH_2–S), 2.38 (t, J = 6.4 Hz, 2×C≡C–CH_2), 1.74 (m, 20 H alkyl), 1.42 (m, 12 H alkyl), 1.27 (m, 48 H alkyl), 0.87 (t, J = 6.8 Hz, 6×CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 163.0 (dd, J = 252.5, J = 6.7 Hz, 4 C), 157.9 (6×), 137.2 (6×), 130.0 (6×), 125.0 (t, J = 11.8 Hz, 2 C), 114.2 (m*, 4 C), 93.6 (2×), 79.3 (t, J = 3.3 Hz, 2 C), 71.6 (2×), 67.8 (6×), 54.7 (2×), 38.2 (2×), 31.8 (6×), 29.4 (6×), 29.3 (12×), 28.2 (2×), 27.0 (2×), 26.1 (6×), 22.7 (6×), 19.0 (2×), 14.1 (6×) ppm. ^{19}F NMR ($CDCl_3$): δ = –108.2 (d, J = 7.2 Hz) ppm. HRMS: calcd. for $[C_{114}H_{146}F_4O_6S_2]^{*+}$ 1751.0492 $[M]^{*+}$; found 1751.0504. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 5: Compound **34** (373 mg, 0.65 mmol) was dissolved in a solution of HCl/MeOH (1 M, 2 mL) with THF (2 mL) and stirred overnight at 50 °C. A saturated solution of I_2 in CH_2Cl_2 was added to this solution until persistence of the brown colouration. The mixture was stirred for 15 min, diluted in CH_2Cl_2 and washed with saturated aqueous $Na_2S_2O_3$ until disappearance of the brown colour. The organic layer was dried with Na_2SO_4 and the solvents were removed under reduced pressure. The crude product was purified by flash chromatography on silica gel with EtOAc/hexanes (4%)as eluent to provide of the title compound **5** (258 mg, 75% yield) as an orange oil. ^1H NMR ($CDCl_3$): δ = 7.26 (br s, 6 H ar.), 7.16 (m, 6 H ar.), 7.05 (m, 12 H ar.), 6.90 (d, J = 7.3 Hz, 4×HC–CF), 2.69 (t, J = 7.1 Hz, 2×CH_2–S), 2.39 (t, J = 6.7 Hz, 2×C≡C–CH_2), 2.28 (s, 6×CH_3), 1.83 (m, 4 H alkyl), 1.66 (m, 4 H alkyl) ppm. ^{13}C NMR ($CDCl_3$): δ = 162.8 (dd, J = 252.5, J = 6.8 Hz, 4 C), 144.6 (2×), 137.6 (2×), 129.9 (2×), 127.8 (2×), 127.7 (2×), 126.3 (2×), 125.0 (t, J = 11.8 Hz, 2 C), 114.2 (m*, 4 C), 107.4 (t, J = 3.1 Hz, 2 C), 102.5 (t, J = 20.2 Hz, 2 C), 93.6 (2×), 79.3 (t, J = 3.5 Hz, 2 C), 72.2 (2×), 56.5 (2×), 38.2 (2×), 28.2 (2×), 27.0 (2×), 21.5 (6×), 19.0 (2×) ppm. ^{19}F NMR ($CDCl_3$): δ = –108.1 (d, J = 7.1 Hz) ppm. HRMS: calcd. for $C_{72}H_{63}F_4S_2$ 1067.4307 $[M + H]^+$; found 1067.4287. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 51: Compound **35** (238 mg, 0.27 mmol) was dissolved in a solution of HCl/MeOH (1 M, 2 mL) with THF (2 mL) and stirred overnight at 50 °C. A saturated solution of I_2 in CH_2Cl_2 was added to this solution until persistence of the brown colouration. The mixture was stirred for 15 min, diluted in CH_2Cl_2 and washed with saturated aqueous $Na_2S_2O_3$ until disappearance of the brown colour. The organic layer was dried with Na_2SO_4 and the solvents were evaporated under reduced pressure. The crude product was purified by preparative TLC on silica gel with EtOAc/hexanes (3%) as eluent to provide the title compound **51** (207 mg, 91% yield) as a pale yellow solid. ^1H NMR ($CDCl_3$): δ = 7.28 (s, 6 H ar.), 7.08 (br s, 12 H ar.), 6.92 (d, J = 7.4 Hz, 4×HC–CF), 2.73 (t, J = 7.1 Hz, 2×CH_2–S), 2.42 (t, J = 6.8 Hz, 2×C≡C–CH_2), 1.86 (m, 4 H alkyl), 1.69 (m, 4 H alkyl), 1.23 (br s, 36×CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 162.9 (dd, J = 252.3, J = 6.7 Hz, 4 C), 149.8 (12×), 144.6 (6×), 124.5 (t, J = 11.7 Hz, 2 C), 123.9 (12×), 119.9 (6×), 114.2 (m*, 4 C), 108.4 (t, J = 2.8 Hz, 2 C), 103.1 (t, J = 20.2 Hz, 2 C), 93.2 (2×), 79.4 (t, J = 3.3 Hz, 2 C), 70.9 (2×), 57.3 (2×), 38.3 (2×), 34.8 (12×), 31.4 (36×), 28.2 (2×), 27.0 (2×), 19.0 (2×) ppm. ^{19}F NMR ($CDCl_3$): δ = –108.5 (d, J = 7.7 Hz) ppm. HRMS: calcd. for $[C_{114}H_{146}F_4S_2]$ 1655.0802 [M]; found 1655.0786. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 36: Compound **11** (1.31 g, 3.91 mmol) and compound **22** (1.08 g, 4.69 mmol) were dissolved in THF (15 mL)and Et_3N (2.61 mL, 18.8 mmol) was added, followed by $PdCl_2(PPh_3)_2$ (132 mg, 0.19 mmol) and CuI (36 mg, 0.19 mmol). The resulting solution was stirred at 60 °C under argon for 2 d. Propargyl alcohol (1 mL) was then added (to remove the unreacted compound **11**)

and the mixture was stirred another day at 60 °C. The mixture was then diluted in CH_2Cl_2 and washed with saturated aqueous NH_4Cl, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude product was purified by flash chromatography on silica gel with EtOAc/hexanes (25%) as eluent to provide the title compound **36** (1.375 g, 80% yield) as a brown solid. ^{1}H NMR ($CDCl_3$): δ = 7.49 (d, J = 8.6 Hz, 2 H ar.), 6.93 (d, J = 7.4 Hz, 2 × HC–CF), 6.87 (d, J = 8.7 Hz, 2 H ar.), 3.96 (t, J = 6.6 Hz, CH_2–O-ar.), 3.71 (t, J = 5.5 Hz, alkyl-CH_2–O), 2.46 (t, J = 6.4 Hz, C≡C–CH_2), 1.77 (m,2 H alkyl), 1.71 (m, 4 H alkyl), 1.44 (m, 2 H alkyl), 1.30 (m, 8 H alkyl), 0.89 (t, J = 6.6 Hz, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 163.1 (dd, J = 252.3, J = 6.8 Hz, 2 C), 159.8, 133.3 (2×), 124.9 (t, J = 11.8 Hz), 114.6 (2×), 114.3 (m*, 2 C), 102.6 (t, J = 20.0 Hz), 100.5 (t, J = 3.1 Hz), 94.0, 79.2 (t, J = 3.7 Hz), 74.9, 68.1, 62.4, 31.8 (2×), 29.4, 29.2 (2×), 26.0, 24.8, 22.7, 19.3, 14.1 ppm. ^{19}F NMR ($CDCl_3$): δ = –108.9 (d, J = 7.6 Hz) ppm. HRMS: calcd. for $[C_{28}H_{32}F_2O_2]^{*+}$ 438.2365 [M]*+; found 438.2367. (*m**: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 37: Compound **11** (1.21 g, 3.60 mmol) and 3-ethynyltoluene (550 mg, 4.74 mmol) were dissolved in THF (10 mL) and Et_3N (2 mL, 14.4 mmol) was added, followed by $PdCl_2(PPh_3)_2$ (101 mg, 0.14 mmol) and CuI (14 mg, 0.14 mmol). The resulting solution was stirred at 60 °C under argon for 2 d. Propargyl alcohol (1 mL) was then added (to remove the unreacted compound **11**) and the mixture was stirred for another day at 60 °C. The mixture was then diluted in CH_2Cl_2 and washed with saturated aqueous NH_4Cl, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude product was purified by flash chromatography on silica gel with EtOAc/hexanes (25%) as eluent to provide the title compound **37**(660 mg, 57% yield) as a brown solid. ^{1}H NMR ($CDCl_3$): δ = 7.35 (m, 2 H ar.), 7.21 (m, 1 H ar.), 7.13 (m, 1 H ar.), 6.92 (d, J = 7.4 Hz, 2 × HC–CF), 3.64 (t, J = 5.8 Hz, CH_2–O), 2.77 (br s, OH), 2.42 (t, J = 6.4 Hz, C≡C–CH_2), 2.31 (s, CH_3), 1.67 (m,4 H alkyl) ppm. ^{13}C NMR ($CDCl_3$): δ = 162.4 (dd, J = 252.9, J = 6.7 Hz, 2 C), 138.1, 132.3, 130.0, 128.9, 128.3, 125.5 (t, J = 11.9 Hz), 122.2, 114.4 (m*, 2 C), 102.3 (t, J = 20.2 Hz), 100.5 (t, J = 2.9 Hz), 94.3, 79.1 (t, J = 3.8 Hz), 75.8, 62.0, 31.8, 24.8, 21.2, 19.3 ppm. ^{19}F NMR ($CDCl_3$): δ = –108.4 (d, J = 7.6 Hz) ppm. HRMS: calcd. for $[C_{21}H_{18}F_2O]^{*+}$ 324.1320 [M]*+; found 324.2520. (*m**: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 38: CBr_4 (2.48 g, 7.47 mmol) and PPh_3 (1.96 mg, 7.47 mmol) were added at room temperature to a solution of compound **36** (1.31 g, 2.99 mmol) in THF (12 mL). The resulting mixture was stirred for 30 min, after which CH_2Cl_2 was added. The organic layer was washed with water and dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude product was filtered through silica gel with EtOAc/hexanes (2%) as eluent to provide the title compound **38** (1.44 g, 96% yield) as a pale yellow solid. ^{1}H NMR ($CDCl_3$): δ = 7.45 (d, J = 8.6 Hz, 2 H ar.), 6.90 (d, J = 7.3 Hz, 2 × HC–CF), 6.82 (d, J = 8.6 Hz, 2 H ar.), 3.88 (t, J = 6.6 Hz, CH_2–O), 3.40 (t, J = 6.6 Hz, CH_2–Br), 2.40 (t, J = 6.9 Hz, C≡C–CH_2), 1.96 (m, 2 H alkyl), 1.71 (m, 4 H alkyl), 1.39 (m, 2 H alkyl), 1.27 (m, 8 H alkyl), 0.88 (t, J = 6.5 Hz, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 163.1 (dd, J = 252.3, J = 6.5 Hz, 2 C), 159.9, 133.3 (2×), 124.8 (t, J = 11.9 Hz), 114.5 (2×), 114.3 (m*, 2 C), 114.2, 102.7 (t, J = 20.1 Hz), 100.8 (t, J = 3.0 Hz), 93.4, 79.4 (t, J = 3.7 Hz), 74.9, 68.1, 33.0, 32.1, 31.8, 29.6, 29.5, 29.4, 26.9, 26.1, 22.8, 18.7, 14.2 ppm. ^{19}F NMR ($CDCl_3$): δ = –108.6 (d, J = 7.2 Hz) ppm. HRMS: calcd. for $[C_{28}H_{31}F_2BrO]^{*+}$ 500.1521 [M]*+; found 500.1519. (*m**: The complex multiplicity of this signal can be attributed to coupling with fluorine*).

Compound 39: CBr_4 (1.44 g, 4.35 mmol) and PPh_3 (1.14 g, 4.35 mmol) were added at room temperature to a solution of compound **37** (565 mg, 1.74 mmol) in THF (4 mL). The resulting mixture was stirred for 30 min, after which CH_2Cl_2 was added. The organic layer was washed with water and dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude product was filtered through silica gel with EtOAc/hexanes (1%) as eluent to provide the title compound **39** (650 mg, 96% yield) as a white solid. ^{1}H NMR ($CDCl_3$): δ = 7.33 (m, 2 H ar.), 7.19 (m, 1 H ar.), 7.12 (m, 1 H ar.), 6.89 (d, J = 7.3 Hz, 2 × HC–CF), 3.39 (t, J = 6.6 Hz, CH_2–Br), 2.39 (t, J = 6.9 Hz, C≡C–CH_2), 2.31 (s, CH_3), 1.94 (m, 2 H alkyl), 1.69 (m, 2 H alkyl) ppm. ^{13}C NMR ($CDCl_3$): δ = 162.4 (dd, J = 253.3, J = 6.7 Hz, 2 C), 138.1, 132.3, 130.0, 128.9, 128.3, 125.3 (t, J = 11.7 Hz), 122.2, 114.3 (m*, 2 C), 102.4 (t, J = 20.2 Hz), 100.6 (t, J = 2.9 Hz), 93.7, 79.3 (t, J = 3.8 Hz), 75.8, 33.0, 31.8, 26.9, 21.2, 18.6 ppm. ^{19}F NMR ($CDCl_3$): δ = –108.2 (d, J = 7.8 Hz) ppm. HRMS: calcd. for $[C_{21}H_{17}BrF_2]^{*+}$ 386.0476 [M]*+; found 386.0478. (*m**: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 40: Compound **38** (1.38 g, 2.74 mmol) and potassium thioacetate (470 mg, 4.11 mmol) were heated at 60 °C overnight in THF (10 mL). The mixture was then diluted in CH_2Cl_2 and washed with water. The organic layer was dried with Na_2SO_4 and the solvents were removed under reduced pressure. The crude product was purified by flash chromatography on silica gel with EtOAc/hexanes (3%) as eluent to provide the title compound **40** (1.29 g, 95% yield) as a yellow solid. ^{1}H NMR ($CDCl_3$): δ = 7.46 (d, J = 8.3 Hz, 2 H ar.), 6.91 (d, J = 7.1 Hz, 2 × HC–CF), 6.83 (d, J = 8.6 Hz, 2 H ar.), 3.90 (t, J = 6.5 Hz, CH_2–O), 2.89 (t, J = 6.9 Hz, CH_2–S), 2.40 (t, J = 7.0 Hz, C≡C–CH_2), 2.31 (s, CH_3–C=O), 1.69 (m, 6 H alkyl), 1.41 (m, 2 H alkyl), 1.27 (m, 8 H alkyl), 0.88, (t, J = 6.3 Hz, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 195.5, 163.1 (dd, J = 252.9, J = 6.9 Hz, 2 C), 159.8, 133.3 (2×), 124.9 (t, J = 11.8 Hz), 114.5 (2×), 114.3 (m*, 2 C), 114.2, 102.7 (t, J = 20.2 Hz), 100.7 (t, J = 2.9 Hz), 93.7, 79.3 (t, J = 3.7 Hz), 74.9, 68.1, 31.9, 30.5, 29.4, 29.3, 29.2, 28.8, 28.5, 27.4, 26.1, 22.7, 19.0, 14.1 ppm. ^{19}F NMR ($CDCl_3$): δ = –108.7 (d, J = 6.8 Hz) ppm. HRMS: calcd. for $[C_{30}H_{34}F_2O_2S]^{*+}$ 496.2242 [M]*+; found 496.2241. (*m**: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 41: Compound **39** (573 mg, 1.48 mmol) and potassium thioacetate (338 mg, 2.96 mmol) were heated at 60 °C in THF (4 mL) overnight. The mixture was then diluted in CH_2Cl_2 and washed with water. The organic layer was dried with Na_2SO_4 and the solvents were removed under reduced pressure. The crude product was purified by flash chromatography on silica gel with EtOAc/hexanes (1%) as eluent to provide the title compound **41**(510 mg, 90% yield) as a white solid. ^{1}H NMR ($CDCl_3$): δ = 7.35 (m, 2 H ar.), 7.22 (m, 1 H ar.), 7.14 (m, 1 H ar.), 6.92 (d, J = 7.4 Hz, 2 × HC–CF), 2.89 (t, J = 7.0 Hz, CH_2–S), 2.40 (t, J = 6.8 Hz, C≡C–CH_2), 2.32 (s, CH_3), 2.31 (s, CH_3), 1.70 (m, 2 H alkyl), 1.64 (m, 2 H alkyl) ppm. ^{13}C NMR ($CDCl_3$): δ = 195.6, 162.4 (dd, J = 252.9, J = 6.5 Hz, 2 C), 138.1, 132.3, 129.9, 128.9, 128.3, 125.4 (t, J = 11.7 Hz), 122.2, 114.4 (m*, 2 C), 102.3 (t, J = 20.0 Hz), 100.5 (t, J = 2.9 Hz), 93.9, 79.2 (t, J = 3.7 Hz), 75.8, 30.6, 28.8, 28.5, 27.3, 21.2, 19.0 ppm. ^{19}F NMR ($CDCl_3$): δ = –108.4 (d, J = 7.5 Hz) ppm. HRMS: calcd. for $[C_{23}H_{20}F_2OS]^{*+}$ 382.1197 [M]*+; found 382.1202. (*m**: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 4: Compound **40** (1.11 g, 2.24 mmol) was dissolved in a solution of HCl/MeOH (1 M, 7 mL) with THF (7 mL) and stirred overnight at 50 °C. A saturated solution of I_2 in CH_2Cl_2 was added to this solution until persistence of the brown colouration. The

mixture was stirred for 15 min, diluted in CH_2Cl_2 and washed with saturated aqueous $Na_2S_2O_3$ until disappearance of the brown colour. The organic layer was dried with Na_2SO_4 and the solvents were removed under reduced pressure. The crude product was purified by flash chromatography on silica gel with EtOAc/hexanes (3%) as eluent to provide the title compound **4** (956 mg, 94% yield) as a white solid. ^{1}H NMR ($CDCl_3$): δ = 7.45 (d, J = 8.4 Hz, 4 H ar.), 6.91 (d, J = 7.3 Hz, 4 × HC–CF), 6.82 (d, J = 8.4 Hz, 4 H ar.), 3.88 (t, J = 6.5 Hz, 2 × CH_2–O), 2.69 (t, J = 6.8 Hz, 2 × CH_2–S), 2.40 (t, J = 6.7 Hz, 2 × C≡C–CH_2), 1.82 (m, 4 H alkyl), 1.73 (m, 4 H alkyl), 1.66 (m, 4 H alkyl), 1.40 (m, 4 H alkyl), 1.27 (m, 16 H alkyl), 0.88 (t, J = 6.1 Hz, 2 × CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 163.1 (dd, J = 252.6, J = 6.8 Hz, 4 C), 159.8 (2×), 124.9 (2×), 133.3 (4×), (t, J = 11.8 Hz, 2 C), 114.5 (4×), 114.3 (m*, 4 C), 114.2 (2×), 102.7 (t, J = 20.1 Hz, 2 C), 100.7 (t, J = 2.8 Hz, 2 C), 93.8 (2×), 79.3 (t, J = 3.6 Hz, 2 C), 74.9 (2×), 68.0 (2×), 38.3 (2×), 31.9 (2×), 29.4 (2×), 29.3 (2×), 29.2 (2×), 28.3 (2×), 27.1 (2×), 26.1 (2×), 22.7 (2×), 19.1 (2×), 14.1 (2×) ppm. ^{19}F NMR ($CDCl_3$): δ = –108.5 (d, J = 7.7 Hz) ppm. HRMS: calcd. for $[C_{56}H_{62}F_4O_2S_2]^{*+}$ 906.4122 [M]*$^+$; found 906.4102. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 6: Compound **41** (402 mg, 1.05 mmol) was dissolved in a solution of HCl/MeOH (1 M, 4 mL) with THF (4 mL) and stirred overnight at 50 °C. A saturated solution of I_2 in CH_2Cl_2 was added to this solution until persistence of the brown colouration. The mixture was stirred for 15 min, diluted in CH_2Cl_2 and washed with saturated aqueous $Na_2S_2O_3$ until disappearance of the brown colour. The organic layer was dried with Na_2SO_4 and the solvents were removed under reduced pressure. The crude product was purified by flash chromatography on silica gel with EtOAc/hexanes (1%) as eluent to provide the title compound **6** (354 mg, 99% yield) as a yellow oil. ^{1}H NMR ($CDCl_3$): δ = 7.35 (m, 4 H ar.), 7.22 (m, 2 H ar.), 7.14 (m, 2 H ar.), 6.92 (d, J = 7.4 Hz, 4 × HC–CF), 2.71 (t, J = 7.2 Hz, 2 × CH_2–S), 2.41 (t, J = 6.8 Hz, 2 × C≡C–CH_2), 2.32 (s, 2 × CH_3), 1.83 (m, 4 H alkyl), 1.67 (m, 4 H alkyl) ppm. ^{13}C NMR ($CDCl_3$): δ = 162.4 (dd, J = 253.2, J = 7.0 Hz, 4 C), 138.1 (2×), 132.3 (2×), 129.9 (2×), 128.9 (2×), 128.3 (2×), 125.3 (t, J = 11.7 Hz, 2 C), 122.2 (2×), 114.4 (m*, 4 C), 102.3 (t, J = 20.1 Hz, 2 C), 100.5 (t, J = 3.0 Hz, 2 C), 94.0 (2×), 79.3 (t, J = 3.8 Hz, 2 C), 75.8 (2×), 38.3 (2×), 28.3 (2×), 27.0 (2×), 21.2 (2×), 19.1 (2×) ppm. ^{19}F NMR ($CDCl_3$): δ = –108.3 (d, J = 7.4 Hz) ppm. HRMS: calcd. for $C_{42}H_{35}F_4S_2$ 679.2111 [M + H]; found 679.2101. (*m*: The complex multiplicity of this signal can be attributed to coupling with fluorine*).

Compound 42: Compound **11** (3.64 g, 10.8 mmol) and TMSA (4.59 mL, 32.5 mmol) were dissolved in THF (55 mL) and Et_3N (6.04 mL, 43.3 mmol) was added, followed by $PdCl_2(PPh_3)_2$ (304 mg, 0.43 mmol) and CuI (83 mg, 0.43 mmol). The resulting solution was stirred at 60 °C under argon for 2 d. The mixture was then diluted in CH_2Cl_2 and washed with saturated aqueous NH_4Cl, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude product was purified by flash chromatography on silica gel with EtOAc/hexanes (25%) as eluent to provide the title compound **42** (3.31 g, 99% yield) as a pale yellow oil. ^{1}H NMR ($CDCl_3$): δ = 6.89 (d, J = 7.5 Hz, 2 × HC–CF), 3.69 (t, J = 5.9 Hz, CH_2–O), 2.45 (t, J = 6.5 Hz, C≡C–CH_2), 1.93 (br s, OH), 1.69 (m,4 H alkyl), 0.27 (s, TMS-C) ppm. ^{13}C NMR ($CDCl_3$): δ = 162.9 (dd, J = 253.6, J = 6.8 Hz, 2 C), 125.8 (t, J = 11.9 Hz), 114.3 (m*, 2 C), 107.0 (t, J = 3.1 Hz), 102.0 (t, J = 20.1 Hz), 94.4, 90.7, 79.0 (t, J = 3.7 Hz), 62.2, 31.8, 24.7, 19.3, –0.3 (3×) ppm. ^{19}F NMR ($CDCl_3$): δ = –108.2 (d, J = 7.5 Hz) ppm. HRMS: calcd. for $[C_{17}H_{20}F_2OSi]$ 306.1251 [M]; found 306.1262. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 43: Compound **42** (1.38 g, 4.50 mmol) was dissolved in acetone (25 mL) at room temperature in darkness, followed by NBS (1.84 g, 10.4 mmol) and $AgNO_3$ (115 mg, 0.68 mmol), and the resulting solution was stirred for 4 h. The mixture was then diluted in CH_2Cl_2 and washed with water, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude product was purified by flash chromatography on silica gel with EtOAc/hexanes (25%) as eluent to provide the title compound **43** (1.07 g, 76% yield) as an orange oil. *Note: It is strongly recommended to use freshly synthesized bromoalkyne **43**. Well stored **43** retains its orange colour whereas improper storage leads to a red bromoalkyne, which is less efficient. Moreover, the compound is degraded to about 50% (by ^{19}F NMR) after one year and optimal efficiency is already lost after one month.* ^{1}H NMR ($CDCl_3$): δ = 6.57 (d, J = 7.4 Hz, 2 × HC–CF), 3.38 (t, J = 5.4 Hz, CH_2–Br), 2.14 (t, J = 5.5 Hz, C≡C–CH_2), 1.40 (m,4 H alkyl) ppm. ^{13}C NMR ($CDCl_3$): δ = 163.7 (dd, J = 253.9, J = 6.3 Hz, 2 C), 126.7 (t, J = 11.8 Hz), 114.8 (m*, 2 C), 101.7 (t, J = 19.8 Hz), 95.5, 79.3 (t, J = 3.5 Hz), 67.8, 62.2, 61.7 (t, J = 2.8 Hz), 32.3, 25.3, 19.7 ppm. ^{19}F NMR ($CDCl_3$): δ = –108.4 (d, J = 7.4 Hz) ppm. HRMS: calcd. for $[C_{14}H_{11}BrF_2O]^{*+}$ 311.9956 [M]*$^+$; found 311.9961. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 44: Compounds**43** (100 mg, 0.32 mmol) and **17** (213 mg, 0.35 mmol) were dissolved in THF (1.5 mL) and DIPEA (0.50 mL, 2.87 mmol) was added, followed by $Pd_2(dba_3)_3$·$CHCl_3$ (17 mg, 0.02 mmol) and CuI (3 mg, 0.02 mmol). The resulting solution was stirred overnight at room temperature under argon. The mixture was then diluted in CH_2Cl_2 and washed with saturated aqueous NH_4Cl, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude product was purified by flash chromatography on silica gel with EtOAc/hexanes (1%) to provide the trityl compound **17** (121 mg, 57% recovery) followed with EtOAc/hexanes (25%) as eluent to provide the title compound **44** (85 mg, 32% yield) as a brown solid. ^{1}H NMR ($CDCl_3$): δ = 7.29 (s, 3 H ar.), 6.99 (br s, 6 H ar.), 6.90 (d, J = 7.4 Hz, 2 × HC–CF), 3.68 (t, J = 5.7 Hz, CH_2–O), 2.45 (t, J = 6.3 Hz, C≡C–CH_2), 1.70 (m, 4 H ar.), 1.23 (br s, 18 × CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 163.6 (dd, J = 254.4, J = 6.3 Hz, 2 C), 150.0 (6×), 143.9 (3×), 126.0 (t, J = 11.9 Hz), 123.8 (6×), 120.2 (3×), 114.3 (m*, 2 C), 101.5 (t, J = 19.9 Hz), 94.9, 92.9, 85.0, (t, J = 2.9 Hz), 79.1 (t, J = 3.6 Hz), 68.3, 63.6, 62.2, 57.3, 34.8 (6×), 31.8, 31.4 (18×), 24.7, 19.3 ppm. ^{19}F NMR ($CDCl_3$): δ = –107.5 (d, J = 7.2 Hz) ppm. HRMS: calcd. for $C_{59}H_{75}F_2O$ 837.5780 [M + H]$^+$; found 837.5815. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 45: CBr_4 (623 mg, 1.88 mmol) and PPh_3 (493 mg, 1.88 mmol) were added at room temperature to a solution of the compound **44** (629 mg, 0.75 mmol) in THF (4 mL)and the resulting mixture was stirred for 30 min. The solution was then diluted in CH_2Cl_2 and washed with water, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude product was filtered through silica gel with EtOAc/hexanes (1%) as eluent to provide the title compound **45** (625 mg, 94% yield) as a yellow solid. ^{1}H NMR ($CDCl_3$): δ = 7.30 (s, 3 H ar.), 7.01 (br s, 6 H ar.), 6.89 (d, J = 7.2 Hz, 2 × HC–CF), 3.39 (t, J = 6.5 Hz, CH_2–Br), 2.42 (t, J = 6.8 Hz, C≡C–CH_2), 1.98 (m, 2 H alkyl), 1.73 (m, 2 H alkyl), 1.24 (br s, 18 × CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 163.6 (dd, J = 254.7, J = 6.3 Hz, 2 C), 150.1 (6×), 144.1 (3×), 125.9 (t, J = 11.6 Hz), 123.8 (6×), 120.2 (3×), 114.3

(m*, 2 C), 101.6 (t, J = 19.9 Hz), 94.4, 93.2, 85.1, (t, J = 2.8 Hz), 79.3 (t, J = 3.5 Hz), 68.4, 63.7, 62.2, 57.5, 34.8 (6×), 32.7, 31.7, 31.4 (18×), 26.7, 18.6 ppm. ^{19}F NMR ($CDCl_3$): δ = –107.2 (d, J = 7.3 Hz) ppm. HRMS: calcd. for $C_{59}H_{74}BrF_2$ 899.4936 $[M + H]^+$; found 899.4942. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 46: Compound **45** (585 mg, 0.66 mmol) and potassium thioacetate (227 mg, 1.99 mmol) were heated at 60 °C in THF (4 mL) overnight. The mixture was then diluted in CH_2Cl_2 and washed with water. The organic layer was dried with Na_2SO_4 and solvents were removed under reduced pressure. The crude product was purified by flash chromatography on silica gel with EtOAc/hexanes (1%) as eluent to provide the title compound **46** (507 mg, 87% yield) as a yellow solid. ^{1}H NMR ($CDCl_3$): δ = 7.30 (s, 3 H ar.), 7.01 (br s, 6 H ar.), 6.90 (d, J = 7.3 Hz, 2× HC–CF), 2.90 (t, J = 6.9 Hz, CH_2–S), 2.42 (t, J = 6.5 Hz, C≡C–CH_2), 2.29 (s, CH_3–C=O), 1.71 (m, 2 H alkyl), 1.65 (m, 2 H alkyl), 1.24 (br s, 18× CH_3) ppm. ^{19}F NMR ($CDCl_3$): δ = –107.3 (d, J = 7.3 Hz) ppm. ^{13}C NMR ($CDCl_3$): δ = 195.4, 163.7 (dd, J = 254.5, J = 6.3 Hz, 2 C), 150.0 (6×), 143.9 (3×), 125.9 (t, J = 11.8 Hz), 123.8 (6×), 120.2 (3×), 114.3 (m*, 2 C), 101.5 (t, J = 19.9 Hz), 94.5, 92.9, 85.1 (t, J = 3.0 Hz), 79.2 (t, J = 3.8 Hz), 68.3, 63.6, 57.3, 34.8 (6×), 31.4 (18×), 30.5, 28.8, 28.4, 27.3, 19.0 ppm. HRMS: calcd. for $C_{61}H_{77}F_2OS$ 895.5658[M + H]$^+$; found 895.5691. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 7: Compound **46** (474 mg, 0.54 mmol) was dissolved in a solution of HCl/MeOH (1 M, 2 mL) with THF (2 mL) and stirred for 4 h at 50 °C. A saturated solution of I_2 in CH_2Cl_2 was added to this solution until persistence of the brown colouration. The mixture was stirred for 15 min, diluted in CH_2Cl_2 and washed with saturated aqueous $Na_2S_2O_3$ until the disappearance of the brown colour. The organic layer was dried with Na_2SO_4 and the solvents were removed under reduced pressure. The crude product was purified by preparative TLC on silica gel with EtOAc/hexanes (2%) as eluent to provide the title compound **7** (378 mg, 82% yield) as a yellow solid, together with residual compound **46** (47 mg, 10% yield). ^{1}H NMR ($CDCl_3$): δ = 7.27 (s, 6 H ar.), 6.97 (br s, 12 H ar.), 6.89 (d, J = 7.4 Hz, 4× HC–CF), 2.73 (t, J = 7.1 Hz, 2× CH_2–S), 2.44 (t, J = 6.9 Hz, 2× C≡C–CH_2), 1.84 (m, 4 H alkyl), 1.70 (m, 4 H alkyl), 1.21 (br s, 36× CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 163.6 (dd, J = 254.4, J = 6.3 Hz, 4 C), 150.0 (12×), 144.0 (6×), 125.9 (t, J = 11.9 Hz, 2 C), 123.8 (12×), 120.2 (6×), 114.3 (m*, 4 C), 101.6 (t, J = 20.1 Hz, 2 C), 94.5 (2×), 93.0 (2×), 85.0 (t, J = 2.3 Hz, 2 C), 79.2 (t, J = 3.6 Hz, 2 C), 68.3 (2×), 63.6 (2×), 57.3 (2×), 38.1 (2×), 34.8 (12×), 31.4 (36×), 28.2 (2×), 26.9 (2×), 19.0 (2×) ppm. ^{19}F NMR ($CDCl_3$): δ = –107.5 (d, J = 7.7 Hz) ppm. HRMS: calcd. for $C_{118}H_{147}F_4S_2$ 1704.0875 $[M + H]^+$; found 1704.0904. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 47: 3,5-Di-*tert*-butylbromobenzene (2.00 g, 7.43 mmol) was dissolved in THF (35 mL) and Et_3N (4.14 mL, 29.7 mmol) was added, followed by $PdCl_2(PPh_3)_2$ (209 mg, 0.30 mmol), CuI (57 mg, 0.30 mmol) and TMSA (3.09 mL, 22.3 mmol). The resulting solution was stirred at 60 °C under argon for two days. The mixture was then diluted in CH_2Cl_2 and washed with saturated aqueous NH_4Cl, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude product was purified by flash chromatography on silica gel with pure hexanes as eluent to provide the title compound **47** (1.99 g, 94% yield) as a white solid. ^{1}H NMR ($CDCl_3$): δ = 7.37 (m, 1 H ar.), 7.32 (m, 2 H ar.), 1.31 (s, 6× CH_3), 0.26 (s, TMS-C) ppm. ^{13}C NMR ($CDCl_3$): δ = 150.8 (2×), 126.4 (2×), 123.1, 122.2, 106.6, 92.6, 34.9 (2×), 31.5 (6×), 0.3 (3×) ppm. HRMS: calcd. for $C_{19}H_{30}Si$, 286.2117 [M]; found 286.2124.

Compound 48: Compound **47** (1.17 g, 4.08 mmol) was dissolved in THF/MeOH/H_2O (18:5:5 mL) in the presence of NaOH (1.63 g, 40.8 mmol) and the mixture was stirred for 90 min at room temperature. The solution was acidified until pH ≈ 6 and extracted three times with CH_2Cl_2, and the combined organic layers were dried with Na_2SO_4. The solvents were removed under reduced pressure and filtration through silica gel with hexanes as eluent afforded the crude deprotected compound, which was dried 30 min prior to use. The previously obtained compound and compound **43** (1.07 g, 3.40 mmol) were then dissolved in THF (17 mL) with DIPEA (5.33 mL, 30.6 mmol), followed by $Pd_2(dba_3)_3$·$CHCl_3$ (176 mg, 0.17 mmol) and CuI (32 mg, 0.17 mmol). The resulting solution was stirred under argon overnight at room temperature. The mixture was then diluted in CH_2Cl_2 and washed with saturated aqueous NH_4Cl, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude product was purified by flash chromatography on silica gel with EtOAc/hexanes (25%) as eluent to provide the title compound **48** (1.02 g, 67% yield) as a brown solid. ^{1}H NMR ($CDCl_3$): δ = 7.47 (s, 1 H ar.), 7.40 (m, 2 H ar.), 6.90 (d, J = 7.4 Hz, 2× HC–CF), 3.67 (t, J = 5.8 Hz, CH_2–O), 2.62 (s, OH), 2.44 (t, J = 6.2 Hz, C≡C–CH_2), 1.69 (m, 4 H alkyl), 1.32 (br s, 6× CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 163.5 (dd, J = 254.8, J = 6.1 Hz, 2 C), 151.1 (2×), 126.8 (2×), 126.5 (t, J = 11.9 Hz), 124.3, 120.3, 114.4 (m*, 2 C), 101.2 (t, J = 20.1 Hz), 95.3, 85.7, 84.5 (t, J = 2.7 Hz), 79.1 (t, J = 3.7 Hz), 72.4, 67.6, 62.0, 34.8 (2×), 31.8, 31.2 (6×), 24.8, 19.3 ppm. ^{19}F NMR ($CDCl_3$): δ = –107.3 (d, J = 7.5 Hz) ppm. HRMS: calcd. for $C_{30}H_{33}F_2O$ 447.2494 $[M + H]^+$; found 447.2497. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 49: CBr_4 (1.80 g, 5.43 mmol) and PPh_3 (1.42 g, 5.43 mmol) were added at room temperature to a solution of compound **48** (970 mg, 2.17 mmol) in THF (6 mL) and the resulting mixture was stirred for 30 min. The solution was then diluted in CH_2Cl_2 and washed with water, and the organic layer was dried with Na_2SO_4. The solvents were removed under reduced pressure and the crude product was filtered through silica gel with EtOAc/hexanes (1%) as eluent to provide the title compound **49** in quantitative yield as a yellow oil. ^{1}H NMR ($CDCl_3$): δ = 7.46 (s, 1 H ar.), 7.40 (m, 2 H ar.), 6.89 (d, J = 7.4 Hz, 2× HC–CF), 3.44 (t, J = 6.6 Hz, CH_2–Br), 2.45 (t, J = 6.9 Hz, C≡C–CH_2), 2.00 (m, 2 H alkyl), 1.75 (m, 2 H alkyl), 1.32 (br s, 6× CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 163.4 (dd, J = 254.4, J = 6.1 Hz, 2 C), 151.0 (2×), 126.7 (2×), 126.2 (t, J = 11.9 Hz), 124.2, 120.1, 114.4 (m*, 2 C), 101.2 (t, J = 20.1 Hz), 94.6, 85.7, 84.4 (t, J = 2.7 Hz), 79.2 (t, J = 3.7 Hz), 72.4, 67.5, 34.7 (2×), 31.7, 31.2 (6×), 26.7, 18.6 ppm. ^{19}F NMR ($CDCl_3$): δ = –107.0 (d, J = 7.4 Hz) ppm. HRMS: calcd. for $[C_{30}H_{31}BrF_2]^{*+}$ 508.1572 $[M]^{*+}$; found 508.1572. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 50: Compound **49** (1.13 g, 2.22 mmol) and potassium thioacetate (760 mg, 6.65 mmol) in THF (10 mL) was heated at 60 °C overnight. The mixture was then diluted in CH_2Cl_2 and washed with water. The organic layer was dried with Na_2SO_4 and the solvents were removed under reduced pressure. The crude product was purified by flash chromatography on silica gel with EtOAc/hexanes (1%) as eluent to provide the title compound **50** (807 mg, 72% yield) as a yellow solid. ^{1}H NMR ($CDCl_3$): δ = 7.47 (s, 1 H ar.), 7.41 (m, 2 H ar.), 6.90 (d, J = 7.4 Hz, 2× HC–CF), 2.90 (t, J = 6.9 Hz, CH_2–S), 2.42 (t, J = 6.6 Hz, C≡C–CH_2), 2.31 (s, CH_3–C=O), 1.69 (m, 4 H alkyl), 1.32 (br s, 6× CH_3) ppm. ^{13}C NMR

($CDCl_3$): δ = 195.5, 163.5 (dd, J = 254.6, J = 6.1 Hz, 2 C), 151.1 (2×), 126.8 (2×), 126.4 (t, J = 12.0 Hz), 124.2, 120.3, 114.4 (m*, 2 C), 101.2 (t, J = 19.9 Hz), 94.9, 85.7, 84.4 (t, J = 2.8 Hz), 79.1 (t, J = 3.6 Hz), 72.4, 67.6, 34.8 (2×), 31.2 (6×), 30.5, 28.8, 28.5, 27.3, 19.0 ppm. ^{19}F NMR ($CDCl_3$): δ = –107.2 (d, J = 7.5 Hz) ppm. HRMS: calcd. for $[C_{32}H_{34}F_2OS]^{*+}$ 504.2293 $[M]^{*+}$; found 504.2309. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

Compound 8: Compound **50** (736 mg, 1.46 mmol) was dissolved in a solution of HCl/MeOH (1 M, 6 mL) with THF (6 mL) and stirred 4 h at 50 °C. A saturated solution of I_2 in CH_2Cl_2 was added to this solution until persistence of the brown colouration. The mixture was stirred for 15 min, diluted in CH_2Cl_2 and washed with saturated aqueous $Na_2S_2O_3$ until the disappearance of the brown colour. The organic layer was dried with Na_2SO_4 and the solvents were removed under reduced pressure. The crude product was purified by preparative TLC on silica gel with EtOAc/hexanes (2%) as eluent to provide the title compound **8** (503 mg, 75% yield) as a yellow solid, together with residual compound **50**(65 mg, 9% yield). ^1H NMR ($CDCl_3$): δ = 7.47 (s, 2 H ar.), 7.40 (m, 4 H ar.), 6.90 (d, J = 7.4 Hz, 4×HC–CF), 2.72 (t, J = 7.1 Hz, 2×CH_2–S), 2.43 (t, J = 6.9 Hz, 2×C≡C–CH_2), 1.83 (m, 4 H alkyl), 1.70 (m, 4 H alkyl), 1.32 (br s, 12×CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 163.5 (dd, J = 254.7, J = 6.2 Hz, 4 C), 151.1 (4×), 126.8 (4×), 126.4 (t, J = 11.8 Hz, 2 C), 124.2 (2×), 120.2 (2×), 114.4 (m*, 4 C), 101.2 (t, J = 20.0 Hz, 2 C), 95.0 (2×), 85.7 (2×), 84.5 (t, J = 2.6 Hz, 2 C), 79.2 (t, J = 3.8 Hz, 2 C), 72.4 (2×), 67.6 (2×), 38.2 (2×), 34.8 (4×), 31.2 (12×), 28.2 (2×), 27.0 (2×), 19.1 (2×) ppm. ^{19}F NMR ($CDCl_3$): δ = –107.1 (d, J = 7.3 Hz) ppm. HRMS: calcd. for $C_{60}H_{63}F_4S_2$ 923.4302 $[M + H]^+$; found 923.4311. (*m*: The complex multiplicity of this signal is attributed to coupling with fluorine*).

General Procedure for the Preparation of NP1–NP8: A solution of tetraoctylammonium bromide (0.034 M, 5 equiv.) in toluene was added to a stirred solution of $HAuCl_4$ (0.032 M, 2 equiv.) in nanopure H_2O and stirred vigorously for 15 min. The two phases were separated and the aqueous phase was discarded. The disulfide (1 equiv.) in a minimal volume of toluene was then added to the brown organic phase and stirred for 5 min. A freshly prepared solution of $NaBH_4$ (0.39 M, 20 equiv.) in nanopure H_2O was then quickly added and the resulting mixture was vigorously stirred for one hour. The two phases were then separated and the black organic layer was washed once with H_2SO_4 (0.1 M), once with NaOH (0.1 M) and once with H_2O. The solvent was removed in vacuo until ≈3 mL of toluene remained. The crude nanoparticles were then precipitated with ethanol (≈150 mL) and centrifuged for 15 min, washed with ethanol and dissolved again in a minimal volume of toluene (≈2 mL), and the purification process was then repeated again as described previously to provide the gold nanoparticles **NP1**–**NP4** as black solids. These products were further purified by size exclusion chromatography (SEC) on Bio-Beads® S-X1 (Bio-Rad Laboratories, Hercules, USA) with toluene as eluent. The gold nanoparticles **NP5**–**NP8** were precipitated once and purified on Bio-Beads® S-X1 as described previously. For **NP5**–**NP6**, a further purification step was as follows: the compounds were each dissolved in a minimal amount of CH_2Cl_2 (≈2 mL), precipitated in hexanes (≈ 200 mL) and centrifuged for 15 min to provide gold nanoparticles **NP5** and **NP6** as black solids.

Quantities of reagents used and purification techniques for the synthesis of compounds NP1–NP8.

NP1: $HAuCl_4$: 118 mg, 0.30 mmol; TOAB: 410 mg, 0.75 mmol; compound **1**: 250 mg, 0.15 mmol; $NaBH_4$: 113 mg, 3.00 mmol. Amount of nanoparticles recovered after purification: 99 mg.

NP2: $HAuCl_4$: 191 mg, 0.49 mmol; TOAB: 664 mg, 1.22 mmol; compound **2**: 200 mg, 0.24 mmol; $NaBH_4$: 184 mg, 4.86 mmol. Amount of nanoparticles recovered after purification: 136 mg.

NP3: $HAuCl_4$: 138 mg, 0.35 mmol; TOAB: 477 mg, 0.87 mmol; compound **3**: 306 mg, 0.17 mmol; $NaBH_4$: 132 mg, 3.49 mmol. Amount of nanoparticles recovered after purification: 79 mg.

NP4: $HAuCl_4$: 174 mg, 0.44 mmol; TOAB: 603 mg, 1.10 mmol; compound **4**: 200 mg, 0.22 mmol; $NaBH_4$: 167 mg, 4.41 mmol. Amount of nanoparticles recovered after purification: 121 mg.

NP5: $HAuCl_4$: 179 mg, 0.46 mmol; TOAB: 622 mg, 1.14 mmol; compound **5**: 243 mg, 0.23 mmol; $NaBH_4$: 172 mg, 4.55 mmol. Amount of nanoparticles recovered after purification: 143 mg.

NP6: $HAuCl_4$: 308 mg, 0.78 mmol; TOAB: 1.07 g, 1.96 mmol; compound **6**: 266 mg, 0.39 mmol; $NaBH_4$: 296 mg, 7.84 mmol. Amount of nanoparticles recovered after purification: 245 mg.

NP7: $HAuCl_4$: 162 mg, 0.41 mmol; TOAB: 561 mg, 1.03 mmol; compound **7**: 350 mg, 0.21 mmol; $NaBH_4$: 155 mg, 4.11 mmol. Amount of nanoparticles recovered after purification: 114 mg.

NP8: $HAuCl_4$: 256 mg, 0.65 mmol; TOAB: 888 mg, 1.62 mmol; compound **8**: 300 mg, 0.32 mmol; $NaBH_4$: 246 mg, 6.50 mmol. Amount of nanoparticles recovered after purification: 205 mg.

Supporting Information (see footnote on the first page of this article): ^1H and ^{13}C NMR spectra of all new compounds, transmission electron microscope (TEM) images, thermogravimetric analysis (TGA) and calculation details of the organic/gold ratio for the nanoparticles.

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