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Regioselective access to substituted oxindoles via rhodium-catalyzed carbene C–H insertion

Delphine Gauthier, Robert H. Dodd, Philippe Dauban *

Centre de Recherche de Gif-sur-Yvette, Institut de Chimie des Substances Naturelles, UPR 2301 CNRS, Avenue de la Terrasse, 91198 Gif-sur-Yvette Cedex, France

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ABSTRACT

Rhodium-catalyzed decomposition of diazoamides followed by insertion of the resulting carbenes into an aromatic C–H bond gives access to substituted oxindoles. The reaction takes place with aromatic rings substituted by either electron-donating or -withdrawing groups at *ortho*, *meta* or *para* positions and the regioselectivity can be controlled by a substitution α to the diazo functionality. In the presence of an ester, the reaction leads to the formation of 2-silyloxyindole-3-carboxylates in 40–85% yields and regioselectivities up to 80% are observed in the case of *meta*-substituted substrates. This selectivity mainly relies on steric factors and use of a more bulky *N*,*N*-diethylamide then affords 2-silyloxyindole-3-carboxamides in 42–91% yields with complete regioselectivity.

1. Introduction

Indolic compounds hold a paramount position in the family of alkaloids and have therefore received considerable attention from the synthetic organic and medicinal chemistry communities.[1] The comparable prominent importance of their oxidized analogs has also recently been acknowledged since oxindoles can be found in a growing number of natural products and pharmaceutical agents.[2] This motif is present, for example, in the structure of horsfiline,[3] spirotryprostatins,[4] and welwitindolinones,[5] to name but a few. Moreover, several oxindole-derived compounds have been approved for the treatment of Parkinson's disease (Ropinirole),[6] arthritis (Tenidap)[7] or renal cell carcinoma (SU11248).[8] As a consequence, several strategies have been devised for the preparation of the oxindole nucleus. Classical methodologies involve oxidative rearrangements of indoles,[1,2a,9] chemical modifications of isatins,[10] radical cyclization,[11] and Gassman synthesis from anilines.[12] Not surprisingly, the advent of transition metal-catalyzed transformations has recently led to the development of numerous new entries to functionalized oxindoles. These can thus be obtained either by catalytic intramolecular amidation of haloarenes,[13] palladium-catalyzed intramolecular α-arylation of amides,[14] Heck-type carbocyclization applied to *N*-(aryl)-acrylamides[15] and -propynamides[16] or catalytic addition to arylisocyanates.[17] More interestingly, transition metal-catalyzed protocols have recently emerged that afford a direct access to oxindoles starting from non *ortho*-substituted anilines[18] via a C–H functionalization process.[19] Such transformations could greatly simplify the synthesis of oxindoles since they circumvent the need to prepare the *ortho*-halogenated anilines necessary for the aforementioned catalytic reactions.

In the course of a medicinal chemistry program aimed at developing proteasome inhibitors as new potential antitumor agents,[20] we sought to prepare analogs of TMC-95A **1** (Fig. 1). The latter isolated from the fermentation broth of *Apiospora montagnei* Sacc. TC 1093 is a cyclic peptide displaying potent inhibitory activity of the proteasome in the nanomolar range as well as cytotoxic

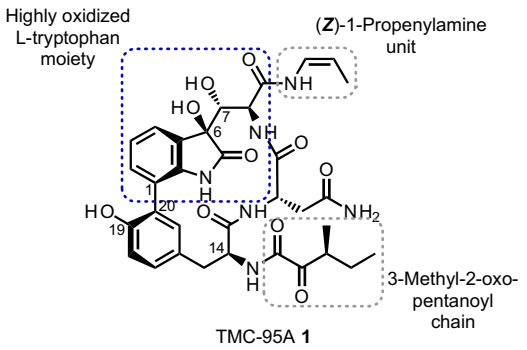

Figure 1. Structure of TMC-95A.

* Corresponding author. Tel.: +33 (0)1 69 82 45 60; fax: +33 (0)1 69 07 72 47.
E-mail address: philippe.dauban@icsn.cnrs-gif.fr (P. Dauban).

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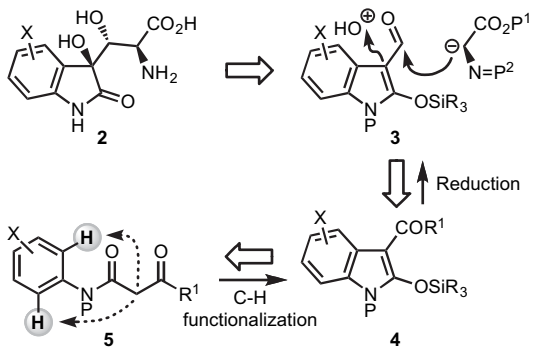
activities against various cancer cell lines.[21] Compared to previously described inhibitors,[20] the novelty of TMC-95A lies in its unique mode of action, i.e., **1** binds non-covalently to the proteasome active sites via a hydrogen bond network[22] as well as in its structural complexity. In particular, this cyclic tripeptide is characterized by a highly oxidized L-tryptophan moiety linked to a tyrosine residue by a biaryl bond.

These unusual features have spurred several groups to embark on synthetic studies that have culminated in the publication of three total syntheses.[23–25] Particular attention has been paid to the preparation of the highly functionalized oxindole part of TMC-95A, which was found to be accessible via application of a Heck reaction starting from dibromoaniline derivatives,[23,24,26] functional group transformations of isatin[25,27] or oxidative rearrangement of indoles.[28] In parallel to these accomplishments, several SAR studies have been conducted thereby delineating the structural requirements for potent proteasome inhibition.[29] Surprisingly, despite several site modifications, the introduction of substituents on the aromatic part of the oxindole and the resulting influence on biological activity have not been investigated so far. It was therefore with the intention of studying such modifications that we have initiated a program aimed at developing a versatile access to substituted oxindoles. In order to avoid the use of *ortho*-haloaniline derivatives, we have devised a strategy based on a C–H functionalization process allowing a straightforward preparation of the expected products (Scheme 1).



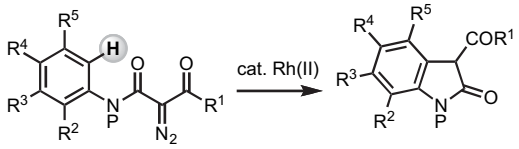
Scheme 1. Retrosynthesis of the oxidized tryptophan moiety.

The retrosynthetic disconnection envisaged for the highly oxidized tryptophan moiety **2** first involves an enolate hydroxylation and condensation of a chiral glycine anion equivalent. The required aldehyde **3** could in turn be obtained by reduction of a keto derivative **4** (i.e., an ester or an amide), the latter being the product of a C–H functionalization reaction applied to dicarbonyl compounds of type **5**. However, such a transformation inevitably poses the problem of regioselectivity with respect to the substitution on the aryl ring. In this article, we thus present the results of our investigations directed towards the formation of substituted oxindoles involving selective functionalization of a C_{sp2}–H bond.

2. Results and discussion

2.1. Selection of C–H functionalization process

Guided by our recent studies devoted to intermolecular C–H amination via catalytic nitrene insertion,[30] we decided to study the analogous carbene transfer for the direct functionalization of aromatic rings. Such reagents can be efficiently generated by catalytic decomposition of a diazo compound, the resulting metallacarbene then inserting into C–H bonds with good yields and selectivities.[31,32] The power of this C–C bond formation is testified by its application to the total syntheses of natural products, heterocycles, and drugs.[33] In particular, Doyle and Durst first recognized the utility of intramolecular carbene C–H insertions for the preparation of oxindoles.[34] Moody and Padwa then demonstrated the superior performance of rhodium(II) perfluorocarboxamide as catalyst for this transformation,[35] which was successfully applied to the syntheses of convolutamydine C[36a] and horsfiline.[36b] In the context of our planned SAR studies, we decided to enhance the scope of this reaction studied thus far in a limited number of cases with a particular emphasis on its regioselectivity, a point that has been overlooked in preceding work (Scheme 2).



Scheme 2. Intramolecular rhodium-catalyzed carbene C–H insertion for the formation of oxindoles.

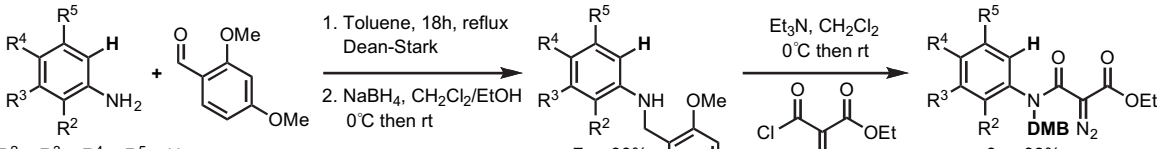
2.2. Synthesis of oxindole 3-carboxylates

We first studied the reactivity of diazomalonamic acid ethyl esters **9** the preparation of which relies on the acylation of substituted anilines of type **7** with ethyl 2-diazomalonyl chloride **8** (Scheme 3). The DMB-protected compounds **7** (DMB: 2,4-dimethoxybenzyl)[36] were in turn isolated in very good yields (generally greater than 83%) via reductive amination of anilines **6** with 2,4-dimethoxybenzaldehyde while diazo derivative **8** was prepared by reaction of triphosgene with commercially available ethyl diazoacetate according to a published procedure.[37] Acylation of **7a–m** finally occurred in the presence of triethylamine to afford the expected diazo precursors **9a–m** in modest to excellent yields.

In the case **7a** and of *para*- or *meta*-substituted derivatives **7b–f** and **7j–m**, the condensation reaction efficiently takes place in the presence of either electron-withdrawing or -donating substituents and allows isolation of the corresponding compounds **9a–f** and **9j–m** with yields in the 64–99% range.[38] However, acylation of the *ortho*-bromo analogs **7g–i** proved to be more sluggish probably as a result of steric hindrance and the corresponding diazos **9g–i** were obtained with non-optimized yields ranging from 22 to 30%.

Compounds **9** were then engaged in the rhodium-catalyzed transformation into indoles **10** (Table 1). As previously described,[35] higher conversions are observed at room temperature in the presence of rhodium(II) trifluoroacetamide prepared according to a recently published procedure.[39] This catalyst, which is more electrophilic than the classical rhodium(II) acetate, induces the formation of a metallacarbene the cationic nature of which favors aromatic substitution.[31e,40] Moreover, based on Padwa's recommendation,[35a] the oxindoles were isolated as their more stable 2-silyl enol ethers. In the case of diazoamides **9a–e**, the corresponding 2-silyloxyindoles **10a–e** are formed in good yields ranging from 68% to 78% (entries 1–5). The yields appear to weakly depend on electronic factors. Thus, while the *p*-trifluoromethyl derivative **10e** is isolated with a yield of 72% (entry 5), the presence of a *p*-methoxy group leads to the 5-methoxyindole **10b** with a comparable yield of 68% (entry 2). Though the presence of two *meta* electrondonating group in substrate **9f** should have improved this result, such was not the case since the corresponding product **10f** was isolated in 65% yield (entry 6). As a possible explanation, the favorable *ortho,para*-electronic effects could be counterbalanced by steric factors.

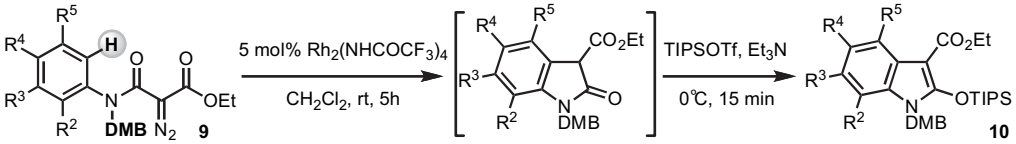
More interestingly, we were very pleased to observe that the reaction occurs efficiently starting from *ortho*-bromo derivatives **9g–i** (entries 7–9), a key result in the context of the preparation of TMC-95A analogs because it affords the opportunity to form the biaryl C1–C20 bond via palladium-catalyzed coupling. Of particular

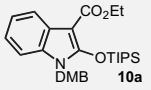
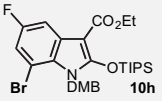
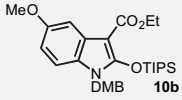
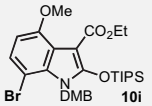
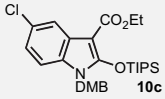
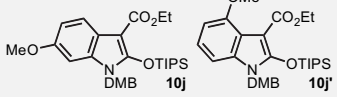
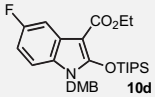
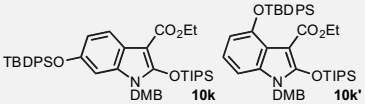
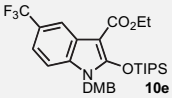
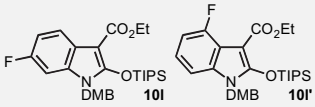
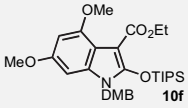
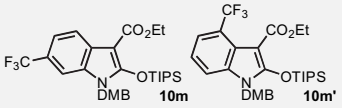
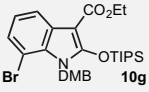


6a: $R^2 = R^3 = R^4 = R^5 = H$	**7a:** 90%	**9a:** 93%
6b: $R^2 = R^3 = R^5 = H$; **R^4 = OMe**	**7b:** 83%	**9b:** 78%
6c: $R^2 = R^3 = R^5 = H$; **R^4 = Cl**	**7c:** 96%	**9c:** 99%
6d: $R^2 = R^3 = R^5 = H$; **R^4 = F**	**7d:** 99%	**9d:** 64%
6e: $R^2 = R^3 = R^5 = H$; **$R^4 = CF_3$**	**7e:** 97%	**9e:** 67%
6f: $R^2 = R^4 = H$; **$R^3 = R^5$ = OMe**	**7f:** 93%	**9f:** 83%
6g: **R^2 = Br**; $R^3 = R^4 = R^5 = H$	**7g:** 89%	**9g:** 28%
6h: **R^2 = Br**; $R^3 = R^5 = H$; **R^4 = F**	**7h:** 36%	**9h:** 30%
6i: **R^2 = Br**; $R^3 = R^4 = H$; **R^5 = OMe**	**7i:** 95%	**9i:** 22%
6j: $R^2 = R^4 = R^5 = H$; **R^3 = OMe**	**7j:** 70%	**9j:** 78%
6k: $R^2 = R^4 = R^5 = H$; **R^3 = OTBDPS**	**7k:** 91%	**9k:** 88%
6l: $R^2 = R^4 = R^5 = H$; **R^3 = F**	**7l:** 96%	**9l:** 90%
6m: $R^2 = R^4 = R^5 = H$; **$R^3 = CF_3$**	**7m:** 86%	**9m:** 71%

Scheme 3. Preparation of diazo compounds **9**, precursors of oxindole 3-carboxylates.

Table 1
Rhodium-catalyzed carbene C–H insertion for the formation of 2-silyloxyindole-3-carboxylates **10**



Entry	Compound	Product	Yield[a] %	Entry	Compound	Product	Yield[a] %
1	**9a**	 **10a**	78	8	**9h**	 **10h**	40
2	**9b**	 **10b**	68	9	**9i**	 **10i**	67
3	**9c**	 **10c**	70	10	**9j**	 **10j** **10j'**	95 (73:27)
4	**9d**	 **10d**	71	11	**9k**	 **10k** **10k'**	93 (90:10)
5	**9e**	 **10e**	72	12	**9l**	 **10l** **10l'**	93 (73:27)
6	**9f**	 **10f**	65	13	**9m**	 **10m** **10m'**	69 (64:36)
7	**9g**	 **10g**	85				

[a] Isolated yields after flash chromatography on SiO_2. Values in parentheses indicate the ratio of regioisomers.

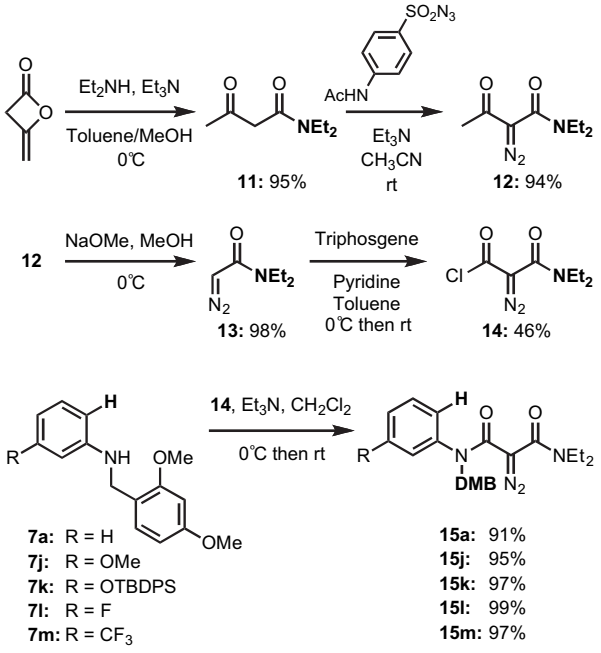
note are the isolated yields of 85% and 67% obtained for products **10g**,**i** (entries 7 and 9) since, when compared to the preceding substrates **9a–f**, there is only one C–H bond available for carbene insertion.

The reaction with substrates **9j–m** then allowed us to study the influence of the substitution on the regioselectivity of the C–H functionalization. Excellent yields up to 95% were obtained with these derivatives (entries 10–13). However, contrary to the

complete regioselectivity observed with a *meta*-methoxy substituted diazoacetamide described in Doyle et al.'s monograph,[31b] the *meta*-methoxy diazo **9j** leads to a mixture of indoles **10j**,**j′** with a 73:27 ratio in favor of the 6-substituted derivative (entry 10). These regioisomers are easily distinguishable by ^{1}H NMR. Compound **10j** is characterized by a downshielded doublet corresponding to H_4 (δ 7.9 ppm) while the coupling constant for H_7 (~3.0 Hz) is smaller than that of H_7 in isomer **10j′** (~8.0 Hz). This result can be attributed to either the nature of the substituent α- to the diazo or a ligand effect since the above mentioned complete regioselectivity was observed starting from a diazoacetamide in the presence of $Rh_2(OAc)_4$.[31b] Such an influence of the diazo substitution and the rhodium(II) catalyst on the regio- and chemoselectivity is well known and documented in several previous reports.[31e,f,40] Replacement of the methoxy group by a bulkier *tert*-butyldiphenylsilyloxy group significantly improves the regioselectivity, a higher ratio of 90:10 in favor of the 6-silyloxy regioisomer **10k** being recorded (entry 11). This observation tends to prove that the course of the reaction can be controlled by steric factors. However, electronic effects also play an important role as suggested by the replacement of the *m*-methoxy group by the less sterically demanding fluorine atom that leads to the same proportion, i.e., 73:27, of regioisomers **10l**,**l′** (entry 12). Finally, the presence of the *m*-trifluoromethyl group in diazo **9m** induces a decrease of reactivity and also of selectivity (entry 13).

2.3. Synthesis of oxindole 3-carboxamides

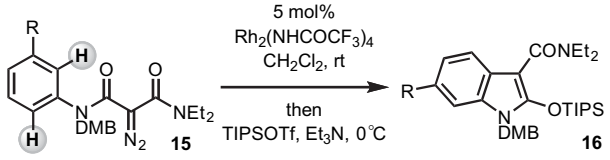
Based on the postulated influence of steric effects, we then planned to improve the regioselectivity of the carbene C–H insertion by studying the case of more sterically demanding diazoamides. We thus turned our attention to *N*,*N*-diethylamide derivatives of type **15** that can in principle be reduced under mild conditions via hydrozirconation using $Cp_2Zr(H)Cl$.[41] Isolation of these starting materials required the initial preparation of diazomalonamyl chloride **14** synthesized from diketene in four steps and 40% overall yield (Scheme 4).[42] Condensation of the latter with anilines **7** then afforded the expected diazo compounds **15** in excellent yields greater than 90%.

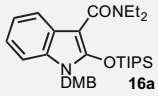
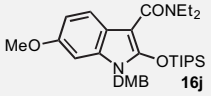
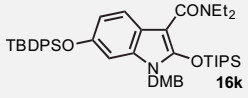
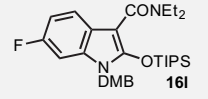
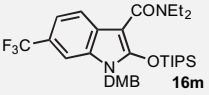


Scheme 4. Preparation of acyl chloride **14** and diazos compounds **15**.

Rhodium-catalyzed decomposition of diazos **15** was then investigated by application of the conditions already used for diazos **9** (Table 2). The *N*,*N*-diethyl 2-silyloxyindole-3-carboxamide **16a** was thus obtained with a yield of 88%, better than that observed for the indole-3-carboxylate **10a** (entry 1). More importantly, the *meta*-substituted substrates **15j**–**m** led to a single regioisomer thereby corroborating the influence of steric hindrance on the course of the reaction. Thus, the 6-OMe **16j**, 6-OTBDPS **16k**, 6-F **16l**, and 6-CF_3 **16m** indole derivatives were isolated in 88, 91, 72, and 42% yields, respectively (entries 2–5). These results clearly indicate that the regioselective formation of substituted oxindoles via C–H functionalization is indeed possible by carefully choosing the substitution pattern on the precursor. A bulky amide is likely to favor reaction at the *para* position with electron-donating groups, 6-substituted indoles **16j**,**k** being isolated with better yields when compared to products **10j**,**k**. However, the same sterically demanding substitution appears to have a different influence on the reactivity in the presence of electron-withdrawing groups. Inhibition of C–H insertion at the *ortho*-position is indeed suggested by comparing the results obtained in the cases of fluoro derivatives **10l** and **16l**, and of trifluoromethyl compounds **10m** and **16m**. Yields are roughly the same for the *para*-adducts (70% vs 72% and 44% vs 42%) while formation of the *ortho*-isomer is no longer observed in the case of the amide.

Table 2
Rhodium-catalyzed carbene C–H insertion for the formation of 2-silyloxyindole-3-carboxamides **16**



Entry	Compound	Product	Yield[a] %
1	**15a**	 **16a**	88
2	**15j**	 **16j**	88
3	**15k**	 **16k**	91
4	**15l**	 **16l**	72
5	**15m**	 **16m**	42

[a] Isolated yields after flash chromatography on SiO_2.

3. Conclusion

Rhodium-catalyzed carbene aromatic C–H insertion has been found to occur in moderate to very good yields in the presence of either electron-donating or -withdrawing groups. *ortho*, *meta*, and *para* Substitutions are well tolerated. More importantly, the reaction can take place with very high regioselectivity in the case of *meta*-substituted starting materials. This selectivity can be fine-tuned by carefully choosing the substituents. In this context, while the importance of electronic effects was previously highlighted,[31b] we have demonstrated that steric hindrance plays a key role in

directing the C–H insertion to a selected position. Work is now in progress to apply these results to the preparation of highly oxidized tryptophan moieties for incorporation into the structure of cyclic tripeptides analogous to TMC-95A.

4. Experimental

4.1. General methods

Melting points (mp [°C]), measured in capillary tubes, are uncorrected. IR spectra were recorded on an FT-IR spectrometer. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded at ambient temperature on a Bruker spectrometer at 300 MHz or 500 MHz, in $CDCl_3$ unless otherwise stated. Chemical shifts (δ) are reported in parts per million with reference to $CDCl_3$ (^{1}H: 7.27, ^{13}C: 77.00). The following abbreviations are used for the proton spectra multiplicities: s: singlet, d: doublet, t: triplet, q: quartet, qu: quintuplet, hep: heptuplet, m: multiplet, br: broad. Coupling constants (J) are reported in hertz (Hz). The carbon bearing the diazo group (C=N_2) was not detected on the ^{13}C NMR spectra. Mass spectra were obtained using electrospray ionization and a Time of Flight analyzer (ESI-MS) for high resolution mass spectra (HRMS). The reactions were performed under an atmosphere of dry nitrogen in flame-dried glassware and were monitored by thin-layer chromatography (TLC) analysis using silica gel (60 F_{254}) plates. The compounds were visualized by UV irradiation and/or with a solution of *p*-anisaldehyde (5%) in ethanol/H_2SO_4/AcOH (90/5/1) or a solution of ninhydrin (2% in ethanol). Column chromatography was performed on silica gel 60 (230–400 mesh, 0.040–0.063 mm) at medium pressure (300 mbar). All solvents were freshly distilled when required. Elemental analyses were performed at the ICSN, CNRS, Gif-sur-Yvette, France.

4.2. 2-Bromo-5-methoxyaniline 6i[43]

To a solution of 4-bromo-3-nitroanisole (3.45 g, 14.87 mmol, 1 equiv) in ethanol (50 mL) were added iron powder (2.48 g, 44.48 mmol, 6.2 equiv) and concd HCl (8.15 mL, 8.28 mmol, 1.2 equiv). After 3 h of reflux, the mixture was cooled to room temperature and Na_2CO_3 was added by portions until gas evolution ceased. After filtration over Celite, the filtrate was extracted with Et_2O and the combined organic fractions were washed with H_2O and a saturated solution of NaCl. The organic layer was then dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual oil was purified by distillation under vacuum (bp 130–135 °C; 0.3 mbar) to give **6i** (2.63 mg, 88%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, J=8.7 Hz, 1H), 6.30 (d, J=2.8 Hz, 1H), 6.21 (dd, J=8.7, 2.8 Hz, 1H), 4.00 (s, 2H), 3.72 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.2, 145.0, 133.0, 105.7, 101.5, 100.7, 55.5; IR (neat, cm^{-1}) 3466, 3370, 3000, 2961, 1574, 1299, 1262, 1170, 1147, 1047, 778; HRMS (ES$^+$) m/z [M+H]$^+$ calcd for $C_7H_9{}^{79}BrNO$: 201.9868; found: 201.9866; calcd for $C_7H_9{}^{81}BrNO$: 203.9847; found: 203.9846.

4.3. 3-(*tert*-Butyldiphenylsilyloxy)aniline 6k

To a solution of 3-aminophenol (750 mg, 6.90 mmol, 1 equiv) in acetonitrile (12.5 mL) were added dropwise, under argon, distilled Et_3N (6.0 mL, 42.80 mmol, 6.2 equiv) and *tert*-butylchlorodiphenylsilane (2.2 mL, 8.30 mmol, 1.2 equiv). After 4 h of reflux, the mixture was cooled to room temperature and concentrated in vacuo. The residue was then dissolved in CH_2Cl_2 and the solution was washed with H_2O, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (heptane/EtOAc, 8/2) to give **6k** (1.40 g, 58%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73–7.70 (m, 4H), 7.41–7.35 (m, 6H), 6.87–6.81 (m, 1H), 6.21–6.14 (m, 3H), 3.43 (br s, 2H), 1.08 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.8, 147.6, 135.7 (4C), 133.4 (2C), 130.0 (2C), 129.9, 127.9 (4C), 110.5, 108.5, 106.7, 26.7 (3C), 19.7; IR (neat, cm^{-1}): 3377, 3069, 3044, 2955, 1617, 1461, 1389, 1111, 820; HRMS (ES$^+$) m/z [M+H]$^+$ calcd for $C_{22}H_{26}NOSi$: 348.1784; found: 348.1786.

4.4. General procedure (A) for the synthesis of 2,4-dimethoxybenzyl-protected compounds 7

*4.4.1. N-(2,4-Dimethoxybenzyl)aniline (**7a**).* A solution of aniline **6a** (0.752 mL, 8.25 mmol, 1 equiv) and 2,4-dimethoxybenzaldehyde (1.40 g, 8.42 mmol, 1.02 equiv) in toluene (10 mL) was stirred at 165 °C for 18 h in a 50 mL flask equipped with a Dean–Stark water trap. After cooling to room temperature, the solvent was removed under reduced pressure and the crude imine was re-dissolved in CH_2Cl_2/EtOH (10 mL, 1:1). Sodium borohydride (0.487 g, 12.87 mmol, 1.6 equiv) was slowly added to the solution cooled at 0 °C and the reaction mixture was allowed to stir for 12 h. The reaction mixture was then poured into ice. Concd HCl and 5 M NaOH were added successively until the pH of the mixture was, respectively, acidic and basic. The mixture was then transferred to a separatory funnel and the layers separated. The aqueous portion was extracted with CH_2Cl_2 (3×). The combined organic fractions were then dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (heptane/EtOAc, 7/3) to give **7a** (1.81 g, 90%) as a white solid; mp 99–100 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19 (d, J=8.2 Hz, 1H), 7.15–7.12 (m, 2H), 6.70–6.63 (m, 3H), 6.47 (d, J=2.3 Hz, 1H), 6.42 (dd, J=8.2, 2.3 Hz, 1H), 4.24 (br s, 2H), 4.03 (br s, 1H), 3.82 (s, 3H), 3.78 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.4, 158.6, 148.7, 129.9, 129.3 (2C), 120.0, 117.5, 113.3 (2C), 104.1, 98.9, 55.6 (2C), 43.4; IR (neat, cm^{-1}): 3370, 2939, 1601, 1504, 1433, 1319, 1254, 1206, 1130, 1034, 747; HRMS (ES$^+$) m/z [M+Na]$^+$ calcd for $C_{15}H_{17}NO_2Na$: 266.1157; found: 266.1144.

*4.4.2. N-(2,4-Dimethoxybenzyl)-4-methoxyaniline (**7b**)[36b].* Compound **7b** was prepared according to the general procedure (A) reported for **7a** starting from 4-methoxyaniline **6b** (1.02 g, 8.25 mmol, 1 equiv) and 2,4-dimethoxybenzaldehyde (1.40 g, 8.42 mmol, 1.02 equiv). Flash column chromatography on silica gel (heptane/EtOAc, 7/3) afforded **7b** (1.87 g, 83%) as a white solid; mp 72–73 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.17 (d, J=8.2 Hz, 1H), 6.75 (dd, J=8.9, 3.5 Hz, 2H), 6.61 (dd, J=8.9, 3.5 Hz, 2H), 6.45 (d, J=2.4 Hz, 1H), 6.40 (dd, J=8.2, 2.4 Hz, 1H), 4.18 (s, 2H), 3.89 (s, 1H), 3.81 (s, 3H), 3.73 (s, 3H), 3.71 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.4, 158.7, 152.4, 142.9, 130.0, 120.1, 115.0 (2C), 114.8 (2C), 104.1, 98.8, 56.0, 55.6 (2C), 44.5; IR (neat, cm^{-1}) 3371, 2955, 2835, 1614, 1586, 1505, 1462, 1235, 1210, 1130, 1029, 813; HRMS (ES$^+$) m/z [M+H]$^+$ calcd for $C_{16}H_{20}NO_3$: 274.1443; found: 274.1431.

*4.4.3. 4-Chloro-N-(2,4-dimethoxybenzyl)aniline (**7c**).* Compound **7c** was prepared according to the general procedure (A) reported for **7a** starting from 4-chloroaniline **6c** (1.05 g, 8.25 mmol, 1 equiv) and 2,4-dimethoxybenzaldehyde (1.40 g, 8.42 mmol, 1.02 equiv). Flash column chromatography on silica gel (heptane/EtOAc, 8/2) afforded **7c** (2.20 g, 96%) as a white solid; mp 52–53 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (d, J=8.2 Hz, 1H), 7.07 (dd, J=2.1, 8.8 Hz, 2H), 6.54 (dd, J=8.8, 2.1 Hz, 2H), 6.46 (d, J=2.4 Hz, 1H), 6.41 (dd, J=8.2, 2.4 Hz, 1H), 4.20 (s, 2H), 4.05 (br s, 1H), 3.81 (s, 3H), 3.78 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.5, 158.6, 147.1, 129.8, 129.1 (2C), 122.0, 119.4, 114.4 (2C), 104.1, 98.9, 55.6 (2C), 43.5; IR (neat, cm^{-1}): 3387, 2940, 1615, 1585, 1401, 1261, 1176, 1093, 1027, 844; HRMS (ES$^+$) m/z [M+H]$^+$ calcd for $C_{15}H_{17}{}^{35}ClNO_2$: 278.0948; found: 278.0964. Anal. Calcd for $C_{15}H_{16}ClNO_2$: C, 64.87; H, 5.81; N, 5.04. Found: C, 64.71; H, 5.89; N, 5.01.

*4.4.4. N-(2,4-Dimethoxybenzyl)-4-fluoroaniline (**7d**).* Compound **7d** was prepared according to the general procedure (A) reported for

7a starting from 4-fluoroaniline **6d** (0.92 g, 8.25 mmol, 1 equiv) and 2,4-dimethoxybenzaldehyde (1.40 g, 8.42 mmol, 1.02 equiv). Flash column chromatography on silica gel (heptane/EtOAc, 7/3) afforded **7d** (2.13 g, 99%) as a beige solid; mp 66–67 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.16 (d, J=8.2 Hz, 1H), 6.89–6.81 (m, 2H), 6.60–6.53 (m, 2H), 6.46 (d, J=2.3 Hz, 1H), 6.42 (dd, J=8.3, 2.3 Hz, 1H), 4.19 (s, 2H), 3.81 (s, 3H), 3.78 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.5, 158.7, 156.1 (d, J=235.0 Hz), 144.9, 130.0, 119.7, 115.7 (d, J=22.0 Hz, 2C), 114.2 (d, J=7.7 Hz, 2C), 104.1, 98.9, 55.6 (2C), 44.2; ^{19}F NMR (282 MHz, $CDCl_3$) δ −128.34; IR (neat, cm^{-1}) 3366, 2960, 1607, 1589, 1510, 1466, 1207, 1130, 1036, 828; HRMS (ES$^+$) m/z $[M+H]^+$ calcd for $C_{15}H_{17}FNO_2$: 262.1243; found: 262.1240.

*4.4.5. N-(2,4-Dimethoxybenzyl)-4-(trifluoromethyl)aniline (**7e**).* Compound **7e** was prepared according to the general procedure (A) reported for **7a** starting from 4-(trifluoromethyl)aniline **6e** (1.33 g, 8.25 mmol, 1 equiv) and 2,4-dimethoxybenzaldehyde (1.40 g, 8.42 mmol, 1.02 equiv). Flash column chromatography on silica gel (heptane/EtOAc, 6/4) afforded **7e** (2.49 g, 97%) as a white solid; mp 79–80 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (d, J=8.7 Hz, 2H), 7.15 (d, J=8.1 Hz, 1H), 6.62 (d, J=8.7 Hz, 2H), 6.48 (d, J=2.3 Hz, 1H), 6.43 (dd, J=8.1, 2.3 Hz, 1H), 4.37 (br s, 1H), 4.27 (br s, 2H), 3.83 (s, 3H), 3.79 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.7, 158.6, 150.9, 129.8, 126.7 (q, J=3.3 Hz, 2C), 125.3 (q, J=268.1 Hz), 119.0, 118.9 (q, J=33.5 Hz), 112.3 (2C), 104.1, 98.9, 55.6 (2C), 43.0; ^{19}F NMR (282 MHz, $CDCl_3$) δ −61.50; IR (neat, cm^{-1}) 3387, 2923, 1613, 1509, 1463, 1325, 1258, 1151, 1094, 822; HRMS (ES$^-$) m/z $[M-H]^-$ calcd for $C_{16}H_{15}F_3NO_2$: 310.1055; found: 310.1042. Anal. Calcd for $C_{16}H_{16}F_3NO_2$: C, 61.73; H, 5.18; N, 4.50. Found: C, 61.83; H, 5.47; N, 4.38.

*4.4.6. N-(2,4-Dimethoxybenzyl)-3,5-dimethoxyaniline (**7f**).* Compound **7f** was prepared according to the general procedure (A) reported for **7a** starting from 3,5-dimethoxyaniline **6f** (1.26 g, 8.25 mmol, 1 equiv) and 2,4-dimethoxybenzaldehyde (1.40 g, 8.42 mmol, 1.02 equiv). Flash column chromatography on silica gel (heptane/EtOAc, 6/4) afforded **7f** (2.33 g, 93%) as a pale-yellow solid; mp 71–72 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.17 (d, J=8.3 Hz, 1H), 6.44 (d, J=2.3 Hz, 1H), 6.40 (dd, J=8.3, 2.3 Hz, 1H), 5.86–5.83 (m, 3H), 4.20 (s, 2H), 4.03 (br s, 1H), 3.81 (s, 3H), 3.78 (s, 3H), 3.72 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.9 (2C), 160.4, 158.6, 150.6, 130.0, 119.9, 104.2, 98.8, 92.1 (2C), 89.9, 55.6 (2C), 55.3 (2C), 43.3; IR (neat, cm^{-1}) 3414, 2948, 1611, 1588, 1505, 1462, 1286, 1201, 1172, 1146, 1130, 1042, 808; HRMS (ES$^+$) m/z $[M+H]^+$ calcd for $C_{17}H_{22}NO_4$: 304.1549; found: 304.1524.

*4.4.7. 2-Bromo-N-(2,4-dimethoxybenzyl)aniline (**7g**).* Compound **7g** was prepared according to the general procedure (A) reported for **7a** starting from 2-bromoaniline **6g** (1.42 g, 8.25 mmol, 1 equiv) and 2,4-dimethoxybenzaldehyde (1.40 g, 8.42 mmol, 1.02 equiv). Flash column chromatography on silica gel (heptane/EtOAc, 6/4) afforded **7g** (2.36 g, 89%) as a pale-yellow solid; mp 47–48 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (dd, J=7.8, 1.3 Hz, 1H), 7.15 (d, J=8.3 Hz, 1H), 7.14–7.09 (m, 1H), 6.66 (dd, J=8.2, 1.1 Hz, 1H), 6.53 (dt, J=7.8, 1.1 Hz, 1H), 6.46 (d, J=2.3 Hz, 1H), 6.42 (dd, J=8.3, 2.3 Hz, 1H), 4.78 (br s, 1H), 4.30 (s, 2H), 3.83 (s, 3H), 3.78 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.5, 158.6, 145.3, 132.5, 129.6, 128.6, 119.2, 117.9, 112.1, 110.1, 104.1, 98.9, 55.6 (2C), 43.3; IR (neat, cm^{-1}) 3412, 2932, 1583, 1503, 1415, 1320, 1237, 1206, 1132, 1072, 928; HRMS (ES$^+$) m/z $[M+Na]^+$ calcd for $C_{15}H_{16}{}^{79}BrNO_2Na$: 344.0262; found: 343.9991; calcd for $C_{15}H_{16}{}^{81}BrNO_2Na$: 346.0242; found: 345.9873.

*4.4.8. 2-Bromo-N-(2,4-dimethoxybenzyl)-4-fluoroaniline (**7h**).* Compound **7h** was prepared according to the general procedure (A) reported for **7a** starting from 2-bromo-4-fluoroaniline **6h** (1.57 g, 8.25 mmol, 1 equiv) and 2,4-dimethoxybenzaldehyde (1.40 g, 8.42 mmol, 1.02 equiv). Flash column chromatography on silica gel (heptane/EtOAc, 7/3) afforded **7h** (1.01 g, 36%) as a white solid; mp 44–45 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21 (dd, J=7.9, 2.7 Hz, 1H), 7.17 (d, J=8.2 Hz, 1H), 6.90 (dt, J=8.2, 2.7 Hz, 1H), 6.61 (dd, J=8.8, 4.9 Hz, 1H), 6.51 (d, J=1.8 Hz, 1H), 6.45 (dd, J=8.2, 1.8 Hz, 1H), 4.65 (br s, 1H), 4.30 (s, 2H), 3.85 (s, 3H), 3.80 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.5, 158.5, 154.5 (d, J=238.2 Hz), 142.1, 129.5, 119.4 (d, J=25.2 Hz), 118.9, 115.0 (d, J=21.4 Hz), 112.0 (d, J=7.7 Hz), 109.1 (d, J=9.9 Hz), 104.0, 98.8, 55.4 (2C), 43.7; ^{19}F NMR (282 MHz, $CDCl_3$) δ −127.18; IR (neat, cm^{-1}) 3405, 2936, 1613, 1587, 1503, 1264, 1206, 1155, 1033, 795; HRMS (ES$^+$) m/z $[M+H]^+$ calcd for $C_{15}H_{16}{}^{79}BrFNO_2$: 340.0348; found: 340.0322.

*4.4.9. 2-Bromo-N-(2,4-dimethoxybenzyl)-5-methoxyaniline (**7i**).* Compound **7i** was prepared according to the general procedure (A) reported for **7a** starting from 2-bromo-5-methoxyaniline **6i** (1.67 g, 8.25 mmol, 1 equiv) and 2,4-dimethoxybenzaldehyde (1.40 g, 8.42 mmol, 1.02 equiv). Flash column chromatography on silica gel (heptane/EtOAc, 7/3) afforded **7i** (2.76 g, 95%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (dd, J=8.7 Hz, 1H), 7.17 (d, J=8.2 Hz, 1H), 6.48 (dd, J=8.2, 2.3 Hz, 1H), 6.44 (d, J=8.2 Hz, 1H), 6.27 (d, J=2.9 Hz, 1H), 6.14 (dd, J=8.7, 2.9 Hz, 1H), 4.78 (br s, 1H), 4.30 (s, 2H), 3.84 (s, 3H), 3.78 (s, 3H), 3.72 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.4, 160.3, 158.5, 146.1, 132.5, 129.6, 119.0, 104.1, 102.7, 101.2, 98.7, 98.6, 55.4 (3C), 43.0; IR (neat, cm^{-1}) 3405, 2933, 2832, 1587, 1504, 1454, 1285, 1205, 1155, 1034, 822; HRMS (ES$^+$) m/z $[M+Na]^+$ calcd for $C_{16}H_{18}{}^{79}BrNO_3Na$: 374.0368; found: 374.0384.

*4.4.10. N-(2,4-Dimethoxybenzyl)-3-methoxyaniline (**7j**).* Compound **7j** was prepared according to the general procedure (A) reported for **7a** starting from 3-methoxyaniline **6j** (1.02 g, 8.25 mmol, 1 equiv) and 2,4-dimethoxybenzaldehyde (1.40 g, 8.42 mmol, 1.02 equiv). Flash column chromatography on silica gel (heptane/EtOAc, 7/3) afforded **7j** (1.58 g, 70%) as a white solid; mp 73–74 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (d, J=8.2 Hz, 1H), 7.06 (t, J=8.0 Hz, 1H), 6.45 (d, J=2.3 Hz, 2H), 6.43 (dd, J=8.2, 2.3 Hz, 1H), 6.28–6.24 (m, 2H), 6.21 (t, J=2.2 Hz, 1H), 4.23 (s, 2H), 3.82 (s, 3H), 3.79 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.8, 160.2, 158.4, 149.9, 129.9, 129.7, 119.7, 106.3, 103.9, 102.4, 99.1, 98.6, 55.4 (2C), 55.1, 43.1; IR (neat, cm^{-1}) 3380, 2962, 1603, 1576, 1505, 1462, 1207, 1129, 1035, 827; HRMS (ES$^+$) m/z $[M+H]^+$ calcd for $C_{16}H_{20}NO_3$: 274.1443; found: 274.1438. Anal. Calcd for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.12. Found: C, 70.21; H, 7.09; N, 4.93.

*4.4.11. 3-(tert-Butyldiphenylsilyloxy)-N-(2,4-dimethoxybenzyl)aniline (**7k**).* Compound **7k** was prepared according to the general procedure (A) reported for **7a** starting from 3-(*tert*-butyldiphenylsilyloxy)aniline **6k** (2.87 g, 8.25 mmol, 1 equiv) and 2,4-dimethoxybenzaldehyde (1.40 g, 8.42 mmol, 1.02 equiv). Flash column chromatography on silica gel (heptane/EtOAc, 7/3) afforded **7k** (3.74 g, 91%) as a white solid; mp 100–101 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72–7.70 (m, 4H), 7.40–7.32 (m, 6H), 7.02 (d, J=8.2 Hz, 1H), 6.84 (t, J=7.9 Hz, 1H), 6.42 (d, J=2.1 Hz, 1H), 6.35 (dd, J=8.2, 2.1 Hz, 1H), 6.17 (dd, J=7.9, 1.5 Hz, 1H), 6.13 (dd, J=1.5, 1.2 Hz, 1H), 6.10 (dd, J=7.9, 1.2 Hz, 1H), 4.03 (s, 2H), 3.87 (br s, 1H), 3.78 (s, 3H), 3.77 (br s, 3H), 1.08 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.3, 158.6, 156.8, 149.8, 135.7 (4C), 133.6 (2C), 130.0, 129.9 (2C), 129.7, 127.8 (4C), 119.9, 109.2, 106.8, 104.8, 104.0, 98.7, 55.6, 55.5, 43.3, 26.8 (3C), 19.7; IR (neat, cm^{-1}) 3385, 2854, 1608, 1588, 1506, 1463, 1262, 1187, 1132, 696; HRMS (ES$^+$) m/z $[M+Na]^+$ calcd for $C_{31}H_{35}NO_3SiNa$: 520.2284; found: 520.2233.

*4.4.12. N-(2,4-Dimethoxybenzyl)-3-fluoroaniline (**7l**).* Compound **7l** was prepared according to the general procedure (A) reported for **7a** starting from 3-fluoroaniline **6l** (0.92 g, 8.25 mmol, 1 equiv) and 2,4-dimethoxybenzaldehyde (1.40 g, 8.42 mmol, 1.02 equiv). Flash column chromatography on silica gel (heptane/EtOAc, 7/3) afforded

7l (2.07 g, 96%) as a beige solid; mp 77–78 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.16 (d, J=8.2 Hz, 1H), 7.04 (br q, J=7.5 Hz, 1H), 6.47 (d, J=2.4 Hz, 1H), 6.43 (d, J=8.2, 2.4 Hz, 1H), 6.41–6.32 (m, 3H), 4.21 (s, 2H), 3.81 (s, 3H), 3.78 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.3 (d, J=242.6 Hz), 160.6, 158.6, 150.3 (d, J=10.4 Hz), 130.3 (d, J=10.4 Hz), 129.9, 119.3, 109.2, 104.1, 103.8 (d, J=31.8 Hz), 99.9 (d, J=25.3 Hz), 98.9, 55.6 (2C), 43.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ −113.00; IR (neat, cm^{-1}) 3377, 2935, 1614, 1583, 1505, 1434, 1336, 1252, 1205, 1142, 1041, 819; HRMS (ES^+) m/z $[M+H]^+$ calcd for $C_{15}H_{17}FNO_2$: 262.1243; found: 262.1237.

*4.4.13. N-(2,4-Dimethoxybenzyl)-3-(trifluoromethyl)aniline (**7m**).* Compound **7m** was prepared according to the general procedure (A) reported for **7a** starting from 3-trifluoromethylaniline **6m** (1.33 g, 8.25 mmol, 1 equiv) and 2,4-dimethoxybenzaldehyde (1.40 g, 8.42 mmol, 1.02 equiv). Flash column chromatography on silica gel (heptane/EtOAc, 7/3) afforded **7m** (2.20 g, 86%) as a white solid; mp 88–89 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (br d, J=7.9 Hz, 1H), 7.21 (d, J=8.4 Hz, 1H), 6.92–6.86 (m, 2H), 6.78–6.74 (m, 1H), 6.51 (d, J=2.1 Hz, 1H), 6.47 (dd, J=8.4, 2.1 Hz, 1H), 4.38 (br s, 1H), 4.29 (s, 2H), 3.86 (s, 3H), 3.83 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.6, 158.7, 148.7, 131.4 (q, J=31.3 Hz), 130.1, 129.7, 124.4 (q, J=271.7 Hz), 119.1, 116.1, 113.9 (q, J=2.2 Hz), 109.4 (q, J=4.4 Hz), 104.2, 98.9, 55.6 (2C), 43.2; ^{19}F NMR (282 MHz, $CDCl_3$) δ −62.86; IR (neat, cm^{-1}) 3405, 2930, 1609, 1504, 1436, 1276, 1153, 1108, 1033, 788; HRMS (ES^-) m/z $[M-H]^-$ calcd for $C_{16}H_{15}F_3NO_2$: 310.1055; found: 310.1045. Anal. Calcd for $C_{16}H_{16}F_3NO_2$: C, 61.73; H, 5.18; N, 4.50. Found: C, 61.24; H, 5.24; N, 4.39.

4.5. General procedure (B) for the synthesis of the diazomalonamic acid ethyl esters 9

*4.5.1. Ethyl 2-diazo-3-(N-(2,4-dimethoxybenzyl)-N-(phenyl)amino)-3-oxopropanoate (**9a**).* A solution of *N*-(2,4-dimethoxybenzyl)aniline **7a** (550 mg, 2.26 mmol, 1 equiv) in CH_2Cl_2 (6.30 mL) was cooled to 0 °C under argon. Distilled Et_3N (1.49 mL, 10.60 mmol, 4.7 equiv) and ethyl 2-diazomalonyl chloride **8** (400 mg, 2.26 mmol, 1 equiv) were successively added dropwise. After 6 h of stirring at room temperature, a solution of HCl 1 M (2.60 mL) was added and the mixture was extracted with CH_2Cl_2 (3×). The combined CH_2Cl_2 phases were then dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (heptane/EtOAc, 7/3) to give **9a** (806 mg, 93%) as a yellow solid; mp 57–58 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J=8.3 Hz, 1H), 7.21–7.18 (m, 1H), 7.11 (br d, J=7.7 Hz, 1H), 7.04 (br d, J=7.7 Hz, 2H), 6.36 (dd, J=8.3, 2.4 Hz, 2H), 6.28 (d, J=2.4 Hz, 1H), 4.88 (s, 2H), 3.95 (q, J=7.1 Hz, 2H), 3.70 (s, 3H), 3.53 (s, 3H), 1.06 (t, J=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3, 161.1, 160.5, 158.5, 143.3, 130.7, 129.1 (2C), 126.9, 126.6 (2C), 117.8, 104.3, 98.5, 61.6, 55.5, 55.3, 49.1, 14.4; IR (neat, cm^{-1}) 3060, 2928, 2124, 1765, 1702, 1642, 1493, 1205, 1102, 697; HRMS (ES^+) m/z $[M+Na]^+$ calcd for $C_{20}H_{21}N_3O_5Na$: 406.1379; found: 406.1382. Anal. Calcd for $C_{20}H_{21}N_3O_5 \cdot 0.4AcOEt$: C, 61.97; H, 5.83; N, 10.04. Found: C, 61.98; H, 5.65; N, 9.89.

*4.5.2. Ethyl 2-diazo-3-(N-(2,4-dimethoxybenzyl)-N-(4-methoxyphenyl)-amino)-3-oxopropanoate (**9b**)[36b].* Compound **9b** was prepared according to the general procedure (B) reported for **9a** starting from *N*-(2,4-dimethoxybenzyl)-4-methoxyaniline **7b** (618 mg, 2.26 mmol, 1 equiv), distilled Et_3N (1.49 mL, 10.60 mmol, 4.7 equiv), and ethyl 2-diazomalonyl chloride **8** (400 mg, 2.26 mmol, 1 equiv). Flash column chromatography on silica gel (heptane/EtOAc, 1/1) afforded **9b** (728 mg, 78%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (d, J=8.5 Hz, 1H), 6.98 (dd, J=8.8, 3.6 Hz, 2H), 6.76 (dd, J=8.8, 3.6 Hz, 2H), 6.41 (dd, J=8.5, 2.4 Hz, 1H), 6.33 (d, J=2.4 Hz, 1H), 4.87 (s, 2H), 4.06 (q, J=7.2 Hz, 2H), 3.76 (s, 6H), 3.59 (s, 3H), 1.15 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0, 160.5, 159.5, 158.6, 158.5, 135.5, 131.0, 128.4 (2C), 117.8, 114.3 (2C), 104.3, 98.5, 61.5, 55.6 (2C), 55.4, 48.9, 14.5; IR (neat, cm^{-1}) 3083, 2934, 2113, 1720, 1613, 1505, 1287, 1246, 1207, 1101, 834; HRMS (ES^+) m/z $[M+Na]^+$ calcd for $C_{21}H_{23}N_3O_6Na$: 436.1485; found: 436.1495.

*4.5.3. Ethyl 3-(N-(4-chlorophenyl)-N-(2,4-dimethoxybenzyl)amino)-2-diazo-3-oxopropanoate (**9c**).* Compound **9c** was prepared according to the general procedure (B) reported for **9a** starting from 4-chloro-*N*-(2,4-dimethoxybenzyl)aniline **7c** (628 mg, 2.26 mmol, 1 equiv), distilled Et_3N (1.49 mL, 10.60 mmol, 4.7 equiv), and ethyl 2-diazomalonyl chloride **8** (400 mg, 2.26 mmol, 1 equiv). Flash column chromatography on silica gel (heptane/EtOAc, 7/1) afforded **9c** (934 mg, 99%) as a yellow solid; mp 97–98 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19 (d, J=8.3 Hz, 1H), 7.14 (dd, J=8.7, 2.0 Hz, 2H), 6.96 (dd, J=8.7, 2.0 Hz, 2H), 6.33 (dd, J=8.3, 2.3 Hz, 1H), 6.26 (d, J=2.3 Hz, 1H), 4.83 (s, 2H), 3.95 (q, J=7.1 Hz, 2H), 3.67 (s, 3H), 3.51 (s, 3H), 1.05 (t, J=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.6, 161.1, 160.5, 158.3, 141.5, 132.2, 130.7, 128.9 (2C), 127.9 (2C), 117.2, 104.3, 98.3, 61.4, 55.3, 55.1, 48.9, 14.3; IR (neat, cm^{-1}) 2936, 2120, 1713, 1614, 1491, 1367, 1285, 1207, 1098, 833; HRMS (ES^+) m/z $[M+Na]^+$ calcd for $C_{20}H_{20}{}^{35}ClN_3O_5Na$: 440.0989; found: 440.0997.

*4.5.4. Ethyl 2-diazo-3-(N-(2,4-dimethoxybenzyl)-N-(4-fluorophenyl)-amino)-3-oxopropanoate (**9d**).* Compound **9d** was prepared according to the general procedure (B) reported for **9a** starting from *N*-(2,4-dimethoxybenzyl)-4-fluoroaniline **7d** (590 mg, 2.26 mmol, 1 equiv), distilled Et_3N (1.49 mL, 10.60 mmol, 4.7 equiv), and ethyl 2-diazomalonyl chloride **8** (400 mg, 2.26 mmol, 1 equiv). Flash column chromatography on silica gel (heptane/EtOAc, 7/3) afforded **9d** (580 mg, 64%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J=8.4 Hz, 1H), 7.06–7.00 (m, 2H), 6.96–6.88 (m, 2H), 6.40 (dd, J=8.4, 2.3 Hz, 1H), 6.31 (d, J=2.3 Hz, 1H), 4.88 (s, 2H), 4.03 (q, J=7.2 Hz, 2H), 3.75 (s, 3H), 3.58 (s, 3H), 1.13 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.9, 161.4 (d, J=247.0 Hz), 161.3, 160.7, 158.6, 138.9, 131.1, 128.8 (d, J=8.2 Hz, 2C), 117.5, 115.7 (d, J=23.0 Hz, 2C), 104.4, 98.5, 61.5, 55.5, 55.3, 49.1, 14.4; ^{19}F NMR (282 MHz, $CDCl_3$) δ −114.76; IR (neat, cm^{-1}) 3071, 2937, 2122, 1713, 1624, 1505, 1385, 1261, 1207, 1105, 1027, 833; HRMS (ES^+) m/z $[M+Na]^+$ calcd for $C_{20}H_{20}FN_3O_5Na$: 424.1285; found: 424.1291.

*4.5.5. Ethyl 2-diazo-3-(N-(2,4-dimethoxybenzyl)-N-(4-trifluoromethylphenyl)amino)-3-oxopropanoate (**9e**).* Compound **9e** was prepared according to the general procedure (B) reported for **9a** starting from *N*-(2,4-dimethoxybenzyl)-4-(trifluoromethyl)aniline **7e** (703 mg, 2.26 mmol, 1 equiv), distilled Et_3N (1.49 mL, 10.60 mmol, 4.7 equiv), and ethyl 2-diazomalonyl chloride **8** (400 mg, 2.26 mmol, 1 equiv). Flash column chromatography on silica gel (heptane/EtOAc, 7/3) afforded **9e** (683 mg, 67%) as a yellow solid; mp 108–109 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (br d, J=8.5 Hz, 2H), 7.25 (d, J=8.4 Hz, 1H), 7.18 (br d, J=8.5 Hz, 2H), 6.36 (dd, J=8.4, 2.3 Hz, 1H), 6.27 (d, J=2.3 Hz, 1H), 4.89 (s, 2H), 3.91 (q, J=7.2 Hz, 2H), 3.69 (s, 3H), 3.51 (s, 3H), 1.01 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.7, 161.4, 160.6, 158.3, 146.7, 130.6, 128.4 (q, J=32.4 Hz), 126.5 (2C), 125.9 (q, J=3.3 Hz, 2C), 123.8 (q, J=272.8 Hz), 117.1, 104.4, 98.4, 61.6, 55.5, 55.1, 49.2, 14.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ −62.50; IR (neat, cm^{-1}) 2960, 2126, 1702, 1642, 1610, 1503, 1325, 1205, 1157, 1100, 855; HRMS (ES^+) m/z $[M+Na]^+$ calcd for $C_{21}H_{20}F_3N_3O_5Na$: 474.1253; found: 474.1244.

*4.5.6. Ethyl 2-diazo-3-(N-(2,4-dimethoxybenzyl)-N-(3,5-dimethoxyphenyl)amino)-3-oxopropanoate (**9f**).* Compound **9f** was prepared according to the general procedure (B) reported for **9a** starting from *N*-(2,4-dimethoxybenzyl)-3,5-dimethoxyaniline **7f** (686 mg, 2.26 mmol, 1 equiv), distilled Et_3N (1.49 mL, 10.60 mmol, 4.7 equiv), and ethyl 2-diazomalonyl chloride **8** (400 mg, 2.26 mmol, 1 equiv). Flash column chromatography on silica gel (heptane/EtOAc, 7/3)

afforded **9f** (832 mg, 83%) as a yellow solid; mp 52–53 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18 (d, J=8.3 Hz, 1H), 6.34 (dd, J=8.3, 2.4 Hz, 1H), 6.29 (d, J=2.4 Hz, 1H), 6.21–6.19 (m, 3H), 4.83 (s, 2H), 4.01 (q, J=7.2 Hz, 2H), 3.67 (s, 3H), 3.61 (s, 6H), 3.58 (s, 3H), 1.09 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3, 160.9 (2C), 160.8, 160.3, 158.3, 144.6, 130.4, 117.8, 104.8 (2C), 104.2, 98.8, 98.3, 61.4, 55.4 (2C), 55.3, 55.2, 48.9, 14.3; IR (neat, cm^{-1}) 2935, 2108, 1726, 1707, 1588, 1286, 1202, 1156, 1100, 1032, 830; HRMS (ES$^+$) m/z [M+Na]$^+$ calcd for $C_{22}H_{25}N_3O_7Na$: 466.1590; found: 466.1591.

*4.5.7. Ethyl 3-(N-(2-bromophenyl)-N-(2,4-dimethoxybenzyl)amino)-2-diazo-3-oxopropanoate (**9g**).* Compound **9g** was prepared according to the general procedure (B) reported for **9a** starting from 2-bromo-*N*-(2,4-dimethoxybenzyl)aniline **7g** (728 mg, 2.26 mmol, 1 equiv), distilled Et_3N (1.49 mL, 10.60 mmol, 4.7 equiv), and ethyl 2-diazomalonyl chloride **8** (400 mg, 2.26 mmol, 1 equiv). Flash column chromatography on silica gel (heptane/EtOAc, 7/3) afforded **9g** (293 mg, 28%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (dd, J=7.7, 1.8 Hz, 1H), 7.33 (d, J=8.4 Hz, 1H), 7.11 (dt, J=7.6, 1.8 Hz, 1H), 7.07 (dt, J=7.7, 2.0 Hz, 1H), 6.92 (dd, J=7.6, 2.0 Hz, 1H), 6.38 (dd, J=8.4, 2.4 Hz, 1H), 6.25 (d, J=2.4 Hz, 1H), 5.22 (d, J=14.3 Hz, 1H), 4.53 (d, J=14.3 Hz, 1H), 4.05 (q, J=7.2 Hz, 2H), 3.74 (s, 3H), 3.44 (s, 3H), 1.13 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3, 161.1, 160.8, 158.9, 140.4, 133.3, 132.4, 131.6, 129.1, 127.6, 124.0, 117.0, 104.2, 98.2, 61.4, 55.5, 55.1, 47.5, 14.5; IR (neat, cm^{-1}) 2936, 2116, 1713, 1612, 1505, 1473, 1385, 1286, 1207, 1099, 750; HRMS (ES$^+$) m/z [M+Na]$^+$ calcd for $C_{20}H_{20}{}^{79}BrN_3O_5Na$: 484.0484; found: 484.0480; calcd for $C_{20}H_{20}{}^{81}BrN_3O_5Na$: 486.0464; found: 484.0467.

*4.5.8. Ethyl 3-(N-(2-bromo-4-fluorophenyl)-N-(2,4-dimethoxybenzyl)-amino)-2-diazo-3-oxopropanoate (**9h**).* Compound **9h** was prepared according to the general procedure (B) reported for **9a** starting from 2-bromo-*N*-(2,4-dimethoxybenzyl)-4-fluoroaniline **7h** (769 mg, 2.26 mmol, 1 equiv), distilled Et_3N (1.49 mL, 10.60 mmol, 4.7 equiv), and ethyl 2-diazomalonyl chloride **8** (400 mg, 2.26 mmol, 1 equiv). Flash column chromatography on silica gel (heptane/EtOAc, 7/3) afforded **9h** (326 mg, 30%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28–7.26 (m, 2H), 6.89–6.82 (m, 2H), 6.38 (dd, J=8.0, 2.3 Hz, 1H), 6.27 (d, J=2.3 Hz, 1H), 5.18 (d, J=14.2 Hz, 1H), 4.48 (d, J=14.2 Hz, 1H), 4.05 (q, J=7.2 Hz, 2H), 3.75 (s, 3H), 3.50 (s, 3H), 1.14 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.0, 161.5, 161.3 (d, J=252.5 Hz), 161.0, 159.0, 136.7, 132.9 (d, J=8.8 Hz), 132.6, 124.5 (d, J=11.0 Hz), 120.2 (d, J=25.2 Hz), 116.7, 114.6 (d, J=22.5 Hz), 104.3, 98.2, 61.5, 55.5, 55.2, 47.7, 14.5; ^{19}F NMR (282 MHz, $CDCl_3$) δ −62.86; IR (neat, cm^{-1}) 2937, 2836, 2120, 1713, 1612, 1506, 1486, 1379, 1286, 1207, 1099, 1033; HRMS (ES$^+$) m/z [M+Na]$^+$ calcd for $C_{20}H_{19}{}^{79}BrFN_3O_5Na$: 502.0390; found: 502.0390; calcd for $C_{20}H_{19}{}^{81}BrFN_3O_5Na$: 504.0369; found: 504.0368.

*4.5.9. Ethyl 3-(N-(2-bromo-5-methoxyphenyl)-N-(2,4-dimethoxybenzyl)amino)-2-diazo-3-oxopropanoate (**9i**).* Compound **9i** was prepared according to the general procedure (B) reported for **9a** starting from 2-bromo-*N*-(2,4-dimethoxybenzyl)-5-methoxyaniline **7i** (796 mg, 2.26 mmol, 1 equiv), distilled Et_3N (1.49 mL, 10.60 mmol, 4.7 equiv), and ethyl 2-diazomalonyl chloride **8** (400 mg, 2.26 mmol, 1 equiv). Flash column chromatography on silica gel (heptane/EtOAc, 7/3) afforded **9i** (245 mg, 22%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 (d, J=8.9 Hz, 1H), 7.30 (d, J=8.4 Hz, 1H), 6.66 (dd, J=8.9, 2.9 Hz, 1H), 6.45 (d, J=2.9 Hz, 1H), 6.39 (dd, J=8.4, 2.3 Hz, 1H), 6.32 (d, J=2.3 Hz, 1H), 5.20 (d, J=14.2 Hz, 1H), 4.44 (d, J=14.2 Hz, 1H), 4.07 (q, J=7.1 Hz, 2H), 3.71 (s, 3H), 3.55 (s, 3H), 3.47 (s, 3H), 1.12 (t, J=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.4, 161.0, 160.9, 159.0 (2C), 141.0, 133.4, 132.5, 117.1, 116.9, 115.7, 114.4, 104.2, 98.3, 61.5, 55.8, 55.6, 55.3, 47.6, 14.5; IR (neat, cm^{-1}) 2936, 2115, 1764, 1677, 1587, 1506, 1463, 1286, 1207, 1157, 1028; HRMS (ES$^+$) m/z [M+Na]$^+$ calcd for $C_{21}H_{22}{}^{79}BrN_3O_6Na$: 514.0590; found: 514.0563; calcd for $C_{21}H_{22}{}^{81}BrN_3O_6Na$: 516.0569; found: 516.0547.

*4.5.10. Ethyl 2-diazo-3-(N-(2,4-dimethoxybenzyl)-N-(3-methoxyphenyl)amino)-3-oxopropanoate (**9j**).* Compound **9j** was prepared according to the general procedure (B) reported for **9a** starting from *N*-(2,4-dimethoxybenzyl)-3-methoxyaniline **7j** (618 mg, 2.26 mmol, 1 equiv), distilled Et_3N (1.49 mL, 10.60 mmol, 4.7 equiv), and ethyl 2-diazomalonyl chloride **8** (400 mg, 2.26 mmol, 1 equiv). Flash column chromatography on silica gel (heptane/EtOAc, 7/3) afforded **9j** (730 mg, 78%) as a yellow solid; mp 97–98 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, J=8.2 Hz, 1H), 7.15 (t, J=8.2 Hz, 1H), 6.72–6.69 (m, 2H), 6.64 (t, J=2.4 Hz, 1H), 6.41 (dd, J=8.2, 2.1 Hz, 1H), 6.34 (d, J=2.1 Hz, 1H), 4.91 (s, 2H), 4.04 (q, J=7.0 Hz, 2H), 3.75 (s, 6H), 3.62 (s, 3H), 1.14 (t, J=7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.4, 161.1, 160.5, 160.2, 158.5, 144.3, 130.6, 129.8, 118.9, 117.9, 112.5, 112.4, 104.3, 98.5, 61.5, 53.6 (2C), 53.4, 49.1, 14.4; IR (neat, cm^{-1}) 3059, 2973, 2130, 1688, 1601, 1584, 1488, 1372, 1276, 1193, 1027, 744; HRMS (ES$^+$) m/z [M+Na]$^+$ calcd for $C_{21}H_{23}N_3O_6Na$: 436.1485; found: 436.1489.

*4.5.11. Ethyl 3-(N-(3-(tert-butyldiphenylsilyloxy)phenyl)-N-(2,4-dimethoxybenzyl)amino)-2-diazo-3-oxopropanoate (**9k**).* Compound **9k** was prepared according to the general procedure (B) reported for **9a** starting from 3-(*tert*-butyldiphenylsilyloxy)-*N*-(2,4-dimethoxybenzyl)aniline **7k** (1.125 g, 2.26 mmol, 1 equiv), distilled Et_3N (1.49 mL, 10.60 mmol, 4.7 equiv), and ethyl 2-diazomalonyl chloride **8** (400 mg, 2.26 mmol, 1 equiv). Flash column chromatography on silica gel (heptane/EtOAc, 6/4) afforded **9k** (1.268 g, 88%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57–7.53 (m, 4H), 7.34–7.21 (m, 6H), 7.02 (d, J=8.8 Hz, 1H), 6.91–6.84 (m, 1H), 6.56–6.53 (m, 1H), 6.50–6.47 (m, 2H), 6.25–6.20 (m, 2H), 4.68 (s, 2H), 3.95 (q, J=7.2 Hz, 2H), 3.65 (s, 3H), 3.48 (s, 3H), 1.06 (t, J=7.2 Hz, 3H), 0.97 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3, 160.6, 160.3, 158.3, 156.1, 143.8, 135.5 (4C), 132.6 (2C), 130.3, 130.1 (2C), 129.4, 128.0 (4C), 119.3, 118.4, 117.8, 117.3, 104.1, 98.4, 61.4, 55.4, 55.2, 49.0, 26.6 (3C), 19.5, 14.4; IR (neat, cm^{-1}) 2937, 2852, 2118, 1723, 1587, 1484, 1372, 1285, 1207, 1105, 700; HRMS (ES$^+$) m/z [M+Na]$^+$ calcd for $C_{36}H_{39}N_3O_6SiNa$: 660.2506; found: 660.2505.

*4.5.12. Ethyl 2-diazo-3-(N-(2,4-dimethoxybenzyl)-N-(3-fluorophenyl)-amino)-3-oxopropanoate (**9l**).* Compound **9l** was prepared according to the general procedure (B) reported for **9a** starting from *N*-(2,4-dimethoxybenzyl)-3-fluoroaniline **7l** (591 mg, 2.26 mmol, 1 equiv), distilled Et_3N (1.49 mL, 10.60 mmol, 4.7 equiv), and ethyl 2-diazomalonyl chloride **8** (400 mg, 2.26 mmol, 1 equiv). Flash column chromatography on silica gel (heptane/EtOAc, 7/3) afforded **9l** (816 mg, 90%) as a yellow solid; mp 82–83 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, J=8.3 Hz, 1H), 7.22–7.16 (m, 1H), 6.91–6.84 (m, 3H), 6.41 (dd, J=8.3, 2.4 Hz, 1H), 6.34 (d, J=2.4 Hz, 1H), 4.92 (s, 2H), 4.01 (q, J=7.2 Hz, 2H), 3.76 (s, 3H), 3.62 (s, 3H), 1.12 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.8 (d, J=247.0 Hz), 161.8, 161.4, 160.6, 158.4, 144.9 (d, J=10.4 Hz), 130.7, 130.0 (d, J=9.3 Hz), 122.2 (d, J=2.7 Hz), 117.5, 113.8 (d, J=23.1 Hz), 113.6 (d, J=20.9 Hz), 104.4, 98.5, 61.6, 55.6, 55.3, 49.2, 12.4; ^{19}F NMR (282 MHz, $CDCl_3$) δ −111.81; IR (neat, cm^{-1}) 3062, 2931, 2124, 1698, 1606, 1586, 1503, 1256, 1205, 1102, 1042; HRMS (ES$^+$) m/z [M+Na]$^+$ calcd for $C_{20}H_{20}FN_3O_5Na$: 424.1285; found: 424.1272.

*4.5.13. Ethyl 2-diazo-3-(N-(2,4-dimethoxybenzyl)-N-(3-trifluoromethylphenyl)amino)-3-oxopropanoate (**9m**).* Compound **9m** was prepared according to the general procedure (B) reported for **9a** starting from *N*-(2,4-dimethoxybenzyl)-3-(trifluoromethyl)aniline **7m** (703 mg, 2.26 mmol, 1 equiv), distilled Et_3N (1.49 mL, 10.60 mmol, 4.7 equiv), and ethyl 2-diazomalonyl chloride **8** (400 mg, 2.26 mmol, 1 equiv). Flash column chromatography on

silica gel (heptane/EtOAc, 7/3) afforded **9m** (724 mg, 71%) as a yellow solid; mp 78–79 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52–7.11 (m, 4H), 7.24 (d, J=8.4 Hz, 1H), 6.34 (dd, J=8.4, 2.3 Hz, 1H), 6.24 (d, J=2.3 Hz, 1H), 4.87 (s, 2H), 3.99 (q, J=7.2 Hz, 2H), 3.67 (s, 3H), 3.48 (s, 3H), 1.00 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.5, 161.4, 160.7, 158.4, 143.7, 132.2 (q, J=31.3 Hz), 131.3, 130.0, 129.3, 123.8 (q, J=271.7 Hz), 123.6 (q, J=3.3 Hz), 123.2 (q, J=2.7 Hz), 117.1, 104.4, 98.3, 61.4, 55.4, 55.0, 49.0, 14.2; ^{19}F NMR (282 MHz, $CDCl_3$) δ −62.7; IR (neat, cm^{-1}) 2960, 2126, 1702, 1640, 1613, 1587, 1337, 1304, 1156, 1091, 1039, 701; HRMS (ES$^+$) m/z [M+Na]$^+$ calcd for $C_{21}H_{20}F_3N_3O_5Na$: 474.1253; found: 474.1247.

4.6. General procedure (C) for the synthesis of the 2-silyloxyindole-3-carboxylates 10

*4.6.1. Ethyl 1-N-(2,4-dimethoxybenzyl)-2-(triisopropylsilyloxy)-1H-indole-3-carboxylate (**10a**).* $Rh_2(NHCOCF_3)_4$ (13 mg, 0.02 mmol, 5 mol %) was added to a solution of ethyl 2-diazo-3-(*N*-(2,4-dimethoxybenzyl)-*N*-(phenyl)amino)-3-oxopropanoate **9a** (153 mg, 0.40 mmol, 1 equiv) in CH_2Cl_2 (2 mL) held under argon at room temperature. After stirring for 5 h, the solution was cooled to 0 °C and distilled Et_3N (171 μL, 2.50 mmol, 6.25 equiv) was added followed by TIPSOTf (135 μL, 0.50 mmol, 1.25 equiv). The solution was allowed to stir at 0 °C for 15 min before quenching with H_2O (2 mL) and extracted with CH_2Cl_2 (3×). The combined CH_2Cl_2 extracts were then dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (heptane/EtOAc/Et_3N, 6/3.8/0.2) to give **10a** (160 mg, 78%) as a white solid; mp 84–85 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (d, J=7.9 Hz, 1H), 7.15 (ddd, J=7.9, 6.2, 2.3 Hz, 1H), 7.08–7.01 (m, 2H), 6.45 (d, J=8.5 Hz, 1H), 6.44 (d, J=2.3 Hz, 1H), 6.23 (dd, J=8.5, 2.3 Hz, 1H), 5.17 (s, 2H), 4.36 (q, J=7.2 Hz, 2H), 3.87 (s, 3H), 3.72 (s, 3H), 1.44 (hep, J=7.5 Hz, 3H), 1.42 (t, J=7.2 Hz, 3H), 1.04 (d, J=7.5 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.1, 160.3, 157.5, 153.6, 131.4, 127.6, 125.5, 121.8, 121.3, 120.9, 117.2, 109.5, 104.1, 98.5, 89.3, 59.2, 55.5 (2C), 39.8, 18.1 (6C), 15.0, 14.5 (3C); IR (neat, cm^{-1}) 2941, 2864, 1693, 1614, 1590, 1534, 1454, 1207, 1141, 1106; HRMS (ES$^+$) m/z [M+Na]$^+$ calcd for $C_{29}H_{41}NO_5SiNa$: 534.2652; found: 534.2661.

*4.6.2. Ethyl 1-N-(2,4-dimethoxybenzyl)-5-methoxy-2-(triisopropylsilyloxy)-1H-indole-3-carboxylate (**10b**)*[36b]. Compound **10b** was prepared according to the general procedure (C) reported for **10a** starting from ethyl 2-diazo-3-(*N*-(2,4-dimethoxybenzyl)-*N*-(4-methoxyphenyl)amino)-3-oxopropanoate **9b** (165 mg, 0.40 mmol, 1 equiv), $Rh_2(NHCOCF_3)_4$ (13 mg, 0.02 mmol, 5 mol %), distilled Et_3N (171 μL, 2.50 mmol, 6.25 equiv), and TIPSOTf (135 μL, 0.50 mmol, 1.25 equiv). Flash column chromatography on silica gel (heptane/EtOAc/Et_3N, 6/3.8/0.2) afforded **10b** (147 mg, 68%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, J=2.5 Hz, 1H), 6.92 (d, J=8.8 Hz, 1H), 6.68 (dd, J=8.8, 2.5 Hz, 1H), 6.47 (d, J=8.4 Hz, 1H), 6.45 (d, J=2.4 Hz, 1H), 6.24 (dd, J=8.4, 2.4 Hz, 1H), 5.14 (s, 2H), 4.36 (q, J=7.1 Hz, 2H), 3.87 (s, 3H), 3.84 (s, 3H), 3.72 (s, 3H), 1.44 (hep, J=7.6 Hz, 3H), 1.43 (t, J=7.1 Hz, 3H), 1.05 (d, J=7.6 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.1, 160.3, 157.5, 155.8, 153.7, 127.6, 126.2, 126.1, 117.2, 110.2, 109.9, 104.4, 104.2, 98.5, 89.5, 59.1, 55.9, 55.6 (2C), 39.9, 18.1 (6C), 15.0, 14.5 (3C); IR (neat, cm^{-1}) 2942, 2864, 1691, 1617, 1589, 1531, 1454, 1207, 1143, 1108, 1032, 776; HRMS (ES$^+$) m/z [M+Na]$^+$ calcd for $C_{30}H_{43}NO_6SiNa$: 564.2757; found: 564.2723.

*4.6.3. Ethyl 5-chloro-1-N-(2,4-dimethoxybenzyl)-2-(triisopropylsilyloxy)-1H-indole-3-carboxylate (**10c**).* Compound **10c** was prepared according to the general procedure (C) reported for **10a** starting from ethyl 3-(*N*-(4-chlorophenyl)-*N*-(2,4-dimethoxybenzyl)amino)-2-diazo-3-oxopropanoate **9c** (167 mg, 0.40 mmol, 1 equiv), $Rh_2(NHCOCF_3)_4$ (13 mg, 0.02 mmol, 5 mol %), distilled Et_3N (171 μL, 2.50 mmol, 6.25 equiv), and TIPSOTf (135 μL, 0.50 mmol, 1.25 equiv). Flash column chromatography on silica gel (heptane/EtOAc/Et_3N, 6/3.8/0.2) afforded **10c** (153 mg, 70%) as a white solid; mp 63–64 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (d, J=2.0 Hz, 1H), 7.01 (dd, J=8.6, 2.0 Hz, 1H), 6.94 (d, J=8.6 Hz, 1H), 6.45 (d, J=2.3 Hz, 1H), 6.43 (d, J=8.4 Hz, 1H), 6.26 (dd, J=8.2, 2.3 Hz, 1H), 5.16 (s, 2H), 4.38 (q, J=7.0 Hz, 2H), 3.87 (s, 3H), 3.72 (s, 3H), 1.47 (hep, J=7.6 Hz, 3H), 1.43 (t, J=7.0 Hz, 3H), 1.06 (d, J=7.6 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.4, 160.5, 157.5, 154.2, 129.7, 127.5 (2C), 126.6, 121.7, 120.8, 116.8, 110.6, 104.2, 98.6, 89.4, 59.4, 55.6 (2C), 40.0, 18.1 (6C), 15.0, 14.5 (3C); IR (neat, cm^{-1}) 2942, 2865, 1693, 1614, 1591, 1537, 1454, 1208, 1145, 1112, 1034, 771; HRMS (ES$^+$) m/z [M+Na]$^+$ calcd for $C_{29}H_{40}{}^{35}ClNO_5SiNa$: 568.2262; found: 568.2273.

*4.6.4. Ethyl 1-N-(2,4-dimethoxybenzyl)-5-fluoro-2-(triisopropylsilyloxy)-1H-indole-3-carboxylate (**10d**).* Compound **10d** was prepared according to the general procedure (C) reported for **10a** starting from ethyl 2-diazo-3-(*N*-(2,4-dimethoxybenzyl)-*N*-(4-fluorophenyl-amino)-3-oxopropanoate **9d** (161 mg, 0.40 mmol, 1 equiv), $Rh_2(NHCOCF_3)_4$ (13 mg, 0.02 mmol, 5 mol %), distilled Et_3N (171 μL, 2.50 mmol, 6.25 equiv), and TIPSOTf (135 μL, 0.50 mmol, 1.25 equiv). Flash column chromatography on silica gel (heptane/EtOAc/Et_3N, 6/3.8/0.2) afforded **10d** (150 mg, 71%) as a white solid; mp 88–89 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (dd, J=10.3, 2.5 Hz, 1H), 6.92 (dd, J=9.0, 4.5 Hz, 1H), 6.75 (dt, J=9.0, 2.5 Hz, 1H), 6.45 (d, J=8.3 Hz, 1H), 6.45 (d, J=2.3 Hz, 1H), 6.25 (dd, J=8.3, 2.3 Hz, 1H), 5.14 (br s, 2H), 4.35 (q, J=7.2 Hz, 2H), 3.86 (s, 3H), 3.72 (s, 3H), 1.44 (hep, J=7.6 Hz, 3H), 1.41 (t, J=7.2 Hz, 3H), 1.05 (d, J=7.7 Hz, 18H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.8, 160.4, 159.5 (d, J=235.0 Hz), 157.5, 154.3, 127.7, 127.6, 126.2 (d, J=10.9 Hz), 116.9, 110.1 (d, J=9.3 Hz), 109.9 (d, J=25.8 Hz), 106.9 (d, J=25.8 Hz), 104.2, 98.5, 89.8, 59.4, 55.6 (2C), 40.0, 18.1 (6C), 15.0, 14.5 (3C); ^{19}F NMR (282 MHz, $CDCl_3$) δ −122.2; IR (neat, cm^{-1}) 2942, 2865, 1688, 1621, 1591, 1537, 1455, 1209, 1148, 1109, 1034, 780; HRMS (ES$^+$) m/z [M+Na]$^+$ calcd for $C_{29}H_{40}FNO_5SiNa$: 552.2558; found: 552.2564.

*4.6.5. Ethyl 1-N-(2,4-dimethoxybenzyl)-5-(trifluoromethyl)-2-(triisopropylsilyloxy)-1H-indole-3-carboxylate (**10e**).* Compound **10e** was prepared according to the general procedure (C) reported for **10a** starting from ethyl 2-diazo-3-(*N*-(2,4-dimethoxybenzyl)-*N*-(4-trifluoromethylphenyl)-amino)-3-oxopropanoate **9e** (180 mg, 0.40 mmol, 1 equiv), $Rh_2(NHCOCF_3)_4$ (13 mg, 0.02 mmol, 5 mol %), distilled Et_3N (171 μL, 2.50 mmol, 6.25 equiv), and TIPSOTf (135 μL, 0.50 mmol, 1.25 equiv). Flash column chromatography on silica gel (heptane/EtOAc/Et_3N, 6/3.8/0.2) afforded **10e** (167 mg, 72%) as a yellow solid; mp 124–125 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (br s, 1H), 7.29 (dd, J=8.6, 1.0 Hz, 1H), 7.09 (d, J=8.6 Hz, 1H), 6.46 (d, J=2.4 Hz, 1H), 6.44 (d, J=8.6 Hz, 1H), 6.26 (dd, J=8.6, 2.4 Hz, 1H), 5.20 (s, 2H), 4.38 (q, J=7.0 Hz, 2H), 3.87 (s, 3H), 3.72 (s, 3H), 1.47 (hep, J=7.6 Hz, 3H), 1.43 (t, J=7.0 Hz, 3H), 1.05 (d, J=7.6 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.6, 160.6, 157.6, 154.6, 127.9, 127.5, 125.5 (q, J=270.3 Hz), 125.1, 124.0 (d, J=31.8 Hz), 118.5 (d, J=4.4 Hz), 118.2 (d, J=3.3 Hz), 116.6, 109.6, 104.3, 98.6, 90.0, 59.6, 55.6 (2C), 40.0, 18.1 (6C), 14.9, 14.6 (3C); ^{19}F NMR (282 MHz, $CDCl_3$) δ −60.6; IR (neat, cm^{-1}) 2943, 2866, 1697, 1618, 1590, 1542, 1454, 1264, 1148, 1111; MS (ES$^+$) m/z 602.3 [M+Na$^+$], 446.1 [M−TIPS+Na$^+$].

*4.6.6. Ethyl 1-N-(2,4-dimethoxybenzyl)-4,6-dimethoxy-2-(triisopropylsilyloxy)-1H-indole-3-carboxylate (**10f**).* Compound **10f** was prepared according to the general procedure (C) reported for **10a** starting from ethyl 2-diazo-3-(*N*-(2,4-dimethoxybenzyl)-*N*-(3,5-dimethoxyphenyl)-amino)-3-oxopropanoate **9f** (177 mg, 0.40 mmol, 1 equiv), $Rh_2(NHCOCF_3)_4$ (13 mg, 0.02 mmol, 5 mol %), distilled Et_3N (171 μL, 2.50 mmol, 6.25 equiv), and TIPSOTf (135 μL, 0.50 mmol, 1.25 equiv). Flash column chromatography on silica gel (heptane/EtOAc/Et_3N, 6/3.8/0.2) afforded **10f** (149 mg, 65%) as a white solid; mp 107–108 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.51 (d,

J=8.5 Hz, 1H), 6.44 (d, J=2.3 Hz, 1H), 6.28 (d, J=2.1 Hz, 1H), 6.25 (dd, J=8.5, 2.3 Hz, 1H), 6.22 (d, J=2.1 Hz, 1H), 5.09 (s, 2H), 4.31 (q, J=7.2 Hz, 2H), 3.86 (s, 3H), 3.85 (s, 3H), 3.72 (s, 3H), 3.70 (s, 3H), 1.38 (hep, J=7.6 Hz, 3H), 1.37 (t, J=7.2 Hz, 3H), 1.03 (d, J=7.6 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 160.3, 157.4, 156.7, 153.8, 150.5, 133.0, 129.7, 127.9, 117.3, 104.2, 98.4, 93.8, 89.7, 86.8, 59.8, 55.8, 55.7, 55.6, 55.3, 39.9, 18.1 (6C), 14.9, 14.3 (3C); IR (neat, cm^{-1}) 2940, 2863, 1675, 1616, 1582, 1533, 1502, 1452, 1207, 1156, 1117, 1034; HRMS (ES^+) m/z $[M+H]^+$ calcd for $C_{31}H_{46}NO_7Si$: 572.3044; found: 572.3041.

*4.6.7. Ethyl 7-bromo-1-N-(2,4-dimethoxybenzyl)-2-(triisopropylsilyloxy)-1H-indole-3-carboxylate (**10g**).* Compound **10g** was prepared according to the general procedure (C) reported for **10a** starting from ethyl 3-(*N*-(2-bromophenyl)-*N*-(2,4-dimethoxybenzyl)-amino)-2-diazo-3-oxopropanoate **9g** (185 mg, 0.40 mmol, 1 equiv), $Rh_2(NHCOCF_3)_4$ (13 mg, 0.02 mmol, 5 mol %), distilled Et_3N (171 μL, 2.50 mmol, 6.25 equiv), and TIPSOTf (135 μL, 0.50 mmol, 1.25 equiv). Flash column chromatography on silica gel (heptane/EtOAc/Et_3N, 6/3.8/0.2) afforded **10g** (201 mg, 85%) as a yellow foam. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (dd, J=7.9, 0.9 Hz, 1H), 7.28 (dd, J=7.9, 0.9 Hz, 1H), 7.04 (t, J=7.9 Hz, 1H), 6.49 (d, J=2.4 Hz, 1H), 6.27 (dd, J=8.2, 2.4 Hz, 1H), 6.23 (d, J=8.2 Hz, 1H), 5.65 (br s, 2H), 4.41 (q, J=7.0 Hz, 2H), 3.90 (s, 3H), 3.76 (s, 3H), 1.47 (hep, J=7.6 Hz, 3H), 1.46 (t, J=7.0 Hz, 3H), 1.04 (d, J=7.6 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.5, 160.0, 156.7, 154.5, 128.5, 128.2, 126.9, 126.4, 122.6, 120.1, 119.4, 103.9, 103.4, 98.3, 89.6, 59.5, 55.4 (2C), 41.6, 18.0 (6C), 14.9, 14.6 (3C); IR (neat, cm^{-1}) 2942, 2864, 1693, 1614, 1590, 1546, 1441, 1108, 1034; HRMS (ES^+) m/z $[M+Na]^+$ calcd for $C_{29}H_{40}{}^{79}BrNO_5SiNa$: 612.1757; found: 612.1743; calcd for $C_{29}H_{40}{}^{81}BrNO_5SiNa$: 614.1736; found: 614.1743.

*4.6.8. Ethyl 7-bromo-1-N-(2,4-dimethoxybenzyl)-5-fluoro-2-(triisopropylsilyloxy)-1H-indole-3-carboxylate (**10h**).* Compound **10h** was prepared according to the general procedure (C) reported for **10a** starting from ethyl 3-(*N*-(2-bromo-4-fluorophenyl)-*N*-(2,4-dimethoxybenzyl)amino)-2-diazo-3-oxopropanoate **9h** (192 mg, 0.40 mmol, 1 equiv), $Rh_2(NHCOCF_3)_4$ (13 mg, 0.02 mmol, 5 mol %), distilled Et_3N (171 μL, 2.50 mmol, 6.25 equiv), and TIPSOTf (135 μL, 0.50 mmol, 1.25 equiv). Flash column chromatography on silica gel (heptane/EtOAc/Et_3N, 6/3.8/0.2) afforded **10h** (97 mg, 40%) as a yellow solid; mp 117–118 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (dd, J=9.7, 2.5 Hz, 1H), 7.00 (dd, J=8.9, 2.5 Hz, 1H), 6.44 (d, J=2.2 Hz, 1H), 6.23 (dd, J=8.4, 2.2 Hz, 1H), 6.15 (d, J=8.4 Hz, 1H), 5.55 (br s, 2H), 4.35 (q, J=7.1 Hz, 2H), 3.84 (s, 3H), 3.72 (s, 3H), 1.42 (hep, J=7.7 Hz, 3H), 1.41 (t, J=7.1 Hz, 3H), 1.00 (d, J=7.7 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.2, 160.1, 158.3 (d, J=238.8 Hz), 156.7, 155.4, 128.8 (d, J=11.0 Hz), 126.3, 124.9, 119.1, 114.6 (d, J=28.0 Hz), 106.2 (d, J=24.7 Hz), 103.9, 102.8 (d, J=11.5 Hz), 98.4, 90.2 (d, J=3.8 Hz), 59.6, 55.5 (2C), 41.6, 18.0 (6C), 14.9, 14.6 (3C); ^{19}F NMR (282 MHz, $CDCl_3$) δ: −121.2; IR (neat, cm^{-1}) 2941, 2864, 1693, 1614, 1590, 1537, 1454, 1207, 1141, 1107, 1034; MS (ES^+) m/z 474 [M−TIPS+Na, ^{79}Br]$^+$, 476 [M−TIPS+Na, ^{81}Br].

*4.6.9. Ethyl 7-bromo-1-N-(2,4-dimethoxybenzyl)-4-methoxy-2-(triisopropylsilyloxy)-1H-indole-3-carboxylate (**10i**).* Compound **10i** was prepared according to the general procedure (C) reported for **10a** starting from ethyl 3-(*N*-(2-bromo-5-methoxyphenyl)-*N*-(2,4-dimethoxybenzyl)-amino)-2-diazo-3-oxopropanoate **9i** (197 mg, 0.40 mmol, 1 equiv), $Rh_2(NHCOCF_3)_4$ (13 mg, 0.02 mmol, 5 mol %), distilled Et_3N (171 μL, 2.50 mmol, 6.25 equiv), and TIPSOTf (135 μL, 0.50 mmol, 1.25 equiv). Flash column chromatography on silica gel (heptane/EtOAc/Et_3N, 6/3.8/0.2) afforded **10i** (166 mg, 67%) as a white solid; mp 114–115 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.12 (d, J=8.5 Hz, 1H), 6.45 (d, J=8.6 Hz, 1H), 6.43 (d, J=1.9 Hz, 1H), 6.21–6.20 (m, 2H), 5.56 (br s, 2H), 4.31 (q, J=7.2 Hz, 2H), 3.85 (s, 3H), 3.83 (s, 3H), 3.72 (s, 3H), 1.37 (t, J=7.2 Hz, 3H), 1.33 (hep, J=7.5 Hz, 3H), 0.99 (d, J=7.5 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 160.0, 156.6, 152.2, 149.8, 128.6, 126.8, 126.7, 126.3, 119.7, 117.3, 103.9(2C), 98.3, 95.2, 60.5, 55.8, 55.5 (2C), 41.4, 18.0 (6C), 14.7, 14.1 (3C); IR (neat, cm^{-1}) 2948, 2871, 1697, 1621, 1590, 1546, 1433, 1259, 1208, 1175, 1031; HRMS (ES^+) m/z $[M+Na]^+$ calcd for $C_{30}H_{42}{}^{79}BrNO_6SiNa$: 642.1862; found: 642.1873; calcd for $C_{30}H_{42}{}^{81}BrNO_6SiNa$: 644.1842; found: 644.1858.

*4.6.10. Ethyl 1-N-(2,4-dimethoxybenzyl)-6-methoxy-2-(triisopropylsilyloxy)-1H-indole-3-carboxylate (**10j**) and ethyl 1-N-(2,4-dimethoxybenzyl)-4-methoxy-2-(triisopropylsilyloxy)-1H-indole-3-carboxylate (**10j′**).* Compounds **10j** and **10j′** were prepared according to the general procedure (C) reported for **10a** starting from ethyl 2-diazo-3-(*N*-(2,4-dimethoxybenzyl)-*N*-(3-methoxyphenyl)-amino)-3-oxopropanoate **9j** (166 mg, 0.40 mmol, 1 equiv), $Rh_2(NHCOCF_3)_4$ (13 mg, 0.02 mmol, 5 mol %), distilled Et_3N (171 μL, 2.50 mmol, 6.25 equiv), and TIPSOTf (135 μL, 0.50 mmol, 1.25 equiv). Flash column chromatography on silica gel (CH_2Cl_2/Et_2O/heptane/Et_3N, 4.9/3/2/0.1) afforded an inseparable mixture of regioisomers **10j**/**10j′** (73:27, respectively, 206 mg, 95%) as a colorless oil. Compound **10j**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, J=8.7 Hz, 1H), 6.81 (dd, J=8.7, 2.3 Hz, 1H), 6.62 (d, J=2.3 Hz, 1H), 6.55 (d, J=8.4 Hz, 1H), 6.47 (d, J=2.4 Hz, 1H), 6.27 (dd, J=8.4, 2.4 Hz, 1H), 5.15 (br s, 2H), 4.36 (q, J=7.1 Hz, 2H), 3.88 (br s, 3H), 3.74 (br s, 3H), 3.72 (br s, 3H), 1.54–1.43 (m, 3H), 1.43 (t, J=7.1 Hz, 3H), 1.07 (d, J=7.5 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.0, 160.3, 157.4, 155.8, 153.0, 132.1, 127.7, 121.6, 119.1, 117.3, 109.8, 104.2, 98.4, 94.6, 88.9, 59.1, 55.7, 55.4 (2C), 39.6, 18.1 (6C), 14.9, 14.5 (3C). Compound **10j′**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.99 (t, J=8.0 Hz, 1H), 6.70 (d, J=8.0 Hz, 1H), 6.62 (d, J=8.0 Hz, 1H), 6.46–6.45 (m, 2H), 6.25–6.22 (m, 1H), 5.17 (br s, 2H), 4.35 (q, J=7.1 Hz, 2H), 3.88 (br s, 3H), 3.75 (br s, 3H), 3.73 (br s, 3H), 1.44–1.41 (m, 3H), 1.30–1.27 (m, 3H), 1.09–1.05 (m, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.7, 160.2, 157.3, 150.8, 132.8, 130.2, 127.5, 121.9, 117.3, 114.5, 104.0, 103.4, 103.1, 98.3, 89.5, 59.8, 55.6 (3C), 40.0, 18.1 (6C), 14.4, 14.2 (3C); HRMS (ES^+) m/z $[M+Na]^+$ calcd for $C_{30}H_{43}NO_6SiNa$: 564.2757; found: 564.2784.

*4.6.11. Ethyl 6-(tert-butyldiphenylsilyloxy)-1-N-(2,4-dimethoxybenzyl)-2-(triisopropylsilyloxy)-1H-indole-3-carboxylate (**10k**) and ethyl 4-(tert-butyldiphenylsilyloxy)-1-N-(2,4-dimethoxybenzyl)-2-(triisopropylsilyloxy)-1H-indole-3-carboxylate (**10k′**).* Compounds **10k** and **10k′** were prepared according to the general procedure (C) reported for **10a** starting from ethyl 3-(*N*-(3-(*tert*-butyldiphenylsilyloxy)phenyl)-*N*-(2,4-dimethoxybenzyl)amino)-2-diazo-3-oxopropanoate **9k** (255 mg, 0.40 mmol, 1 equiv), $Rh_2(NHCOCF_3)_4$ (13 mg, 0.02 mmol, 5 mol%), distilled Et_3N (171 μL, 2.50 mmol, 6.25 equiv), and TIPSOTf (135 μL, 0.50 mmol, 1.25 equiv). Flash column chromatography on silica gel (CH_2Cl_2/Et_2O/heptane/Et_3N, 4.9/3/2/0.1) afforded an inseparable mixture of regioisomers **10k**/**10k′** (90:10, respectively, 285 mg, 93%) as a yellow solid. Compound **10k**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, J=8.8 Hz, 1H), 7.66–7.65 (m, 4H), 7.37–7.32 (m, 2H), 7.29–7.24 (m, 4H), 6.67 (dd, J=8.8, 2.1 Hz, 1H), 6.47 (d, J=2.1 Hz, 1H), 6.39–6.36 (m, 2H), 6.18 (dd, J=8.2, 1.8 Hz, 1H), 4.93 (s, 2H), 4.30 (q, J=7.0 Hz, 2H), 3.76 (s, 3H), 3.75 (s, 3H), 1.44 (hep, J=7.4 Hz, 3H), 1.37 (t, J=7.0 Hz, 3H), 1.05 (br s, 9H), 1.03 (d, J=7.4 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 160.1, 155.3, 151.2, 144.0, 134.8 (4C), 133.2 (2C), 131.5, 129.5 (2C), 127.9 (5C), 120.8, 117.7, 118.2, 112.3, 104.4, 101.6, 97.7, 93.2, 59.5, 55.5, 55.3, 39.7, 26.9 (3C), 18.2, 18.1 (6C), 14.9, 13.6 (3C). Compound **10k′**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66–7.65 (m, 4H), 7.37–7.32 (m, 2H), 7.29–7.24 (m, 4H), 7.01 (t, J=7.8 Hz, 1H), 6.72 (d, J=7.8 Hz, 1H), 6.62 (d, J=7.8 Hz, 1H), 6.46–6.41 (m, 2H), 6.38–6.32 (m, 1H), 4.90 (s, 2H), 4.30 (q, J=7.0 Hz, 2H), 3.74 (s, 3H), 3.71 (s, 3H), 1.42 (hep, J=7.1 Hz, 3H), 1.36 (t, J=6.9 Hz, 3H), 1.03 (d, J=7.1 Hz, 18H), 1.02 (br s, 9H); ^{13}C

NMR (75 MHz, $CDCl_3$) δ 166.5, 161.9, 155.1, 143.9, 141.3 (2C), 135.4 (4C), 132.8 (2C), 132.5, 130.3 (2C), 128.4, 127.8 (4C), 124.0, 120.6, 113.8, 104.9, 99.2, 98.1, 93.2, 59.5, 55.3, 55.1, 37.8, 26.9 (3C), 17.9, 17.7 (6C), 14.9, 13.6 (3C); HRMS (ES^+) m/z $[M+Na]^+$ calcd for $C_{45}H_{59}NO_6Si_2Na$: 788.3779; found: 788.3754.

*4.6.12. Ethyl 1-N-(2,4-dimethoxybenzyl)-6-fluoro-2-(triisopropylsilyloxy)-1H-indole-3-carboxylate (**10l**) and ethyl 1-N-(2,4-dimethoxybenzyl)-4-fluoro-2-(triisopropylsilyloxy)-1H-indole-3-carboxylate (**10l′**).* Compounds **10l** and **10l′** were prepared according to the general procedure (C) reported for **10a** starting from ethyl 2-diazo-3-(*N*-(2,4-dimethoxybenzyl)-*N*-(3-fluorophenyl)-amino)-3-oxopropanoate **9l** (161 mg, 0.40 mmol, 1 equiv), $Rh_2(NHCOCF_3)_4$ (13 mg, 0.02 mmol, 5 mol %), distilled Et_3N (171 μL, 2.50 mmol, 6.25 equiv), and TIPSOTf (135 μL, 0.50 mmol, 1.25 equiv). Flash column chromatography on silica gel (CH_2Cl_2/Et_2O/heptane/Et_3N, 4.9/3/2/0.1) afforded an inseparable mixture of regioisomers **10l**/**10l′** (73:27, respectively, 197 mg, 93%) as a white solid. Compound **10l**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.91 (dd, J=9.4, 2.3 Hz, 1H), 6.91–6.84 (m, 1H), 6.75 (dd, J=8.8, 5.6 Hz, 1H), 6.49 (d, J=8.4 Hz, 1H), 6.46–6.44 (m, 1H), 6.26 (dd, J=8.4, 2.4 Hz, 1H), 5.12 (s, 2H), 4.35 (q, J=7.1 Hz, 2H), 3.87 (s, 3H), 3.73 (s, 3H), 1.49–1.38 (m, 3H), 1.41 (t, J=7.1 Hz, 3H), 1.06–1.03 (m, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.8, 160.5, 159.5 (d, J=236.6 Hz), 157.6, 153.8, 131.5 (d, J=12.1 Hz), 127.7, 121.8 (d, J=8.8 Hz), 121.5 (d, J=1.1 Hz), 116.7, 109.5 (d, J=23.1 Hz), 104.3, 98.6, 96.7 (d, J=26.9 Hz), 89.8, 59.4, 55.6 (2C), 39.9, 18.2 (6C), 15.0, 14.6 (3C); ^{19}F NMR (282 MHz, $CDCl_3$) δ −121.5. Compound **10l′**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.25 (m, 1H), 7.07 (d, J=8.6 Hz, 1H), 6.52 (dd, J=9.0, 6.9 Hz, 1H), 6.52 (d, J=8.2 Hz, 1H), 6.46–6.44 (m, 1H), 6.30 (dd, J=8.2, 2.1 Hz, 1H), 5.10 (s, 2H), 4.31 (q, J=7.0 Hz, 2H), 3.76 (s, 3H), 3.72 (s, 3H), 1.70–1.33 (m, 3H), 1.37 (t, J=7.0 Hz, 3H), 1.04–0.86 (m, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.1, 161.7, 158.3, 152.7 (d, J=220.1 Hz), 148.5, 135.5, 128.5, 124.6 (2C, J=18.7 Hz), 117.1, 107.6 (d, J=21.1 Hz), 104.1, 102.1, 98.2, 87.8, 61.4, 55.3 (2C), 39.2, 18.2 (6C), 14.8, 14.4 (3C); ^{19}F NMR (282 MHz, $CDCl_3$) δ −119.0; HRMS (ES^+) m/z $[M+Na]^+$ calcd for $C_{29}H_{40}FNO_5SiNa$: 552.2558; found: 552.2563.

*4.6.13. Ethyl 1-N-(2,4-dimethoxybenzyl)-6-(trifluoromethyl)-2-(triisopropylsilyloxy)-1H-indole-3-carboxylate (**10m**) and ethyl 1-N-(2,4-dimethoxybenzyl)-4-(trifluoromethyl)-2-(triisopropylsilyloxy)-1H-indole-3-carboxylate (**10m′**).* Compounds **10m** and **10m′** were prepared according to the general procedure (C) reported for **10a** starting from ethyl 2-diazo-3-(*N*-(2,4-dimethoxybenzyl)-*N*-(3-trifluoromethyl-phenyl)amino)-3-oxopropanoate **9m** (181 mg, 0.40 mmol, 1 equiv), $Rh_2(NHCOCF_3)_4$ (13 mg, 0.02 mmol, 5 mol %), distilled Et_3N (171 μL, 2.50 mmol, 6.25 equiv), and TIPSOTf (135 μL, 0.50 mmol, 1.25 equiv). Flash column chromatography on silica gel (CH_2Cl_2/Et_2O/heptane/Et_3N, 4.9/3/2/0.1) afforded an inseparable mixture of regioisomers **10m**/**10m′** (64:36, respectively, 160 mg, 69%) as a yellow solid. Compound **10m**: ^1H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, J=8.7 Hz, 1H), 7.39–7.36 (m, 1H), 7.36 (br s, 1H), 6.53 (d, J=8.5 Hz, 1H), 6.46 (br s, 1H), 6.27 (dd, J=8.5, 2.4 Hz, 1H), 5.20 (s, 2H), 4.37 (q, J=7.2 Hz, 2H), 3.89 (s, 3H), 3.73 (s, 3H), 1.47 (hep, J=7.7 Hz, 3H), 1.42 (t, J=7.2 Hz, 3H), 1.07–1.02 (m, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.7, 160.6, 157.5, 154.9, 130.5, 128.5, 127.9, 123.2 (q, J=31.8 Hz), 118.6 (q, J=3.2 Hz), 118.4 (q, J=256.2 Hz), 113.1 (2C), 106.8 (q, J=3.2 Hz), 104.4, 98.6, 90.0, 59.5, 55.6 (2C), 39.7, 18.1 (6C), 14.9, 14.2 (3C); ^{19}F NMR (282 MHz, $CDCl_3$) δ −60.5. Compound **10m′**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.44 (d, J=7.9 Hz, 1H), 7.20 (d, J=7.9 Hz, 1H), 7.07 (t, J=7.9 Hz, 1H), 6.46–6.43 (m, 2H), 6.27–6.24 (m, 1H), 5.19 (br s, 2H), 4.30 (q, J=7.2 Hz, 2H), 3.88 (br s, 3H), 3.73 (br s, 3H), 1.46–1.37 (m, 3H), 1.34 (t, J=7.2 Hz, 3H), 1.07–1.02 (m, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 160.5, 157.4, 151.9, 132.5, 131.5 (m), 127.6 (2C), 123.5 (q, J=261.3 Hz), 123.3 (q, J=33.2 Hz), 120.3 (m), 116.8, 113.2, 104.2, 98.6, 91.3, 60.6, 55.5 (2C), 40.0, 18.1 (6C), 14.5 (4C); ^{19}F NMR (282 MHz, $CDCl_3$) δ −61.6; HRMS (ES^+) m/z $[M+Na]^+$ calcd for $C_{30}H_{40}F_3NO_5SiNa$: 580.2706; found: 580.2734.

4.7. *N,N*-Diethyl 3-oxobutanamide (11)

To a solution of diketene (2.30 mL, 30 mmol, 2 equiv) in toluene (16.50 mL) held at 0 °C was added a solution of diethylamine (1.60 mL, 15 mmol, 1 equiv) and distilled Et_3N (2.50 mL, 18 mmol, 1.2 equiv) in MeOH (7.5 mL). After completion of the addition, the mixture was stirred at 0 °C for 2 h. The solution was then concentrated in vacuo to afford a crude oil, which was purified by flash column chromatography on silica gel (heptane/EtOAc, 7/3) to give **11** (2.24 g, 95%) as a yellow oil. ^1H NMR (300 MHz, $CDCl_3$) δ 3.40 (s, 2H), 3.29 (q, J=7.2 Hz, 2H), 3.10 (q, J=7.2 Hz, 2H), 2.18 (s, 3H), 1.05 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.9, 166.8, 50.0, 42.7, 40.2, 30.2, 14.2, 13.0; IR (neat, cm^{-1}) 2974, 2934, 1720, 1633, 1590, 1360, 1272, 1153, 1086, 1047, 773; HRMS (ES^+) m/z $[M+Na]^+$ calcd for $C_8H_{15}NO_2Na$: 180.1000; found: 180.0998.

4.8. *N,N*-Diethyl 2-diazo-3-oxobutanamide 12

To a solution of *N,N*-diethyl-3-oxobutanamide **11** (2.03 g, 12.91 mmol) in acetonitrile (17 mL) was added Et_3N (5.43 mL, 14.20 mmol, 1.1 equiv) at 0 °C. *p*-Acetamidobenzenesulfonyl azide (3.41 g, 14.20 mmol, 1.1 equiv) was then introduced by portions. The mixture was warmed to room temperature and stirred for 20 h. The solution was concentrated in vacuo and the residue was triturated with a mixture of Et_2O/petroleum ether (1:1, 35 mL). After removal of the sulfonamide by-product by filtration, the filtrate was concentrated in vacuo and the resulting residue was purified by flash column chromatography on silica gel (Et_2O/EP, 1/1) to give **12** (2.21 g, 94%) as a yellow oil. ^1H NMR (300 MHz, $CDCl_3$) δ 3.28 (q, J=7.1 Hz, 4H), 2.22 (s, 3H), 1.09 (t, J=7.1 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.1, 160.4, 41.9 (2C), 27.3, 13.2 (2C); IR (neat, cm^{-1}) 2974, 2872, 2095, 1621, 1421, 1285, 1257, 1057, 633; MS (ES^+) m/z 206 $[M+Na]^+$.

4.9. *N,N*-Diethyl 2-diazoacetamide 13

To a solution of *N,N*-diethyl-2-diazo-3-oxobutanamide **12** (200 mg, 1.10 mmol) in MeOH (350 μL) held at 0 °C was added MeONa (0.060 g, 1.11 mmol, 1.01 equiv) by portions. After completion of the addition, the mixture was stirred at 0 °C for an additional hour. The reaction solution was then poured into ice water (2.50 mL), and the resulting mixture was extracted with Et_2O. The aqueous phase was saturated with NaCl and extracted with Et_2O. The combined Et_2O extracts were washed with H_2O, dried over Na_2SO_4, and filtered. The solution was then concentrated in vacuo to afford a crude oil, which was distilled (bp 120–125 °C; 2×10^{-1} mbar) to yield **13** (0.152 mg, 98%) as a yellow oil. ^1H NMR (300 MHz, $CDCl_3$) δ 4.91 (s, 1H), 3.19 (br s, 4H), 1.06 (t, J=7.2 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 46.4, 41.4(2C), 13.9 (2C); IR (neat, cm^{-1}) 3065, 2974, 2933, 2095, 1599, 1429, 1354, 1257, 1134, 724; HRMS (ES^+) m/z $[M+Na]^+$ calcd for $C_6H_{11}N_3ONa$: 164.0800; found: 164.0804.

4.10. 2-Diazo-3-(diethylamino)-3-oxopropanoyl chloride 14

To a solution of triphosgene (0.850 g, 2.86 mmol, 0.40 equiv) in toluene (3.80 mL) held at 0 °C was added pyridine (180 μL, 2.2 mmol, 0.30 equiv). A white precipitate was formed and to the mixture was then slowly added 2-diazo-*N,N*-diethylacetamide **13** (1 g, 7.08 mmol). The reaction mixture was warmed to room temperature and stirred for 6 h. After filtration through a pad of Celite, the filtrate was concentrated in vacuo and purified by flash column chromatography on silica gel (Et_2O/petroleum ether, 6/4) to give **14**

(0.674 g, 46%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.35 (q, J=7.1 Hz, 4H), 1.20 (t, J=7.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.6, 154.9, 42.1 (2C), 13.1 (2C); IR (neat, cm^{-1}) 2974, 2937, 2136, 1731, 1632, 1425, 1274, 1247, 1212, 727; HRMS (MALDI$^+$) m/z [M+H]$^+$ calcd for $C_7H_{11}{}^{35}ClN_3O_2$: 204.0534; found: 204.0527.

4.11. General procedure (D) for the synthesis of the diazo malonamides 15

*4.11.1. N^3,N^3-Diethyl-N^1-(2,4-dimethoxybenzyl)-N^1-phenyl-2-diazomalonamide (**15a**).* To a solution of *N*-(2,4-dimethoxybenzyl)aniline **7a** (114 mg, 0.47 mmol, 1 equiv) in CH_2Cl_2 (1.40 mL) held at 0 °C under argon were successively added dropwise distilled Et_3N (0.31 mL, 2.20 mmol, 4.7 equiv) and 2-diazo-3-(diethylamino)-3-oxopropanoyl chloride **14** (96 mg, 0.47 mmol, 1 equiv). After warming to room temperature and stirring for 6 h, a solution of 1 M HCl (0.60 mL) was added and the mixture was extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were then dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (Et_2O/petroleum ether, 6/4) to give **15a** (176 mg, 91%) as a yellow solid; mp 122–123 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (d, J=8.5 Hz, 1H), 7.29–7.15 (m, 3H), 7.11–7.08 (m, 2H), 6.47 (dd, J=8.5, 2.3 Hz, 1H), 6.34 (d, J=2.3 Hz, 1H), 4.95 (s, 2H), 3.78 (s, 3H), 3.57 (s, 3H), 3.13 (q, J=7.2 Hz, 4H), 0.97 (t, J=7.2 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.5, 161.2, 160.4, 158.4, 142.7, 130.7, 128.9 (2C), 127.3 (2C), 127.1, 118.0, 104.3, 98.3, 55.5, 55.2, 48.7, 41.5 (2C), 12.9 (2C); IR (neat, cm^{-1}) 2934, 2087, 1619, 1591, 1421, 1377, 1276, 1207, 1155, 1034, 697; HRMS (ES$^+$) m/z [M+Na]$^+$ calcd for $C_{22}H_{26}N_4O_4Na$: 433.1852; found: 433.1812.

*4.11.2. N^3,N^3-Diethyl-N^1-(2,4-dimethoxybenzyl)-N^1-(3-methoxyphenyl)-2-diazomalonamide (**15j**).* Compound **15j** was prepared according to the general procedure (D) reported for **15a** starting from *N*-(2,4-dimethoxybenzyl)-3-methoxyaniline **7j** (128 mg, 0.47 mmol, 1 equiv), distilled Et_3N (0.31 mL, 2.20 mmol, 4.7 equiv), and 2-diazo-3-(diethylamino)-3-oxopropanoyl chloride **14** (96 mg, 0.47 mmol, 1 equiv). Flash column chromatography on silica gel (Et_2O) afforded **15j** (197 mg, 95%) as a yellow solid; mp 97–98 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, J=8.2 Hz, 1H), 7.12 (t, J=8.1 Hz, 1H), 6.68 (dd, J=8.1, 2.1 Hz, 1H), 6.66 (dd, J=8.1, 2.1 Hz, 1H), 6.60 (t, J=2.1 Hz, 1H), 6.42 (dd, J=8.1, 2.1 Hz, 1H), 6.32 (d, J=2.1 Hz, 1H), 4.90 (s, 2H), 3.74 (s, 3H), 3.68 (s, 3H), 3.57 (s, 3H), 3.13 (q, J=7.1 Hz, 4H), 0.96 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.6, 161.2, 160.4, 160.1, 158.4, 143.8, 130.6, 129.6, 119.5, 118.1, 113.1, 112.4, 104.3, 98.4, 55.5 (2C), 55.3, 48.7, 41.5 (2C), 12.9 (2C); IR (neat, cm^{-1}) 3054, 2933, 2098, 1618, 1587, 1422, 1375, 1282, 1206, 1032, 732; HRMS (ES$^+$) m/z [M+Na]$^+$ calcd for $C_{23}H_{28}N_4O_5Na$: 463.1957; found: 463.1969.

*4.11.3. N^1-(3-(tert-Butyldiphenylsilyloxy)phenyl)-N^3,N^3-diethyl-N^1-(2,4-dimethoxybenzyl)-2-diazomalonamide (**15k**).* Compound **15k** was prepared according to the general procedure (D) reported for **15a** starting from 3-(*tert*-butyldiphenylsilyloxy)-*N*-(2,4-dimethoxybenzyl)aniline **7k** (234 mg, 0.47 mmol, 1 equiv), distilled Et_3N (0.31 mL, 2.20 mmol, 4.7 equiv), and 2-diazo-3-(diethylamino)-3-oxopropanoyl chloride **14** (96 mg, 0.47 mmol, 1 equiv). Flash column chromatography on silica gel (heptane/AcOEt, 7/3) afforded **15k** (303 mg, 97%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, J=7.3 Hz, 4H), 7.40 (t, J=7.3 Hz, 2H), 7.32 (t, J=7.3 Hz, 4H), 7.13 (d, J=8.3 Hz, 1H), 6.94 (t, J=8.0 Hz, 1H), 6.59–6.55 (m, 2H), 6.54–6.53 (m, 1H), 6.33 (dd, J=8.3, 2.3 Hz, 1H), 6.30 (d, J=2.3 Hz, 1H), 4.75 (s, 2H), 3.75 (s, 3H), 3.53 (s, 3H), 3.08 (q, J=7.1 Hz, 4H), 1.05 (s, 9H), 0.98 (t, J=7.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.8, 161.7, 160.3, 158.4, 156.3, 143.5, 135.6 (4C), 132.6 (2C), 130.5, 130.3 (2C), 129.6, 128.0 (4C), 119.8, 118.6, 118.4, 118.0, 104.2, 98.4, 55.5, 55.3, 48.7, 41.7 (2C), 26.6 (3C), 19.6, 12.7 (2C); IR (neat, cm^{-1}) 2931, 2091, 1614, 1587, 1484, 1427, 1377, 1277, 1207, 1106, 1036, 700; HRMS (ES$^+$) m/z [M+Na]$^+$ calcd for $C_{38}H_{44}N_4O_5SiNa$: 687.2979; found: 687.2991.

*4.11.4. N^3,N^3-Diethyl-N^1-(2,4-dimethoxybenzyl)-N^1-(3-fluorophenyl)-2-diazomalonamide (**15l**).* Compound **15l** was prepared according to the general procedure (D) reported for **15a** starting from *N*-(2,4-dimethoxybenzyl)-3-fluoroaniline **7l** (123 mg, 0.47 mmol, 1 equiv), distilled Et_3N (0.31 mL, 2.20 mmol, 4.7 equiv), and 2-diazo-3-(diethylamino)-3-oxopropanoyl chloride **14** (96 mg, 0.47 mmol, 1 equiv). Flash column chromatography on silica gel (heptane/AcOEt, 7/3) afforded **15l** (199 mg, 99%) as a yellow solid; mp 108–109 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (d, J=8.4 Hz, 1H), 7.18 (br q, J=8.0 Hz, 1H), 6.88–6.79 (m, 3H), 6.43 (dd, J=8.4, 2.3 Hz, 1H), 6.32 (d, J=2.3 Hz, 1H), 4.90 (s, 2H), 3.74 (s, 3H), 3.56 (s, 3H), 3.10 (q, J=7.1 Hz, 4H), 0.93 (t, J=7.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.5, 162.7 (d, J=247.6 Hz), 160.7, 160.5, 158.3, 144.4 (d, J=9.9 Hz), 130.7, 129.8 (d, J=9.3 Hz), 122.8 (d, J=2.7 Hz), 117.6, 114.3 (d, J=23.0 Hz), 113.7 (d, J=20.9 Hz), 104.4, 98.4, 55.5, 55.2, 48.8, 41.4 (2C), 12.7 (2C); ^{19}F NMR (282 MHz, $CDCl_3$) δ −111.9; IR (neat, cm^{-1}) 2935, 2091, 1720, 1604, 1587, 1505, 1421, 1376, 1262, 1207, 1155, 1034; HRMS (ES$^+$) m/z [M+Na]$^+$ calcd for $C_{22}H_{25}FN_4O_4Na$: 451.1758; found: 451.1740.

*4.11.5. N^3,N^3-Diethyl-N^1-(2,4-dimethoxybenzyl)-N^1-(3-trifluoromethylphenyl)-2-diazomalonamide (**15m**).* Compound **15m** was prepared according to the general procedure (D) reported for **15a** starting from *N*-(2,4-dimethoxybenzyl)-3-(trifluoromethyl)-aniline **7m** (146 mg, 0.47 mmol, 1 equiv), distilled Et_3N (0.31 mL, 2.20 mmol, 4.7 equiv), and 2-diazo-3-(diethylamino)-3-oxopropanoyl chloride **14** (96 mg, 0.47 mmol, 1 equiv). Flash column chromatography on silica gel (Et_2O) afforded **15m** (218 mg, 97%) as a yellow solid; mp 63–64 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, J=8.2 Hz, 1H), 7.38–7.24 (m, 4H), 6.42 (dd, J=8.2, 2.1 Hz, 1H), 6.27 (d, J=2.1 Hz, 1H), 4.91 (s, 2H), 3.72 (s, 3H), 3.48 (s, 3H), 3.01 (q, J=7.0 Hz, 4H), 0.84 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.9, 160.6, 160.4, 158.3, 143.5, 131.3, 131.0, 130.6 (d, J=32.9 Hz), 129.5, 124.0 (d, J=3.8 Hz), 123.8 (d, J=272.8 Hz), 123.4 (d, J=3.3 Hz), 117.4, 104.4, 98.2, 55.5, 55.0, 48.9, 41.3 (2C), 12.6 (2C); ^{19}F NMR (282 MHz, $CDCl_3$) δ −62.4; IR (neat, cm^{-1}) 2931, 2091, 1614, 1587, 1484, 1427, 1377, 1277, 1207, 1106, 1036, 700; HRMS (ES$^+$) m/z [M+Na]$^+$ calcd for $C_{23}H_{25}F_3N_4O_4Na$: 501.1726; found: 501.1711.

4.12. General procedure (E) for the synthesis of the 2-silyloxyindole-3-carboxamides 16

*4.12.1. N,N-Diethyl-1-N-(2,4-dimethoxybenzyl)-2-(triisopropylsilyloxy)-1H-indole-3-carboxamide (**16a**).* To a solution of compound **15a** (164 mg, 0.40 mmol, 1 equiv) in CH_2Cl_2 (2 mL) held at room temperature under argon was added $Rh_2(NHCOCF_3)_4$ (13 mg, 0.02 mmol, 5 mol %). After 5 h of stirring under argon, the solution was cooled to 0 °C. Distilled Et_3N (171 μL, 2.50 mmol, 6.25 equiv) and TIPSOTf (135 μL, 0.50 mmol, 1.25 equiv) were then successively added. The solution was allowed to stir at 0 °C for 15 min before quenching with H_2O (2 mL) and extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were then dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (CH_2Cl_2/Et_2O/Et_3N, 9/7/0.1) to give **16a** (181 mg, 84%) as a light yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36–7.33 (m, 1H), 7.08–7.00 (m, 3H), 6.45 (d, J=2.4 Hz, 1H), 6.44 (d, J=8.3 Hz, 1H), 6.23 (dd, J=8.3, 2.4 Hz, 1H), 5.16 (s, 2H), 3.86 (s, 3H), 3.72 (s, 3H), 3.51 (q, J=6.7 Hz, 4H), 1.36 (hep, J=7.7 Hz, 3H), 1.16 (t, J=6.7 Hz, 6H), 1.03 (d, J=7.7 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 160.2, 157.5, 146.8, 131.0, 127.6, 125.6, 120.5, 120.4, 118.5, 118.0, 109.4, 104.1, 98.4, 93.3, 55.5 (2C), 41.0 (2C), 39.8, 18.1 (6C), 14.1 (2C), 13.6 (3C); IR (neat, cm^{-1}) 3420, 2937, 2862, 1712, 1613, 1463,

1361, 1207, 1126, 1035, 881, 674; HRMS (ES^+) m/z $[M+H]^+$ calcd for $C_{31}H_{47}N_2O_4Si$: 539.3305; found: 539.3298.

*4.12.2. N,N-Diethyl-1-N-(2,4-dimethoxybenzyl)-6-methoxy-2-(triisopropylsilyloxy)-1H-indole-3-carboxamide (**16j**).* Compound **16j** was prepared according to the general procedure (E) reported for **16a** starting from diazo **15j** (176 mg, 0.40 mmol, 1 equiv), $Rh_2(NHCOCF_3)_4$ (13 mg, 0.02 mmol, 5 mol %), distilled Et_3N (171 μL, 2.50 mmol, 6.25 equiv), and TIPSOTf (135 μL, 0.50 mmol, 1.25 equiv). Flash column chromatography on silica gel (CH_2Cl_2/Et_2O/Et_3N, 5.9/4/0.1) afforded **16j** (200 mg, 88%) as a light yellow oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, J=8.5 Hz, 1H), 6.75 (dd, J=8.5, 2.3 Hz, 1H), 6.64 (d, J=2.3 Hz, 1H), 6.53 (d, J=8.5 Hz, 1H), 6.49 (d, J=2.4 Hz, 1H), 6.29 (dd, J=8.5, 2.4 Hz, 1H), 5.15 (s, 2H), 3.90 (s, 3H), 3.76 (s, 6H), 3.53 (q, J=7.0 Hz, 4H), 1.38 (hep, J=7.5 Hz, 3H), 1.19 (t, J=7.0 Hz, 6H), 1.07 (d, J=7.5 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.8, 160.2, 157.5, 155.4, 145.8, 131.7, 127.8, 119.6, 119.1, 117.9, 109.0, 104.2, 98.3, 94.4, 92.8, 55.8, 55.5, 55.4, 41.5(2C), 39.7, 18.2 (6C), 14.1 (2C), 13.6 (3C); IR (neat, cm^{-1}) 3424, 2938, 2863, 1713, 1614, 1455, 1377, 1260, 1207, 1035, 809; HRMS (ES^+) m/z $[M+Na]^+$ calcd for $C_{32}H_{48}N_2O_5SiNa$: 591.3230; found: 591.3249.

*4.12.3. N,N-Diethyl-6-(tert-butyldiphenylsilyloxy)-1-N-(2,4-dimethoxybenzyl)-2-(triisopropylsilyloxy)-1H-indole-3-carboxamide (**16k**).* Compound **16k** was prepared according to the general procedure (E) reported for **16a** starting from diazo **15k** (266 mg, 0.40 mmol, 1 equiv), $Rh_2(NHCOCF_3)_4$ (13 mg, 0.02 mmol, 5 mol %), distilled Et_3N (171 μL, 2.50 mmol, 6.25 equiv), and TIPSOTf (135 μL, 0.50 mmol, 1.25 equiv). Flash column chromatography on silica gel (CH_2Cl_2/Et_2O/heptane/Et_3N, 4.9/3/2/0.1) afforded **16k** (289 mg, 91%) as a light yellow oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.62 (dd, J=7.9, 1.1 Hz, 4H), 7.35–7.22 (m, 6H), 7.01 (d, J=8.5 Hz, 1H), 6.54 (dd, J=8.5, 2.1 Hz, 1H), 6.42 (d, J=2.1 Hz, 1H), 6.37 (d, J=2.3 Hz, 1H), 6.32 (d, J=8.5 Hz, 1H), 6.15 (dd, J=8.5, 2.3 Hz, 1H), 4.88 (s, 2H), 3.74 (s, 3H), 3.73 (s, 3H), 3.45 (q, J=7.0 Hz, 4H), 1.32–1.22 (m, 3H), 1.13–1.07 (m, 6H), 1.03 (br s, 9H), 0.99 (d, J=7.5 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9, 160.0, 157.3, 150.7, 146.0, 135.8 (4C), 133.7 (2C), 131.6, 129.8 (2C), 127.7 (5C), 119.8, 118.7, 117.9, 113.7, 104.0, 100.6, 98.3, 92.7, 55.5, 55.3, 41.3 (2C), 39.7, 26.9 (3C), 18.2, 18.1 (6C), 17.9 (2C), 14.0 (2C), 13.6 (3C), 12.5; IR (neat, cm^{-1}) 3379, 2932, 2863, 1619, 1483, 1462, 1261, 1207, 1105, 1036, 954, 821; HRMS (ES^+) m/z $[M+Na]^+$ calcd for $C_{47}H_{64}N_2O_5Si_2Na$: 815.4252; found: 815.4264.

*4.12.4. N,N-Diethyl-1-N-(2,4-dimethoxybenzyl)-6-fluoro-2-(triisopropylsilyloxy)-1H-indole-3-carboxamide (**16l**).* Compound **16l** was prepared according to the general procedure (E) reported for **16a** starting from diazo **15l** (171 mg, 0.40 mmol, 1 equiv), $Rh_2(NHCOCF_3)_4$ (13 mg, 0.02 mmol, 5 mol %), distilled Et_3N (171 μL, 2.50 mmol, 6.25 equiv), and TIPSOTf (135 μL, 0.50 mmol, 1.25 equiv). Flash column chromatography on silica gel (CH_2Cl_2/Et_2O/heptane/Et_3N, 4.9/3/2/0.1) afforded **16l** (160 mg, 72%) as a light yellow oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.35–7.24 (m, 1H), 6.82–6.76 (m, 1H), 6.74 (dd, J=9.4, 2.4 Hz, 1H), 6.47 (d, J=8.4 Hz, 1H), 6.45 (d, J=2.4 Hz, 1H), 6.25 (dd, J=8.4, 2.4 Hz, 1H), 5.10 (s, 2H), 3.86 (s, 3H), 3.73 (s, 3H), 3.45 (q, J=7.3 Hz, 4H), 1.32 (hep, J=7.7 Hz, 3H), 1.15 (m, 6H), 1.03 (d, J=7.7 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 160.4, 159.3 (d, J=250.1 Hz), 155.6 (2C), 135.5 (d, J=9.7 Hz), 127.2, 121.7, 119.1 (d, J=9.3 Hz), 117.3, 108.4 (d, J=24.2 Hz), 104.2, 98.5 (2C), 96.5 (d, J=26.3 Hz), 55.6 (2C), 41.1 (2C), 40.0, 18.1 (6C), 15.0 (2C), 14.6 (3C); ^{19}F NMR (282 MHz, $CDCl_3$) δ −122.4; HRMS (ES^+) m/z $[M+Na]^+$ calcd for $C_{31}H_{45}FN_2O_4SiNa$: 556.3133; found: 556.3139.

*4.12.5. N,N-Diethyl-1-N-(2,4-dimethoxybenzyl)-6-(trifluoromethyl)-2-(triisopropylsilyloxy)-1H-indole-3-carboxamide (**16m**).* Compound **16m** was prepared according to the general procedure (E) reported for **16a** starting from diazo **15m** (191 mg, 0.40 mmol, 1 equiv), $Rh_2(NHCOCF_3)_4$ (13 mg, 0.02 mmol, 5 mol %), distilled Et_3N (171 μL, 2.50 mmol, 6.25 equiv), and TIPSOTf (135 μL, 0.50 mmol, 1.25 equiv). Flash column chromatography on silica gel (CH_2Cl_2/Et_2O/Et_3N, 5.9/4/0.1) afforded **16m** (102 mg, 42%) as a light yellow oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.40–7.37 (m, 2H), 7.27 (dd, J=7.8, 1.4 Hz, 1H), 6.50 (d, J=8.5 Hz, 1H), 6.46 (d, J=2.3 Hz, 1H), 6.26 (dd, J=8.5, 2.3 Hz, 1H), 5.19 (s, 2H), 3.88 (s, 3H), 3.73 (s, 3H), 3.48 (q, J=7.1 Hz, 4H), 1.37 (hep, J=7.5 Hz, 3H), 1.15 (t, J=7.1 Hz, 6H), 1.04 (d, J=7.5 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0, 160.6, 157.6, 148.5, 130.0, 128.1, 127.9, 124.1 (q, J=251.3 Hz), 122.4 (q, J=31.8 Hz), 118.4, 117.35, 117.33 (q, J=3.0 Hz), 106.9 (d, J=4.4 Hz), 104.4, 98.5, 94.0, 55.6, 55.5, 48.9, 41.3 (2C), 18.1 (6C), 14.1 (2C), 13.7 (2C), 12.5 (3C); ^{19}F NMR (282 MHz, $CDCl_3$) δ −60.3; IR (neat, cm^{-1}) 3424, 2940, 2864, 1614, 1557, 1462, 1301, 1208, 1158, 1112, 881; HRMS (ES^+) m/z $[M+Na]^+$ calcd for $C_{32}H_{45}F_3N_2O_4Si$ Na: 629.2998; found: 629.3019.

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