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Asymmetric synthesis of deuterated and fluorinated aromatic α,α-disubstituted amino acid derivatives

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Dedicated to Henri Kagan on the occasion of his 80th birthday

ABSTRACT

We herein present organocatalytic approaches to synthesize fluorinated and deuterated α-substituted phenylglycine derivatives. Whereas the addition of diethyl azodicarboxylate to fluorinated α-substituted aldehydes furnishes chiral non-racemic compounds, the use of chloramine-T as a nitrogen source represents a rapid access to sulfamidated fluorinated amino acid precursors. Additionally, further functionalization was achieved through the palladium-catalyzed coupling of a *p*-bromosubstituted aldehyde with a range of fluorine or deuterium-containing boronic acids. Oxidation of the aldehyde function and cleavage of the protection group of the nitrogen give way to the free fluorinated unnatural amino acids.

1. Introduction

Chiral amino compounds, among them particularly α-amino acids and their derivatives, play a central role in the emergence of life. Numerous examples of non-proteinogenic α-amino acids and related compounds have moved into the focus of biochemical research and drug discovery. They differ from their 'natural' relatives in the composition of the α-carbon centre, displaying either opposite stereochemistry or untypical substitution patterns.

Thus, the presence of a fully substituted α-carbon centre imposes severe conformational restrictions on the molecule and exhibits a pronounced helix-inducing potential when incorporated into peptides.[1] These specific peculiarities of the secondary structure were found to be responsible for the membrane destabilization exerted by peptaibols, a class of peptidic broad-spectrum antibiotics.[2,3]

Since some of the major drawbacks in the application of peptides as pharmaceuticals deal with their conformational flexibility, α,α-disubstituted amino acid derivatives[4] can be used to minimize the nonselective interactions with different receptors. The concept of forcing conformational constraint on otherwise flexible structures was carried further in the targeted synthesis of peptoids, where it was utilized in the design of non-peptidic small molecules to conformationally and functionally mimic biologically active peptides.[5]

The incorporation of fluorine in fluorocarbon compounds clearly demonstrates the unique properties of this outstanding element in organic chemistry. Besides the synthetic potential of fluorine itself and reagents derived from it, numerous fluorinated compounds have gained influence in the development of bioactive molecules.[6] Therefore, the introduction of fluorine has become a very important strategy to overcome serious problems of newly designed active compounds, such as insufficient bioavailability as a result of fast in vivo metabolism or poor transportation or diffusion through the body.[7] The substitution of carbon-bound hydrogen by fluorine to significantly enhance the metabolic stability caused by the strength and chemical stability of the C–F bond can thus improve the pharmacokinetic properties of drugs that are based on a peptide structure. In this context, it has been shown that the incorporation of even one fluorinated amino acid instead of its hydrocarbon analogue can not only have a strong impact on protein structure[8] but does also tremendously increases peptide and protein stability by forming very strong non-natural side chain interaction cores.[9] The modification by fluorine results in a high polarizability of the C–F bond and, consequently, of the entire carbon skeleton, while on the other hand the steric demand of the molecule is not significantly increased. Thus, the replacement of hydrogen with fluorine generally enhances lipophilicity, resulting in improved membrane permeability that facilitates transport through the blood–brain barrier, a property of particular importance in the development of peptide-based drugs.[10] These effects can best be measured by performing a so-called 'fluorine scan', which means systematically exchanging one or more hydrogen for fluorine.[11] Due to the sensitivity of ^{19}F NMR spectroscopy along with large ^{19}F–^{1}H coupling constants and chemical-shift anisotropy, fluorine incorporation has proved to be a particularly powerful tool for dynamic NMR studies of biological processes.[12]

Moreover, fluorinated amino acids have attracted considerable attention as synthetic targets for pharmaceutical and other biological applications.[13] Nevertheless, their application remains strongly

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limited to date. The main reasons for this are the restricted synthetic availability of fluorinated building blocks as well as the elaborate methods often required for their incorporation. For this reason, fast and convenient access to this class of interesting molecules is highly desirable.

Therefore, we decided to investigate the scope of two different organocatalytic approaches toward α,α-disubstituted fluorinated amino acids. Herein, we report the synthesis of a library of fluorinated and deuterated amino acid precursors via organocatalytic amination of aryl aldehydes.[14]

2. Results and discussion

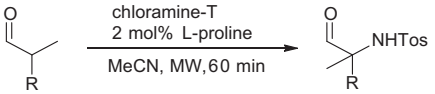
The aldehydes were synthesized according to the literature from the commercially available acetophenones.[15] In the first step a Wittig reaction was carried out with the corresponding acetophenones to yield enol ethers. These could then easily be cleaved by protonation and tautomerized with aq HBr resulting in the desired aldehydes. In the case of the deutero-substituted aldehyde **4f** (Scheme 1), the bromo substituent was supposed to be exchanged with organomagnesium reagents. As the lability of the carbonyl function of the ketone and the aldehyde renders them not useful for Grignard addition, the transformation was performed at this stage in 89% yield. Acidic opening of **3** delivered the *p*-deuterated substrate **4f** in 97% yield.

With the α-substituted aldehydes in hand,[16] we turned our attention toward the α-sulfamidation of 2-arylpropionaldehydes with the inexpensive and environmentally benign reagent chloramine-T. Under these conditions, we had previously been able to show that electron-withdrawing groups or atoms such as fluorine have a stabilizing effect on the reaction which results in higher yields. Electron-donating groups on the other hand lower the yield, most likely because of a halogenation of the electron-rich aromatic ring. The reactions were carried out under microwave conditions according to a literature-known procedure at 60 °C within 60 min and using only 2 mol % L-proline.[17]

In this manner we were able to produce a range of fluoro-containing sulfamidated aldehydes with different aromatic substituents (Table 1).

Here, however, all the substituents on the aromatic backbone seem to have only a small impact on the resulting yields as they all lay in the range between 62% and 85%. Altogether, no trend is perceptible. Apart from fluoro-substituted aldehydes we also submitted deuterated aldehydes to the process (Table 1, entries 6 and 7). Regardless of the altered electronic properties, yields of 86% for **5f** and 74% for **5g** were achieved. Nevertheless, the resulting products could only be obtained as racemic mixtures. It is possible that the reaction proceeds via enolate-intermediates rather than enamines. If so, the chiral catalyst loses its influence on the side of the attack. Recently, other methods for α-functionalization (e.g., chlorination) were published which can be used for the same purpose.[18] The racemic aldehydes can subsequently be oxidized to the corresponding amino acids. In a first step the aldehyde is oxidized with sodium chlorite/hydrogen peroxide.[19] The following

Table 1
α-Sulfamidation of 2-arylpropionaldehydes with chloramine-T[a]



4a-g **5a-g**

Entry	R	Temp[b] (°C)	Power[c] (W)	Product	Yield[d] (%)
1	2-F–C_6H_4	60	200	**5a**	70
2	3-F–C_6H_4	60	200	**5b**	62
3	4-F–C_6H_4	60	200	**5c**[17]	85
4	3-CF_3–C_6H_4	60	200	**5d**	73
5	4-CF_3–C_6H_4	60	200	**5e**[17]	79
6	4-D-C_6H_4	60	200	**5f**	86
7	α-CD_3–C_6H_4	60	200	**5g**	74

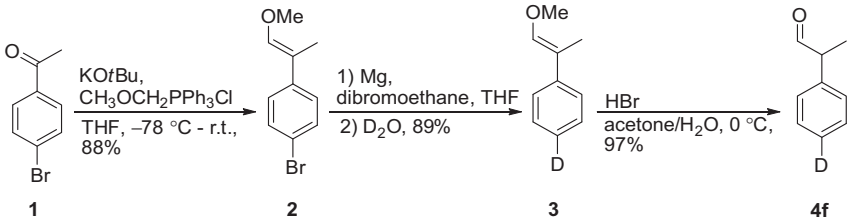
[a] Reaction conditions: 1.0 equiv aldehyde, 1.5 equiv chloramine-T, 2 mol % L-proline.
[b] For cooling, compressed air with a constant pressure of 0.7 bar (10 psi) was used during the entire experiment.
[c] Application of constant microwave power.
[d] Isolated yields.

esterification is performed with trimethylsilyldiazomethane to deliver the fully protected amino acid **7** (Scheme 2). In a last step hydrogen bromide in acetic acid[20] was used to furnish the free α-methylphenylglycine **8** (81% overall yield).

In most cases, however, it is necessary to install enantiomerically pure amino acids. With this goal in mind, a different organocatalytic strategy was considered. We have previously reported the microwave-enhanced addition of diethyl azodicarboxylate to aromatic α-methylaldehydes.[21] When screening the most commonly used solvents, the incapability of low-absorbing solvents such as 1,4-dioxane or chloroform became visible. On the other hand, acetonitrile was found to be the solvent with the best conversion and the best enantiomeric ratio.

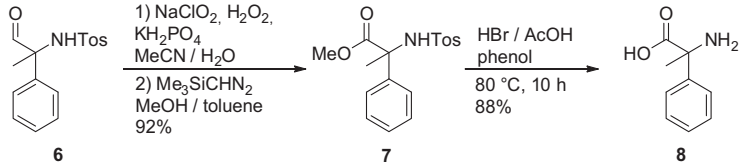
In this study, therefore, the amidation reactions were performed with 50 mol % L-proline, 1.5 equiv diethyl azodicarboxylate in acetonitrile under microwave irradiation at 60 °C within 30–60 min (Table 2).

While the unsubstituted 2-phenylpropionaldehyde gave the amidated product **9l** with complete conversion and good enantioselectivity, moving to 2-naphthylpropionaldehyde resulted in a decrease of yield to 76% for **9m** whereas the enantioselectivity remained the same (90% and 89% ee). A variety of fluoro-substituted aromatic aldehydes were subjected to the reaction conditions. The substitution patterns played a significant role, as electron-withdrawing groups have a stronger impact when they are positioned closer toward the reaction centre. Consequently, when moving from the *ortho*- over *meta*- to the *para*-position, the yield rose significantly from 38% to 91% and the enantioselectivity increased from 69% to 89% (Table 2, **9a** to **9c**). In the case of the trifluoromethyl-substituent, the yield and the ee stayed in the same range (Table 2, entries 6 and 7). Although fluorinated compounds are particularly prone to self-disproportionation of the enantiomers during achiral chromatography, this could not be observed here.[22]



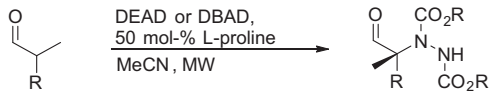
1 **2** **3** **4f**

Scheme 1. Synthesis of deuterated aldehyde **4f**.



Scheme 2. Oxidation and deprotection of sulfamidated aldehydes.

Table 2
α-Amination of 2-arylpropionaldehydes with dialkyl azodicarboxylates[a]



4a-j **9a-m**

Entry	R	Azo-compound	Time (min)	Product	Yield[b] (%)	ee[c,d] (%)
1	C_6H_5	DEAD	30	**9l**[21]	97	89 (*R*)
2	2-Naph	DEAD	30	**9m**[21]	76	90 (*R*)
3	2-F–C_6H_4	DEAD	60	**9a**	38	69 (*R*)
4	3-F–C_6H_4	DEAD	60	**9b**	77	87 (*R*)
5	4-F–C_6H_4	DEAD	60	**9c**[21]	91	89 (*R*)
6	3-CF_3–C_6H_4	DEAD	60	**9d**	65	72 (*R*)
7	4-CF_3–C_6H_4	DEAD	60	**9e**[21]	63	56 (*R*)
8	4-D–C_6H_4	DEAD	60	**9f**	68	n.d.
9	α-CD_3–C_6H_4	DEAD	60	**9g**	88	n.d.
10	4-Br–C_6H_4	DEAD	60	**9h**[21]	75	86 (*R*)
11	4-Br–C_6H_4	DBAD	60	**9i**[21]	72	53 (*R*)
12	4-F–C_6H_4	DBAD	60	**9j**[21]	85	59 (*R*)
13	C_6H_5	DBAD	60	**9k**[21]	83	81 (*R*)[e]

[a] Reaction conditions: 1.0 equiv aldehyde, 0.5 equiv L-proline, 1.5 equiv DEAD, $T = 60$ °C, application of constant microwave power of 200 W. For cooling, compressed air with a constant pressure of 0.7 bar (10 psi) was used during the entire experiment.
[b] Isolated yields.
[c] Determined by HPLC analysis using a chiral column (Chiracel AD); see Section 4.1 for details. n.d. not determined.
[d] Absolute configuration according to correlation with related systems.[16,17,21]
[e] Reaction conditions: solvent = dichloromethane, rt, 5 d.

Furthermore, the products obtained have, despite their fluorine content, a very low vapor pressure, thus change of enantioselectivity due to volatility did not occur in our case.[23]

Besides diethyl azodicarboxylate, also dibenzyl azodicarboxylate could be utilized as nitrogen-transfer reagent under microwave irradiation (Table 2, entries 11–13).

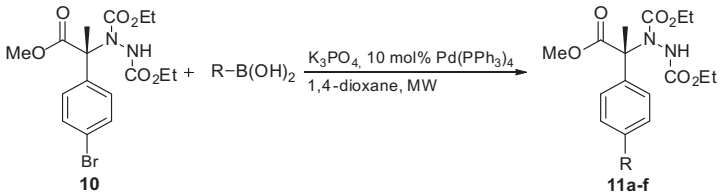
Further functionalization of the aromatic backbone was achieved by introduction of different units through the bromine substituent. Therefore, aldehyde **9h** was first converted to the methylester followed by a Suzuki reaction. In this way the amount of required and the often costly boronic acids could be kept at a minimum.

For the next step, a literature-known procedure for the Suzuki–Miyaura reaction in the microwave was applied (Table 3).[24] The reaction of **10** with phenyl boronic acid in a mixture of toluene/ethanol/water 3:3:1 with tetrakis(triphenylphosphine)-palladium at 100 °C did not result in the formation of the desired product **11a**. Changing the solvent to 1,4-dioxane and raising the temperature to 150 °C, however, resulted in 61% product after 30 min (Table 3, entry 1).[25] By increasing the reaction time to 2 h, 82% of the coupling product **11a** could be obtained. When assigning the reaction conditions to 4-fluorophenyl boronic acid, the level of reactivity remained the same (Table 3, entry 4, **11b**).

Moving to phenyl boronic acids bearing more of the electron-withdrawing fluorine atoms, a drop in yield could be observed which derives from the decreased reactivity of the electronically deactivated boronic acids in the coupling process. The formation of **11f** as a last example goes in line with the unsubstituted compound **11a**.

The deprotection of hydrazino acid precursors can be achieved in very good yields (Scheme 3).[16] Oxidation of the aldehyde **9k** with sodium chlorite and subsequent treatment with trimethylsi-

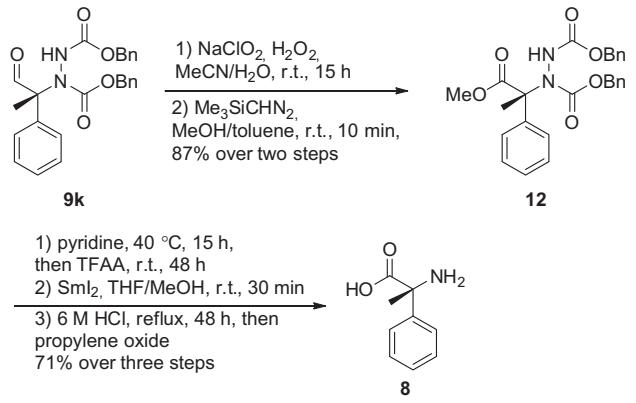
Table 3
Suzuki–Miyaura reaction of an aminoacid precursor with functionalized phenyl boronic acid[a]



10 **11a-f**

Entry	R	Time (h)[b]	Product	Yield[c] (%)
1	C_6H_5	0.5	**11a**	61
2	C_6H_5	1	**11a**	79
3	C_6H_5	2	**11a**	82
4	4-F–C_6H_4	2	**11b**	88
5	3,4,5-F–C_6H_2	2	**11c**	61
6	2,3,4,5,6-F–C_6	2	**11d**	69
7	4-CF_3–C_6H_4	2	**11e**	69
8	2,3,4,5,6-D-C_6	2	**11f**	81

[a] Reaction conditions: 1.0 equiv **10**, 1.5 equiv boronic acid, 3 equiv K_3PO_4, 10 mol % $Pd(PPh_3)_4$, 6 mL 1,4-dioxane per mmol substrate, $T = 150$ °C, application of constant microwave power of 200 W.
[b] For cooling, compressed air with a constant pressure of 0.7 bar (10 psi) was used during the entire experiment.
[c] Isolated yields.



Scheme 3. Oxidation of the aldehyde **9k** and cleavage of the protecting groups.

lyldiazomethane furnished the completely protected methyl ester **12** in 87% yield.

Applying then a selective benzyloxycarbonyl deprotection using trifluoroacetanhydride (TFAA), cleavage of the hydrazine with SmI_2 and finally hydrolysis of the ester function gave 71% of the phenylglycine derivative **8**.

3. Conclusions

In summary, we presented an easy and fast method to access a variety of fluorinated or deuterated configurationally stable α,α-disubstituted amino acid precursors. Starting from easily accessible aromatic aldehydes, different organocatalytic strategies could be applied successfully to fluorinated and deuterated aromatic aldehydes. Using chloramine-T as a nitrogen source, the racemic sulfamidated products could be obtained in good to very good yields within 1 h. For enantiomerically enriched compounds, the addition of diethyl azodicarboxylate to the above-mentioned aldehydes could be performed under microwave irradiation to furnish the amidated compounds in good to excellent yields and up to 90% ee. Further functionalities could be introduced through a Suzuki–Miyaura reaction on the aromatic backbone to deliver the biphenyl-bearing amino acid precursor in 61–82% yield. These products can easily be oxidized and deprotected to the corresponding unnatural amino acids, thus opening a way to a range of substituted amino acid moieties which then can be further utilized or manipulated.

4. Experimental section

4.1. General

All chemicals were purchased and used without further purification. The aldehydes and the enol ether **3** were synthesized according to the literature.[17] The products were purified by flash chromatography[26] using silica 60 from SDS (0.035–0.070 mm) or Merck (0.040–0.063 mm) and sea sand (purified with acid and calcined) from Merck. The solvents were purified by distillation and were determined by volume. The microwave-assisted reactions were conducted using a focused microwave unit (Discover® Reactor from CEM Corporation). The instrument consists of a continuous focused microwave power delivery system with operator-selectable power output from 0 to 300 W. In all experiments, the microwave power was held constant to ensure reproducibility. Reactions were performed in 10 mL glass vessels, which were sealed with a septum and locked into a pressure device, which controlled the pressure in the reaction vessel (maximum 10 bar). The specified reaction time corresponds to the irradiation time. The temperature was monitored by an infrared temperature sensor positioned below the reaction vessel. The indicated temperature corresponds to the maximum temperature reached during each experiment.

^{1}H NMR spectra were recorded at 400 MHz on Bruker AM400, the ^{13}C NMR spectra were recorded at 100 MHz, respectively. The chemical shifts are reported in parts per million (ppm) relative to the solvent residual peak.[27] HPLC was performed on an Agilent 1100 Series using Diacel Chiralpak AS (250 × 4.6 mm) or Diacel Chiracel OD (250 × 4.0 mm, 10 μm). Rotational values were determined on a Perkin Elmer 241 Polarimeter at λ = 589 nm (sodium D-Line). The concentration *c* is given in (g/100 mL). The ee's were determined by comparison with the racemic products obtained by application of DL-proline as a catalyst.

4.1.1. GP 1: General procedure for the proline-catalyzed α-sulfamidation under microwave irradiation

In a 10 mL vessel were placed 1.00 mmol (1.0 equiv) of the aldehyde, 0.02 mmol (2 mol %) L-proline, 1.50 mmol (1.5 equiv) chloramine-T, 5 mL acetonitrile, and a magnetic stir bar. The vessel was sealed with a septum, placed in a MW cavity, and locked with the pressure device. Constant microwave irradiation of 200 W as well as simultaneous air-cooling (0.7 bar, 10 psi) was used during the entire reaction time (30 min, 60 °C). After cooling to rt, the solvent was removed under reduced pressure, and the product was purified by column chromatography (diethyl ether/*n*-pentane) to afford the α-sulfamidated aldehyde as a colorless solid.

4.1.2. GP 2: General procedure for the synthesis of *N,N′*-bis(ethoxycarbonyl)-2-hydrazino-2-phenylpropionaldehyde under microwave irradiation

In a 10 mL vessel were placed 1.0 mmol (1.0 equiv) of the aldehyde, 0.5 mmol (50 mol %) L-proline, 1.5 mmol (1.5 equiv) diethyl azodicarboxylate, 5 mL acetonitrile, and a magnetic stir bar. The vessel was sealed with a septum, placed in a MW cavity, and locked with the pressure device. Constant microwave irradiation of 200 W as well as simultaneous air-cooling (0.7 bar, 10 psi) was used during the entire reaction time (60 min, 60 °C). After cooling to rt, the solvent was removed under reduced pressure and the product was purified by column chromatography (*n*-pentane/diethyl ether) to afford the α-aminated aldehyde as an oil.

4.1.3. GP 3: General procedure for the synthesis of *N,N′*-bis(ethoxycarbonyl)-2-hydrazino-2-phenylpropionaldehyde at room temperature

In a 10 mL vessel was placed 1.0 mmol of the aldehyde (1.0 equiv), 1.5 mmol diethyl azodicarboxylate (1.5 equiv), 0.5 mmol L-proline (50 mol %), 5 mL acetonitrile, and a magnetic stir bar. The reaction mixture was vigorously stirred at rt until TLC indicated complete conversion. The solvent was removed under reduced pressure and the product was purified by column chromatography (*n*-pentane/diethyl ether) to afford the α-aminated carbonyl compound as an oil.

4.1.4. GP 4: General procedure for the esterification of α-sulfamidated or α-aminated aldehydes

At first, 1.00 mmol (1.00 equiv) of the aldehyde was dissolved in 5.0 mL of acetonitrile along with 0.28 mmol (0.28 equiv) KH_2PO_4 in 2.0 mL water and 0.5 mL (1.00 mmol, 1.00 equiv) 35% H_2O_2. To the resulting mixture was added a solution of 1.74 mmol (1.74 equiv) $NaClO_2$ in 5.0 mL of water dropwise, keeping the temperature of the mixture below 10 °C. After the mixture was stirred for 12 h, 0.08 mmol (0.08 equiv) of Na_2SO_3 was added and the resulting mixture was partitioned between brine and dichloromethane, the layers were separated, and the aqueous layer was extracted with

dichloromethane. The combined organic extracts were washed with brine, dried, and concentrated under reduced pressure to give a residue that was taken up in toluene/methanol 1:2 and treated with an ethereal solution of trimethylsilyldiazomethane at 0 °C for five minutes until bubbling subsided. The excess trimethylsilyldiazomethane was quenched with a few drops of acetic acid and the solvent was removed in vacuo. Column chromatography (*n*-pentane/diethyl ether) delivered the product as a colorless solid.

4.1.5. GP 5: General procedure for the Suzuki-coupling of diethyl 1-(2-(4-bromophenyl)-1-methoxy-1-oxopropan-2-yl) hydrazine-1,2-dicarboxylate with phenyl boronic acids under microwave irradiation

In a 10 mL vessel under argon were placed 0.50 mmol (1.0 equiv) of the ester, 0.75 mmol (1.5 equiv) phenyl boronic acid, 1.00 mmol (2.0 equiv) K_3PO_4, 0.05 mmol (10 mol %) tetrakis(triphenylphosphine)palladium, 3 mL dioxane, and a magnetic stir bar. The vessel was sealed with a septum, placed in a MW cavity, and locked with the pressure device. Constant microwave irradiation of 200 W as well as simultaneous air-cooling (0.7 bar, 10 psi) was used during the entire reaction time (120 min, 150 °C). After cooling to rt, the resulting mixture was partitioned between brine and dichloromethane, the layers were separated, and the aqueous layer was extracted with dichloromethane. The combined organic extracts were washed with brine, dried, and the solvent was removed in vacuo. The product was purified by column chromatography (*n*-pentane/diethyl ether) to afford the coupling product as an oil.

4.2. 4-Deutero-4-(2-methoxy-1-methylvinyl)-benzene 3

Under argon, 90 mg (40 mmol) of magnesium and 20 mL of dry THF were placed together in a column fixed with a reflux condenser and a magnetic stir bar. To activate magnesium, five drops of dibromoethane were added and the mixture was quickly heated with the heat gun. Then 1130 mg (5.0 mmol) of 1-bromo-4-(1-methoxyprop-1-en-2-yl)-benzene was added and the reaction mixture was stirred at rt for three hours. After this time 1.01 mL D_2O was added and after three more hours of stirring at rt the reaction mixture was filtered over Celite and the solvent was removed in vacuo. Flash chromatography on silica with *n*-pentane/diethyl ether 40:1 delivered 669 mg (4.45 mmol, 89%) of a mixture of *E*/*Z*-isomers (*E*/*Z* 1.48:1, determined by integration of the methyl signals) a colorless oil. R_f = 0.32 (*n*-pentane/diethyl ether 40:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.02, 2.10 (d, J = 1.4 Hz, 3H, CH_3), 3.75, 3.80 (s, 3H, OCH_3), 6.21, 6.51 (q, J = 1.4 Hz, 1H, CHvinyl), 7.39–7.43 (m, 4H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 12.6, 18.3 (CCH_3), 59.9, 60.1 (OCH_3), 110.9, 114.5 (CCH_3), 127.1, 127.8 (C-3′, C-5′), 125.0, 128.2 (C-2′, C-6′), 132.1 (t, J = 17.5 Hz, C-4′), 138.4 (C-1′), 140.7 ($CHOCH_3$), 144.6, 145.2 ($CHOCH_3$) ppm. IR (KBr): υ^{-1} = 3027 (w), 2932 (w), 2833 (w), 1654 (m), 1595 (w), 1493 (w), 1458 (w), 1409 (w), 1223 (m), 1135 (m), 1113 (w), 1010 (w), 982 (vw), 860 (w) cm^{-1}. MS (EI, 70 eV): *m/z* (%): 149 (100) [M^+], 134 (18) [$C_9H_8DO^+$], 196 (85) [$C_8H_7D^+$], 78 (17) [$C_8H_7D^+$]. HRMS ($C_{10}H_{11}DO$): calcd: 149.0951, found: 149.0956.

4.3. 2-(4′-Deuterophenyl)propanal 4f

A solution of 639 mg (4.20 mmol) 4-deutero-4-(2-methoxy-1-methylvinyl)-benzene in 80 mL acetone/water 4:1 was treated with 4.6 mL aq HBr at 0 °C. The reaction mixture was stirred for 24 h and the procedure was repeated, until no further change of product/starting material ratio could be seen by TLC. The aqueous phase was neutralized with satd $NaHCO_3$ and then extracted with dichloromethane. The organic phase was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography on silica with *n*-pentane/diethyl ether 5:1 delivered 409 mg (4.16 mmol, 99%) of a colorless oil. R_f = 0.35 (pentane/diethyl ether 5:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36 (d, J = 7.1 Hz, 3H, $CHCH_3$), 3.55 (dq, J = 7.1, 1.3 Hz, 1H, $CHCH_3$), 7.13 (d, J = 8.1 Hz, 2H, 3′-H, 5′-H), 7.30 (d, J = 8.1 Hz, 2H, 2′-H, 6′-H), 9.60 (d, J = 1.3 Hz, 1H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.6 ($CHCD_3$), 53.0 ($CHCD_3$), 127.3 (t, J = 24.4 Hz, C-4′), 129.0 (C-3′, C-5′), 129.1 (C-2′, C-6′), 137.8 (C-1′), 201.1 (CHO) ppm. IR (KBr): υ^{-1} = 3078 (m), 2978 (m), 2934 (m), 2817 (m), 2719 (w), 1920 (w), 1722 (s), 1599 (m), 1492 (m), 1454 (m), 1417 (w), 1371 (m), 1211 (w), 1065 (m), 1020 (m), 856 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%): 135 (13) [M^+], 106 (100) [M^+−CO], 78 (14) [$C_6H_4D^+$]. HRMS (C_9H_9DO): calcd: 135.0794, found: 135.797.

4.4. *N*-(2-(2′-Fluorophenyl)-1-oxopropan-2-yl)-4-methylbenzenesulfonamide 5a (Table 1, entry 1)

The product was synthesized following **GP 1**, using 0.152 g (1.00 mmol) of 2-(2′-fluorophenylphenyl)propanal, 0.423 g (1.50 mmol) chloramine-T, 3 mg (0.02 mmol) L-proline, and 5 mL acetonitrile. Flash chromatography on silica with *n*-pentane/diethyl ether 2:1 delivered 0.223 g (0.70 mmol, 70%) of a colorless solid. R_f = 0.12 (*n*-pentane/diethyl ether 2:1). Mp = 138 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.85 (s, 3H, CCH_3), 2.24 (s, 3H, $C^{4''}{}_{Ts}CH_3$), 6.00 (br s, 1H, NH), 6.44 (dd, J = 11.3, 7.9 Hz, 1H, 3′-H), 6.89 (d, J = 8.0 Hz, 2H, 3″-H_{Ts}, 5″-H_{Ts}), 7.07–7.13 (m, 2H, 4′-H, 5′-H), 7.16 (d, J = 8.1 Hz, 2H, 2″-H_{Ts}, 6″-H_{Ts}), 7.42 (d, J = 7.8 Hz, 1H, 6′-H), 9.11 (s, 1H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.5 (CCH_3), 21.4 ($C^{4''}{}_{Ts}CH_3$), 66.4 (CCH_3), 115.6 (d, J = 21.7 Hz, C-3′), 121.6 (d, ^3J = 11.3 Hz, C-4′), 124.5 (d, J = 2.9 Hz, C-5′), 126.5 (C_{Ts}-2″, C_{Ts}-6″), 128.9 (C_{Ts}-3″, C_{Ts}-5″), 129.57 (d, J = 3.1 Hz, C-6′), 131.28 (d, J = 8.8 Hz, C-1′), 138.1 (C_{Ts}-1″), 142.5 (C_{Ts}-4″), 160.3 (d, J = 249.6 Hz, C-2′), 193.4 (CHO) ppm. ^{19}F NMR (400 MHz, $CDCl_3$): δ = −111.9 ppm. IR (KBr): υ^{-1} = 3259 (m), 3070 (w), 2984 (w), 2835 (w), 1742 (m), 1599 (w), 1487 (w), 1445 (w), 1365 (w), 1328 (m), 1164 (m), 816 (w), 765 (m), 706 (w) cm^{-1}. FAB-MS: *m/z* (%) = 322 (90) [M+H$^+$], 292 (100) [M^+–CHO], 172 (87) [$C_7H_8NO_2S^+$], 154 (98) [$C_7H_7SO_2^+$], 136 (75) [$C_8H_8FN^+$] HRMS ($C_{16}H_{17}FNO_3S$): calcd: 322.0913, found: 322.0916. Anal. Calcd for $C_{16}H_{16}FNO_3S$ (321.08 g/mol): C, 59.80; H, 5.02; N, 4.36; S, 9.98. Found: C, 58.96; H, 4.88; N, 4.78; S, 10.04.

4.5. *N*-(2-(3′-Fluorophenyl)-1-oxopropan-2-yl)-4-methylben 5b (Table 1, entry 2)

The product was synthesized following **GP 1**, using 0.152 g (1.00 mmol) of 2-(3′-fluorophenyl)propanal, 0.423 g (1.50 mmol) chloramine-T, 0.003 g (0.02 mmol) L-proline, and 5 mL acetonitrile. Flash chromatography on silica with *n*-pentane/diethyl ether 2:1 delivered 0.189 g (0.62 mmol, 62%) of a colorless solid. Mp = 101 °C. R_f = 0.12 (*n*-pentane/diethyl ether 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.86 (s, 3H, CCH_3), 2.35 (s, 3H, $C^{4''}{}_{Ts}CH_3$), 6.05 (br s, 1H, NH), 6.76–6.79 (m, 1H, 4′-H), 6.89–6.95 (m, 2H, 5′-H, 6′-H), 7.08 (d, J = 8.0 Hz, 2H, 2″-H_{Ts}, 6″-H_{Ts}), 7.17 (dt, J = 8.1, 5.9 Hz, 1H, 2′-H), 7.38 (d, J = 8.1 Hz, 2H, 3″-H_{Ts}, 5″-H_{Ts}), 9.11 (s, 1H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.0 (CCH_3), 21.3 ($C^{4''}{}_{Ts}CH_3$), 66.4 (CCH_3), 114.8 (d, J = 22.8 Hz, C-4′), 115.6 (d, J = 22.0 Hz, C-2′), 126.6 (C_{Ts}-2″, C_{Ts}-6″), 123.1 (C-6′), 129.2 (C_{Ts}-3″, C_{Ts}-5″), 129.4 (C-1′), 130.3 (d, J = 8.3 Hz, C-5′), 138.8 (C_{Ts}-1″), 143.1 (C_{Ts}-4″), 162.8 (d, J = 247.7 Hz, C-3′), 193.7 (CHO) ppm. ^{19}F NMR (400 MHz, $CDCl_3$): δ = −111.3 ppm. IR (KBr): υ^{-1} = 3274 (m), 3067 (w), 2985 (w), 2867 (w), 2710 (vw), 1731 (s), 1612 (m), 1592 (s), 1489 (s), 1384 (s), 1329 (s), 1161 (vs), 1093 (s), 964 (m), 815 (m), 787 (m), 739 (w), 696 (w) cm^{-1}. FAB-MS: *m/z* (%): 322 (36) [M+H$^+$], 292 (51) [M^+–CHO], 172 (55) [$C_7H_8NO_2S^+$], 155 (63) [$C_7H_7SO_2^+$], 136 (100) [$C_8H_8FN^+$], 107 (34) [$C_7H_4F^+$], 91 (59) [$C_7H_7^+$], 77 (29) [$C_6H_4^+$]. HRMS ($C_{16}H_{17}FNO_3S$): calcd: 322.0913,

found: 322.0916. Anal. Calcd for $C_{16}H_{16}FNO_3S$ (321.08 g/mol): C, 59.80; H, 5.02; N, 4.36; S, 9.98. Found: C, 59.38; H, 5.34; N, 4.03; S, 9.39.

4.6. 4-Methyl-*N*-(1-oxo-2-(3-(trifluoromethyl)phenyl)propan-2-yl)benzenesulfonamide 5d (Table 1, entry 4)

The product was synthesized following **GP 1**, using 0.202 g (1.00 mmol) of 2-(3′-trifluoromethy)propanal, 0.423 g (1.50 mmol) chloramine-T, 0.003 g (0.02 mmol) L-proline, and 5 mL acetonitrile. Flash chromatography on silica with *n*-pentane/diethyl ether 2:1 delivered 0.269 g (0.73 mmol, 73%) of a colorless solid. R_f = 0.10 (*n*-pentane/diethyl ether 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.88 (s, 3H, CC*H*$_3$), 2.25 (s, 3H, C$^{4''}{}_{Ts}$CH$_3$), 6.04 (br s, 1H, NH), 6.96 (d, *J* = 8.0 Hz, 2H, 3″-H$_{Ts}$, 5″-H$_{Ts}$), 7.14 (s, 1H, 2′-H), 7.23 (d, *J* = 8.3 Hz, 2H, 2″-H$_{Ts}$, 6″-H$_{Ts}$), 7.30 (d, *J* = 7.7 Hz, 1H, 5′-H), 7.36 (d, *J* = 8.0 Hz, 1H, 4′-H), 7.40 (d, ^{3}*J* = 7.7 Hz, 1H, 6′-H), 9.05 (s, 1H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.2 (*C*CH$_3$), 21.3 (C$^{4''}{}_{Ts}$CH$_3$), 66.4 (*C*CH$_3$), 124.5 (C-4′), 126.9 (C-3′), 126.4 (C$_{Ts}$-2″, C$_{Ts}$-6″), 129.3 (C-5′), 129.4 (C$_{Ts}$-3″, C$_{Ts}$-5″), 131.1 (q, *J* = 32.7 Hz, C-4′), 135.1 (C-1′), 138.6 (C$_{Ts}$-1″), 143.3 (C$_{Ts}$-4″), 193.7 (CHO) ppm. IR (KBr): υ^{-1} = 3239 (m), 3067 (w), 2978 (w), 2844 (w), 2730 (w), 1738 (m), 1598 (m), 1496 (m), 1441 (m), 1402 (m), 1330 (s), 1148 (m), 1093 (m), 1072 (m), 878 (m), 811 (m), 704 (m) cm^{-1}. FAB-MS: *m/z* (%): 372 (35) [M$^+$], 342 (100) [M$^+$–CHO], 239 (52), 188 (49), 172 (93) [$C_9H_7F_3^+$], 155 (74) [$C_7H_7SO_2^+$], 139 (27), 91 (82) [$C_7H_7^+$]. HRMS ($C_{17}H_{17}F_3NO_3S$): calcd: 372.0881, found: 372.0883. Anal. Calcd $C_{17}H_{16}F_3NO_3S$ (371.08 g/mol): C, 54.98; H, 4.34; N, 3.77; S, 8.63. Found: C, 54.47; H, 4.43; N, 4.02; S, 8.24.

4.7. *N*-(2-(4-Deuterophenyl)-1-oxopropan-2-yl)-4-methylbenzene 5f (Table 1, entry 6)

The product was synthesized following **GP 1**, using 0.125 g (0.93 mmol) of 2-(4′-deuterophenyl)propanal, 0.391 g (1.40 mmol) chloramine-T, 0.003 g (0.02 mmol) L-proline, and 5 mL acetonitrile. Flash chromatography on silica with *n*-pentane/diethyl ether 1:1 delivered 0.242 g (0.80 mmol, 86%) of a colorless solid. Mp = 105 °C. R_f = 0.25 (*n*-pentane/diethyl ether 1:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.88 (s, 3H, CC*H*$_3$), 2.34 (s, 3H, C$^{4'}{}_{Ts}$CH$_3$), 5.98 (br s, 1H, NH), 7.05 (d, *J* = 7.9 Hz, 2H, 3″-H$_{Ts}$, 5″-H$_{Ts}$), 7.11 (d, *J* = 8.4 Hz, 2H, 2′-H, 6′-H), 7.18 (d, *J* = 8.4 Hz, 2H, 3′-H, 5′-H), 7.35 (d, *J* = 8.4 Hz, 2H, 2″-H$_{Ts}$, 6″-H$_{Ts}$), 9.13 (s, 1H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.6 (CH$_3$), 21.4 (C$^{4'}{}_{Ts}$CH$_3$), 66.8 (*C*CH$_3$), 126.6 (C-4′), 127.5 (C-3′, C-5′), 128.7 (C$_{Ts}$-2″, C$_{Ts}$-6″), 129.2 (C-2′, C-6′), 129.5 (C$_{Ts}$-3″, C$_{Ts}$-5″), 134.1 (C-1′), 139.1 (C$_{Ts}$-1″), 142.8 (C$_{Ts}$-4″), 194.3 (CHO) ppm. IR (KBr): υ^{-1} = 3253 (m), 3068 (w), 2975 (w), 2842 (w), 2722 (w), 1743 (m), 1599 (w), 1495 (w), 1403 (m), 1365 (m), 1328 (m), 1160 (m), 902 (m), 817 (m), 707 (m) cm^{-1}. FAB-MS: *m/z* (%): 305 (36) [M+H$^+$], 275 (100) [M$^+$ − CHO], 239 (50), 172 (55) [$C_7H_8NO_2S^+$], 155 (42) [$C_7H_7SO_2^+$], 91 (33) [$C_7H_7^+$]. HRMS ($C_{16}H_{17}DNO_3S$): calcd: 305.1070, found: 305.1066. Anal. Calcd for $C_{16}H_{16}DNO_3S$ (304.10 g/mol): C, 63.13; H, 5.96; N, 4.60; S, 10.53. Found: C, 62.42; H, 5.89; N, 4.81; S, 10.33.

4.8. *N*-(2-Phenyl-1-oxo-2-trideutero-propan-2-yl)-4-methyl 5g (Table 1, entry 7)

The product was synthesized following **GP 1**, using 0.085 g (0.62 mmol) of α,α,α-trideutero-2-phenylpropanal, 0.262 g (0.93 mmol) chloramine-T, 0.002 g (0.01 mmol) L-proline, and 5 mL acetonitrile. Flash chromatography on silica with *n*-pentane/diethyl ether 2:1 delivered 0.140 g (0.46 mmol, 74%) of a colorless solid. Mp = 112 °C. R_f = 0.17 (*n*-pentane/diethyl ether 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.27 (s, 3H, C$^{4'}{}_{Ts}$CH$_3$), 5.93 (br s, 1H, NH), 6.98 (d, *J* = 8.2 Hz, 2H, 3″-H$_{Ts}$, 5″-H$_{Ts}$), 7.05 (d, *J* = 7.6 Hz, 2H, CH$_{Ph}$), 7.09–7.19 (m, 3H, CH$_{Ph}$), 7.28 (d, *J* = 8.2 Hz, 2H, 2″-H$_{Ts}$, 6″-H$_{Ts}$), 9.06 (s, 1H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.8–20.0 (m, CD_3), 21.4 (C$^{4'}{}_{Ts}$CH$_3$), 66.7 (*C*CD_3), 126.6 (C-4′), 127.5 (C$_{Ts}$-2″, C$_{Ts}$-6″), 128.6 (C-2′, C-6′), 128.8 (C-3′, C-5′), 129.2 (C$_{Ts}$-3″, C$_{Ts}$-5″), 134.1 (C-1′), 139.1 (C$_{Ts}$-1″), 142.8 (C$_{Ts}$-4″), 194.4 (CHO) ppm. IR (KBr): υ^{-1} = 3254 (m), 3069 (w), 2951 (w), 2843 (w), 2727 (w), 1732 (m), 1599 (w), 1583 (w), 1495 (m), 1449 (m), 1405 (m), 1378 (w), 1329 (m), 1167 (m), 818 (m), 764 (m) cm^{-1}. FAB-MS: *m/z* (%): 277 (100) [M$^+$], 155 (48) [$C_7H_7SO_2^+$], 91 (74) [$C_7H_7^+$]. HRMS ($C_{16}H_{14}D_3NO_3S$): calcd: 307.1195, found: 307.1191. Anal. Calcd for $C_{16}H_{15}D_3NO_3S$ (306.11 g/mol): C, 62.72; H, 6.58; N, 4.57; S, 10.47. Found: C, 62.35; H, 5.69; N, 4.93; S, 10.42.

4.9. Diethyl (*R*)-1-(2-(2′-fluorophenyl)-1-oxopropan-2-yl)hydra-1,2-dicarboxylate 9a (Table 2, entry 3)

The product was synthesized following **GP 2**, using 0.152 g (1.00 mmol) of 2-(2′-fluorophenyl)propanal, 0.261 g (1.50 mmol) diethyl azodicarboxylate, 0.058 g (0.50 mmol) L-proline, and 5 mL acetonitrile. Flash chromatography on silica with *n*-pentane/diethyl ether 2:1 delivered 0.124 g (0.38 mmol, 38%) of a colorless oil in 69% ee. R_f = 0.16 (*n*-pentane/diethyl ether 2:1). $[\alpha]_D$ = −3.0 (*c* 2.9, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.16–1.33 (m, 6H, OCH$_2$C*H*$_3$), 1.84 (s, 3H, CC*H*$_3$), 4.19 (q, *J* = 7.1 Hz, 4H, OC*H*$_2$CH$_3$), 6.70 (br s, 1H, NH rotamers), 7.05–7.44 (m, 4H, 3′-H, 4′-H, 5′-H, 6′-H), 9.80, 9.93 (2 × s, 1H, CHO rotamers) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 14.4 (OCH$_2$*C*H$_3$), 18.5 (*C*CH$_3$), 62.3, 63.2 (O*C*H$_2$CH$_3$), 77.1 (*C*CH$_3$), 116.0 (d, *J* = 23.4 Hz, C-3′), 116.4 (d, *J* = 23.0 Hz, C-1′), 124.7 (C-5′), 129.0 (d, *J* = 22.1 Hz, C-4′), 130.4 (d, *J* = 8.4 Hz, C-6′), 156.0 (q, NCO_2), 160.4 (d, *J* = 247.0 Hz, C-2′), 194.1 (CHO) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = −115.47 ppm. IR (KBr): υ^{-1} = 3301 (m), 2984 (m), 1734 (s), 1613 (w), 1582 (w), 1489 (m), 1448 (m), 1379 (s), 1341 (s), 1244 (s), 1176 (m), 1096 (m), 1065 (s), 925 (vw), 819 (w), 762 (m) cm^{-1}. FAB-MS: *m/z* (%) = 297 (26) [M$^+$–CHO], 225 (100) [$C_{11}H_{15}FN_2O_2^+$], 210 (29) [$C_{11}H_{13}FNO_2^+$], 179 (54), 176 (41), 136 (55) [$C_9H_8F^+$], 123 (93), 104 (91) [$C_8H_8^+$]. HRMS ($C_{15}H_{20}FN_2O_5$): calcd: 327.1356, found: 327.1353. Anal. Calcd for $C_{15}H_{19}FN_2O_5$ (326.13 g/mol): C, 55.21; H, 5.87; N, 8.58. Found: C, 54.21; H, 5.85; N, 8.83.

4.10. Diethyl (*R*)-1-(2-(3′-fluorophenyl)-1-oxopropan-2-yl) hydra-1,2-dicarboxylate 9b (Table 2, entry 4)

The product was synthesized following **GP 2**, using 0.152 mg (1.00 mmol) of 2-(3′-fluorophenyl)propanal, 0.261 g (1.50 mmol) diethyl azodicarboxylate, 0.058 g (0.50 mmol) L-proline, and 5 mL acetonitrile. Flash chromatography on silica with *n*-pentane/diethyl ether 2:1 delivered 0.250 g (0.77 mmol, 77%) of a colorless oil in 87% ee. R_f = 0.13 (*n*-pentane/diethyl ether 2:1). $[\alpha]_D$ = −5.0 (*c* 4.4, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.14–1.33 (m, 6H, OCH$_2$C*H*$_3$), 1.83 (s, 3H, CCH$_3$), 4.18 (q, *J* = 7.1 Hz, 4H, OC*H*$_2$CH$_3$), 6.59 (br s, 1H, NH rotamers), 7.03–7.43 (m, 4H, 2′-H, 4′-H, 5′-H, 6′-H), 9.78, 9.92 (2 × d, ^{3}*J* = 6.8, 2.9 Hz, 1H, CHO rotamers) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 14.4 (OCH$_2$CH$_3$), 18.5 (CCH$_3$), 62.3, 63.2 (OCH$_2$CH$_3$), 77.1 (q, *C*CH$_3$), 116.3 (C-2′, C-4′), 124.7 (C-5′, C-6′), 129.5 (q, C-1′), 156.0 (q, NCO_2), 160.4 (d, *J* = 246.5 Hz, C-3′), 194.1 (CHO) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = −112.52 ppm. IR (KBr): υ^{-1} = 3302 (m, υ[NH]), 2984 (m, υ[CH$_3$]), 1734 (s, υ[CO]), 1613 (w), 1582 (w), 1489 (s), 1448 (s), 1378 (s), 1341 (s), 1244 (s), 1176 (m), 1096 (m), 1065 (s), 924 (w), 819 (w), 762 (s) cm^{-1}. MS (EI, 70 eV): *m/z* (%): 297 (31) [M$^+$–CHO], 225 (100) [$C_{11}H_{15}FN_2O_2^+$], 210 (16) [$C_{11}H_{13}FNO_2^+$], 179 (47), 176 (25), 136 (32) [$C_9H_8F^+$], 123 (28). HRMS ($C_{15}H_{20}FN_2O_5$): calcd: 327.1356, found: 327.1353.

4.11. Diethyl (*R*)-1-(1-oxo-2-(3-(trifluoromethyl)phenyl) propan-2-yl)hydrazine-1,2-dicarboxylate 9d (Table 2, entry 6)

The product was synthesized following **GP 3**, using 0.202 g (1.00 mmol) of 2-(3′-trifluoromethylphenyl)propanal, 0.261 g (1.50 mmol) diethyl azodicarboxylate, 0.058 g (0.50 mmol) L-proline, and 5 mL acetonitrile. Flash chromatography on silica with *n*-pentane/diethyl ether 1:1 delivered 0.243 g (0.65 mmol, 65%) of a colorless oil in 72% ee. R_f = 0.20 (*n*-pentane/diethyl ether 1:1). $[\alpha]_D$ = +31.6 (*c* 1.2, $CHCl_3$). HPLC (Chiralcel OD, *n*-heptane/isopropanol 70:30, 0.5 mL/min): R_t(maj) = 10.1 min, R_t(min) = 12.2 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.28 (t, *J* = 7.1 Hz, 6H, OCH_2CH_3), 1.73 (s, 3H, CCH_3), 4.14 (q, *J* = 7.1 Hz, 4H, OCH_2CH_3), 6.89, 7.01 (2 × br s, 1H, NH rotamers), 7.45–7.61 (m, 4H, 2′-H, 4′-H, 5′-H, 6′-H), 9.61, 9.69 (2 × s, 1H, CHO rotamers) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 14.2 (OCH_2CH_3), 18.8 (CCH_3), 62.2, 62.5 (OCH_2CH_3), 72.6 (CCH_3), 123.9 (q, ^1J = 275.0 Hz, CF_3), 123.4 (C-4′), 124.87 (C-5′), 124.90 (C-2′), 129.3 (C-6′), 131.1 (q, ^2J = 32.4 Hz, C-3′), 138.6 (C-1′), 156.0, 156.9 (NCO_2), 194.3 (CHO) ppm. IR (KBr): ν^{-1} = 3301 (m), 2987 (w), 1736 (s), 1515 (m), 1446 (m), 1406 (m), 1330 (s), 1241 (m), 1169 (m), 1127 (m), 1072 (m), 923 (w), 805 (w), 766 (w) cm^{-1}. MS (EI, 70 eV): *m/z* (%): 347 (14) [M^+–CHO], 303 (16), 275 (100) [$C_{12}H_{14}F_3N_2O_2^+$], 215 (31), 188 (19) [$C_9H_9F_3N^+$], 173 (44) [$C_9H_8F_3^+$], 145 (37) [$C_7H_4F_3^+$], 104 (87) [$C_8H_7^+$]. HRMS ($C_{16}H_{20}F_3N_2O_5$): calcd: 377.1324, found: 377.1328.

4.12. Diethyl (*R*)-1-(1-oxo-2-(4-deuterophenyl)propan-2-yl)hydrazine-1,2-dicarboxylate 9f (Table 2, entry 8)[16]

The product was synthesized following **GP 2**, using 0.154 g (1.14 mmol) of 2-(4′-deuteromethylphenyl)propanal, 0.298 g (1.71 mmol) diethyl azodicarboxylate, 0.066 g (0.75 mmol) L-proline, and 5 mL acetonitrile to afford 0.240 g (0.77 mmol, 68%) of a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26 (t, *J* = 7.1 Hz, 6H, OCH_2CH_3), 1.75 (s, 3H, CCH_3), 4.16 (q, *J* = 7.1 Hz, 4H, OCH_2CH_3), 6.93 (br s, 1H, NH), 7.25–7.52 (m, 4H, 2′-H, 3′-H, 5′-H, 6′-H), 9.55, 9.70 (2 × s, 1H, CHO rotamers) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 14.4 (OCH_2CH_3), 17.6 (CCH_3), 62.3, 63.2 (OCH_2CH_3), 73.2 (CCH_3), 124.7 (C-2′, C-6′), 126.9–128.8 (C-3′, C-5′), 136.7 (C-1′), 156.6 (NCO_2R), 193.1 (CHO) ppm. IR (KBr): ν^{-1} = 3302 (m), 2985 (m), 1733 (vs), 1513 (m), 1493 (m), 1410 (m), 1378 (s), 1241 (s), 1185 (m), 1065 (m), 1028 (m), 925 (w), 858 (w), 766 (m) cm^{-1}. FAB-MS: *m/z* (%) = 310 (100) [$M+H^+$], 280 (18) [M^+–CHO], 208 (18) [$C_{10}H_8DN_2O_3^+$], 177 (32) [$C_9H_7DN_2O_2^+$], 154 (25). HRMS ($C_{15}H_{20}DN_2O_5$): calcd: 310.1513, found: 310.1517. Anal. Calcd for $C_{15}H_{19}DN_2O_5$ (309.14 g/mol): C, 58.24; H, 6.84; N, 9.06. Found: C, 57.33; H, 6.48; N, 9.13.

4.13. Diethyl (*R*)-1-(1-oxo-2-trideuteromethyl-2-phenyl) propan-2-yl)hydrazine-1,2-dicarboxylate 9g (Table 2, entry 9)

The product was synthesized following **GP 2**, using 0.137 g (1.00 mmol) of α,α,α-trideutero-2-phenylpropanal, 0.261 g (1.50 mmol) diethyl azodicarboxylate, 0.058 g (0.50 mmol) L-proline, and 5 mL acetonitrile. Flash chromatography on silica with *n*-pentane/diethyl ether 2:1 delivered 0.290 g (0.93 mmol, 88%) of a colorless solid. R_f = 0.08 (*n*-pentane/diethyl ether 2:1). $[\alpha]_D$ = +11.2 (*c* 4.8, MeOH). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (t, *J* = 7.2 Hz, 6H, OCH_2CH_3), 4.16 (q, *J* = 7.1 Hz, 4H, OCH_2CH_3), 6.71, 6.80 (2 × br s, 1H, NH, rotamers), 7.28–7.37 (m, 5H, 2′-H, 3′-H, 4′-H, 5′-H, 6′-H), 9.58, 9.73 (2 × s, 1H, CHO rotamers) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 14.4 (OCH_2CH_3), 14.1–14.35 (m, CCD_3), 14.35, 15.2 (OCH_2CH_3, rotamers), 62.2, 64.2 (OCH_2CH_3), 73.1 (CCD_3), 126.9 (C-2′), 128.2 (C-4′), 129.0 (C-3′), 136.8 (C-1′), 156.5 (NCO_2), 192.9 (CHO) ppm. IR (KBr): ν^{-1} = 3300 (w), 3060 (w), 2985 (w), 2937 (w), 1735 (m), 1602 (vw), 1584 (vw), 1449 (w), 1408 (w), 1340 (m), 1241 (w), 1187 (w), 1095 (w), 1060 (w), 928 (w), 866 (w), 762 (w) cm^{-1}. FAB-MS: *m/z* (%) = 312 (100) [$M+H^+$], 282 (24) [M^+–CHO], 210 (22) [$C_{10}H_8D_3N_2O_3^+$], 154 (31), 137 (50) [$C_9H_6D_3O^+$]. HRMS ($C_{15}H_{18}D_3N_2O_5$): calcd: 312.1639, found: 312.1642.

4.14. Diethyl (*R*)-1-(2-(4-bromophenyl)-1-methoxy-1-oxopropan-2-yl)hydrazine-1,2-dicarboxylate 10

The product was synthesized following **GP 4**, using 5.20 g (13.47 mmol) of diethyl 1-(1-oxo-2-(4-bromophenyl)propan-2-yl)hydrazine-1,2-dicarboxylate. Flash chromatography on silica with *n*-pentane/diethyl ether 5:1 delivered 4.68 g (11.26 mmol, 84%) of a colorless oil. R_f = 0.32 (*n*-pentane/diethyl ether 5:1). $[\alpha]_D$ = −53.4 (*c* 1.75, $CHCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.14 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3), 1.23 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3), 1.64, 1.97 (2 × br s, 3H, CCH_3 rotamers), 3.64 (s, 3H, OCH_3), 3.89–3.99 (m, 2H, OCH_2CH_3), 4.05–4.17 (m, 2H, OCH_2CH_3), 6.20, 6.54 (2 × br s, 1H, NH rotamers), 7.33 (d, ^3J = 8.4 Hz, 2H, 2′-H, 6′-H), 7.36 (d, ^3J = 8.7 Hz, 2H, 3′-H, 5′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.35, 14.44 (CH_2CH_3), 21.8 (CCH_3), 52.9 (OCH_3), 62.1, 62.9 (OCH_2CH_3), 70.5 (CCH_3), 122.6 (C-4′), 128.2 (C-2′, C-6′), 131.0 (C-3′, C-5′), 137.1 (C-1′), 157.0, 155.9 (NCO_2), 172.2 ($COOCH_3$) ppm. IR (KBr): ν^{-1} = 3305 (m), 2985 (m), 2910 (w), 1744 (m), 1492 (m), 1400 (m), 1376 (m), 1242 (m), 1062 (m), 1010 (m), 916 (w), 829 (w), 764 (w) cm^{-1}. FAB-MS: *m/z* (%) = 417 (48) [M+1], 241 (97) [$C_{10}H_{10}BrO_4^+$], 177 (100) [$C_6H_{11}N_2O_4^+$]. HRMS ($C_{16}H_{22}BrN_2O_6$): calcd: 417.0661, found: 417.0665. Anal. Calcd for $C_{16}H_{21}BrN_2O_6$ (416.06 g/mol): C, 46.06; H, 5.07; N, 6.71. Found: C, 45.64; H, 5.50; N, 6.97.

4.15. Diethyl (*R*)-1-(2-(biphenyl-4-yl)-1-methoxy-1-oxopropan-2-yl)hydrazine-1,2-dicarboxylate 11a (Table 3, entry 1–3)

The product was synthesized following **GP 5**, using 0.208 g (0.50 mmol) of a diethyl 1-(2-(4-bromophenyl)-1-methoxy-1-oxopropan-2-yl)hydrazine-1,2-dicarboxylate and 0.092 g (0.75 mmol) phenyl boronic acid. Flash chromatography on silica with *n*-pentane/diethyl ether 1:1 delivered 0.176 g (0.42 mmol, 82%) of a colorless oil. R_f = 0.17 (*n*-pentane/diethyl ether 1:1). $[\alpha]_D$ = −56.8 (*c* 6.4, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.02 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3), 1.17 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3), 1.76, 2.08 (2 × br s, 3H, CCH_3 rotamers), 3.68, 3.73 (2 × br s, 3H, OCH_3 rotamers), 3.89–3.90 (m, 2H, OCH_2CH_3), 4.07–4.17 (m, 2H, OCH_2CH_3), 6.41, 6.72 (2 × br s, 1H, NH rotamers), 7.23–7.28 (m, 1H, CH_{ar}), 7.31–7.36 (m, 2H, CH_{ar}), 7.44–7.51 (m, 6H, CH_{ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.37, 14.43 (CH_2CH_3), 21.9 (CCH_3), 52.8, 52.9 (OCH_3), 61.9, 62.2 (OCH_2CH_3), 70.6, 70.9 (CCH_3), 126.5 (C-3′, C-5′), 127.1 (C-2″, C-6″), 127.9 (C-4″), 128.7 (C-2′, C-6′), 128.9 (C-3″, C-5″), 136.9 (C-4′), 140.2 (C-1″), 141.1 (C-1′), 155.9, 156.1 (NCO_2), 172.4, 172.6 (q, $COCH_3$) ppm. IR (KBr): ν^{-1} = 3309 (m), 2983 (m), 1723 (s), 1517 (m), 1488 (m), 1447 (m), 1402 (m), 1376 (m), 1336 (m), 1238 (m), 1097 (m), 1063 (m), 1008 (m), 842 (w), 763 (w) cm^{-1}. FAB-MS: *m/z* (%) = 415 (25) [$M+H^+$], 239 (100) [$C_{16}H_{15}O_2^+$], 179 (21) [$C_{14}H_{12}^+$], 154 (12) [$C_{12}H_9^+$]. HRMS ($C_{22}H_{26}N_2O_6$): calcd: 415.1869, found: 415.1866.

4.16. Diethyl (*R*)-1-(2-(4′-fluorobiphenyl-4-yl)-1-methoxy-1-oxopropan-2-yl)hydrazine-1,2-dicarboxylate 11b (Table 3, entry 4)

The product was synthesized following **GP 5**, using 0.208 g (0.50 mmol) of diethyl 1-(2-(4-bromophenyl)-1-methoxy-1-oxopropan-2-yl)hydrazine-1,2-dicarboxylate and 0.105 g (0.75 mmol) 4-fluorophenyl boronic acid. Flash chromatography on silica with

n-pentane/diethyl ether 1:1 delivered 0.190 g (0.44 mmol, 88%) of a light yellow oil. R_f = 0.14 (*n*-pentane/diethyl ether 1:1). $[\alpha]_D$ = −54.5 (*c* 1.50, MeOH) ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.02 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3), 1.17 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3), 1.75, 2.06 (s, 3H, CCH_3 rotamers), 3.68, 3.73 (s, 3H, OCH_3, rotamers), 3.88–4.00 (m, 2H, OCH_2CH_3), 4.01–4.20 (m, 2H, OCH_2CH_3), 6.44, 6.76 (2 × br s, 1H, N*H* rotamers), 6.99–7.04 (m, 2H, CH_{ar}), 7.40–7.46 (m, 4H, CH_{ar}), 7.67–7.79 (m, 2H, CH_{ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.4, 14.5 (OCH_2CH_3 rotamers), 21.8 (C-CH_3), 52.8, 52.9 (s, OCH_3, rotamers), 61.9, 62.1 (s, OCH_2CH_3, rotamers), 62.7, 62.8 (s, OCH_2CH_3, rotamers), 79.8 (*C*-CH_3), 114.5 (d, *J* = 21.4 Hz, C-3″), 114.7 (d, *J* = 21.4 Hz, C-5″), 125.4 (C-3′, C-5′), 126.0 (C-2′, C-6′) 127.6 (d, *J* = 8.0 Hz, C-2″, C-6″), 135.1 -135.9 (m, C-1″), 137.8 (C-4′), 139.0 (C-1′), 155.9, 157.0 (s, NCO_2, rotamers), 162.8 (C-4″), 171.4 (d, $COCH_3$) ppm. ^{19}F-NMR (376 MHz, $CDCl_3$): δ = −114.3 ppm. IR (KBr): υ^{-1} = 3310 (w), 2983 (w), 1736 (m), 1497 (m), 1400 (w), 1376 (m), 1336 (m), 1238 (m), 1160 (w), 1063 (w), 1007 (w), 826 (w), 763 (w) cm^{-1}. FAB-MS: *m/z* (%) = 433 (4) [M+H$^+$], 258 (17), 257 (100) [$C_{16}H_{14}FO_2^+$], 197 (18) [$C_{14}H_{11}F^+$]. HRMS ($C_{22}H_{26}FN_2O_6$): calcd: 433.1775, found: 433.1772.

4.17. Diethyl (*R*)-1-(1-methoxy-1-oxo-2-(3′,4′,5′-trifluorobiphenyl-4-yl)propan-2-yl)hydrazine-1,2-dicarboxylate 11c (Table 3, entry 5)

The product was synthesized following **GP 5**, using 0.208 g (0.50 mmol) of diethyl 1-(2-(4-bromophenyl)-1-methoxy-1-oxopropan-2-yl)hydrazine-1,2-dicarboxylate and 0.132 g (0.75 mmol) 2,3,4-trifluorophenyl boronic acid. Flash chromatography on silica with *n*-pentane/diethyl ether 1:1 delivered 0.143 g (0.31 mmol, 61%) of a light yellow oil. R_f = 0.14 (*n*-pentane/diethyl ether 1:1). $[\alpha]_D$ = −41.9 (*c* 7.0, MeOH). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.06 (t, *J* = 7.0 Hz, 3H, OCH_2CH_3), 1.18–1.27 (m, 3H, OCH_2CH_3), 1.74, 2.06 (s, 3H, CCH_3, rotamers), 3.71, 3.77 (s, 3H, OCH_3, rotamers), 3.90–4.04 (m, 2H, OCH_2CH_3), 4.11–4.26 (m, 2H, OCH_2CH_3), 6.25, 6.38 (2 × br s, 1H, NH rotamers), 7.11 (ddd, *J* = 6.8 Hz, 2H, 2″-H, 6″-H), 7.38–7.84 (m, 4H, 2′-H, 3′-H, 5′-H, 6′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 14.4 (OCH_2CH_3, rotamers), 22.0 (CCH_3), 52.9, 53.0 (s, OCH_3, rotamers), 62.2, 62.9 (OCH_2CH_3, rotamers), 70.7 (CCH_3), 110.8–111.2 (m, C-2″, C-6″), 126.3 (C-3′, C-5′), 127.2 (C-2′, C-6′), 128.1 (C-1″), 136.4–137.0 (m, C-4′), 136.9 (C-1′), 150.1–150.3 (m, C-4″), 152.6 (m, C-3″), 155.9–156.0 (m, C-5″), 157.0 (NCO_2), 171.4 ($COCH_3$) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = −133.55, −161.75 ppm. IR (KBr): υ^{-1} = 3313 (w), 2986 (w), 1742 (m), 1536 (m), 1509 (m), 1443 (w), 1376 (m), 1247 (m), 1108 (w), 1049 (m), 1018 (w), 865 (w), 834 (w), 767 (w) cm^{-1}. FAB-MS: *m/z* (%) = 469 (13) [M+H$^+$], 293 (100) [$C_{16}H_{12}F_3O_2^+$]. HRMS ($C_{22}H_{24}F_3N_2O_6$): calc.: 469.1587, found: 469.1593.

4.18. Diethyl (*R*)-1-(1-methoxy-1-oxo-2-(2′,3′,4′,5′,6′-penta-4-yl)propan-2-yl)hydrazine-1,2-di 11d (Table 3, entry 6)

The product was synthesized following **GP 5**, using 0.208 g (0.50 mmol) of diethyl 1-(2-(4-bromophenyl)-1-methoxy-1-oxopropan-2-yl)hydrazine-1,2-dicarboxylate and 0.159 g (0.75 mmol) pentafluorophenyl boronic acid. Flash chromatography on silica with *n*-pentane/diethyl ether 1:1 delivered 0.174 g (0.35 mmol, 69%) of a light yellow oil. R_f = 0.20 (*n*-pentane/diethyl ether 1:1). $[\alpha]_D$ = −100.0 (*c* 2.45, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.18–1.31 (m, 6H, OCH_2CH_3), 1.98, 2.04 (s, 3H, CCH_3, rotamers), 3.71, 3.77 (s, 3H, OCH_3, rotamers), 3.95–4.06 (m, 2H, OCH_2CH_3), 4.11–4.24 (m, 2H, OCH_2CH_3), 6.50, 6.80 (2 × br s, 1H, NH rotamers), 7.30–7.80 (m, 4H, 2′-H, 3′-H, 5′-H, 6′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 14.4 (OCH_2CH_3, rotamers), 21.7 (CCH_3), 52.9, 53.0 (s, OCH_3, rotamers), 61.9, 62.1 (OCH_2CH_3, rotamers), 62.8, 62.9 (OCH_2CH_3, rotamers), 70.6 (CCH_3), 121.2 (*J* = 142.1 Hz, C-1″), 128.3 (C-3′, C-5′), 129.3 (C-1′), 130.9 (C-2′, C-6′), 131.5 (C-4′), 140.6–141.0 (m, C_{ar}F), 155.9 (m, C_{ar}F), 156.0 (m, C_{ar}-F), 156.1 (NCO_2), 157.0 (NCO_2), 172.1 ($COCH_3$) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = −143.2, −155.0, −160.2 ppm. IR (KBr): υ^{-1} = 3311 (m), 2984 (m), 2955 (m), 1724 (m), 1572 (w), 1512 (m), 1467 (m), 1378 (m), 1237 (m), 1063 (m), 1010 (w), 869 (w), 830 (w), 764 (w) cm^{-1}. FAB-MS: *m/z* (%) = 505 (7) [M+H$^+$], 417 (63), 241 (96), 177 (100). HRMS ($C_{22}H_{22}F_5N_2O_6$): calcd: 505.1401, found: 505.1398.

4.19. Diethyl (*R*)-1-(1-methoxy-1-oxo-2-(4′-(trifluoromethyl)biphenyl-4-yl)propan-2-yl)hydrazine-1,2-dicarboxylate 11e (Table 3, entry 7)

The product was synthesized following **GP 5**, using 0.208 g (0.50 mmol) of diethyl 1-(2-(4-bromophenyl)-1-methoxy-1-oxopropan-2-yl)hydrazine-1,2-dicarboxylate and 0.143 g (0.75 mmol) 4-trifluoromethylphenyl boronic acid. Flash chromatography on silica with *n*-pentane/diethyl ether 1:1 delivered 0.163 g (0.34 mmol, 69%) of a light yellow oil. R_f = 0.16 (*n*-pentane/diethyl ether 1:1). $[\alpha]_D$ = −46.2 (*c* 7.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.10 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3), 1.21–1.33 (m, 3H, OCH_2CH_3), 1.82, 2.14 (s, 3H, CCH_3, rotamers), 3.77, 3.82 (s, 3H, OCH_3, rotamers), 3.97–4.09 (m, 2H, OCH_2CH_3), 4.14–4.32 (m, 2H, OCH_2CH_3), 6.49, 6.80 (2 × br s, 1H, NH rotamers), 7.41–7.46 (m, 2H, 3′-H, 5′-H), 7.6 (d, *J* = 8.7 Hz, 2H, 2″-H, 6″-H), 7.67 (s, 2H, 2′-H, 6′-H), 7.91 (d, *J* = 7.8 Hz, 2H, 3″-H, 5″-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 14.3 (OCH_2CH_3 rotamers), 21.8 (CCH_3), 52.7, 52.9 (s, OCH_3, rotamers), 61.8, 62.1 (s, OCH_2CH_3, rotamers), 62.7, 62.8 (s, OCH_2CH_3, rotamers), 70.6 (CCH_3), 122.9 (q, *J* = 271.8 Hz, CF_3), 125.7, 125.8 (q, *J* = 3.7 Hz, C-3″, C-5″), 127.1, 127.3 (C-3′, C-5′), 128.1, 128.3 (C-2″, C-6″), 129.6 (q, *J* = 32.7 Hz, CCF_3), 130.9, 131.5 (C-2′, C-6′), 138.1, 138.3 (C-4′), 139.6 (C-1′), 143.8 (C-1″), 156.0 (NCO_2), 157.1 (NCO_2), 172.2 ($COCH_3$) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = −62.35 ppm. IR (KBr): υ^{-1} = 3309 (m), 2986 (m), 1741 (m), 1500 (m), 1400 (m), 1377 (m), 1242 (m), 1070 (m), 1008 (m), 859 (m), 828 (m), 764 (m) cm^{-1}. FAB-MS: *m/z* (%) = 483 (17) [M+H$^+$], 307 (100) [$C_{17}H_{14}F_3O_2^+$]. HRMS ($C_{23}H_{26}F_3N_2O_6$): calcd: 483.1742, found: 483.1741.

4.20. Diethyl (*R*)-1-(1-methoxy-1-oxo-2-(2′,3′,4′,5′,6′-pentadeuterobiphenyl-4-yl)propan-2-yl)hydrazine-1,2-dicarboxylate 11f (Table 3, entry 8)

The product was synthesized following **GP 5**, using 0.208 g (0.50 mmol) of diethyl 1-(2-(4-bromophenyl)-1-methoxy-1-oxopropan-2-yl)hydrazine-1,2-dicarboxylate and 0.960 g (0.75 mmol) phenyl-d_5 boronic acid. Flash chromatography on silica with *n*-pentane/diethyl ether 1:1 delivered 0.170 g (0.41 mmol, 81%) of a light yellow oil. R_f = 0.17 (*n*-pentane/diethyl ether 1:1). $[\alpha]_D$ = −54.1 (*c* 4.2, MeOH) ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.22–1.29 (m, 6H, OCH_2CH_3), 2.03, 2.16 (s, 3H, CCH_3, rotamers), 3.76, 3.82 (s, 3H, OCH_3, rotamers), 3.97–4.28 (m, 4H, OCH_2CH_3), 6.48, 6.80 (2 × br s, 1H, NH rotamers), 7.48–7.87 (m, 4H, 2′-H, 3′-H, 5′-H, 6′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 14.4 (OCH_2CH_3, rotamers), 21.0, 21.8 (CCH_3, rotamers), 52.8, 52.9 (s, OCH_3, rotamers), 61.8, 62.7 (OCH_2CH_3, rotamers), 62.1, 62.8 (OCH_2CH_3, rotamers), 70.7 (CCH_3), 126.5 (C-3′, C-5′), 127.9 (C-2′, C-6′), 128.1–128.6 (C-2″, C-3″, C-4″, C-5″, C-6″), 136.9 (C-4′), 140.0 (C-1″), 141.0 (C-1′), 156.0 (NCO_2), 156.7 (NCO_2), 171.8 ($COCH_3$) ppm. IR (KBr): υ^{-1} = 3309 (m), 2983 (m), 2910 (w), 1740 (s), 1611 (w), 1514 (m), 1402 (m), 1376 (w), 1336 (m), 1174 (m), 1064 (m), 849 (m), 762 (m) cm^{-1}. FAB-MS: *m/z* (%) = 420 (18) [M+H$^+$], 244 (100) [$C_{15}H_8D_5N_2O^+$]. HRMS ($C_{22}H_{22}D_5N_2O_6$): calcd: 420.2183, found: 420.2185.

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