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# Asymmetric synthesis of benzofuryl β-amino alcohols by the transfer hydrogenation of α-functionalized ketones

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ABSTRACT

The asymmetric transfer hydrogenation of representative benzofuryl α-sulfonyloxy ketones and *N*-protected α-amino ketones with an azeotropic mixture of formic acid/triethylamine, catalyzed by RhCl[(*R*,*R*)-TsDPEN]($C_5Me_5$), afforded the corresponding 1,2-diol monosulfonates and *N*-substituted β-amino alcohols in high yields and with enantioselectivities up to 99%. Transformation of the reduction products to the chiral benzofuryl β-amino alcohols possessing a primary amine group is also described.



## 1. Introduction

Chiral amino alcohols represent useful structures in organic and medicinal chemistry. β-Amino alcohols are found in the structural units of many building blocks, chiral auxiliaries, and ligands.[1–5] Moreover, optically active β-amino alcohols containing heteroaryl moieties are of great importance as a key intermediates for the synthesis of physiologically active compounds.[6,7] Benzofuran is considered as an important structure due to its diverse biological profile.[8] There have been many reports on the synthesis of benzofuran derivatives because of their clinical importance.[9,10] For example, bufuralol (2-*tert*-butylamino-1-(7-ethylbenzofuran-2-yl)ethanol) is a potent non-selective β-adrenergic receptor antagonist of comparable potency to propranolol, an inhibitor of testosterone 6β-hydroxylase, and commonly used marker of hepatic CYP 2D6 activity.[11–15] 1-(3-Phenethylbenzofuran-2-yl)-2-propylaminoethanol, a propafenone analogue, shows antiarrhythmic activity with a lack of β-adrenoacceptor blocking activity.[16]

Various syntheses of enantiomerically pure β-amino alcohols including: the aminohydroxylation of olefins,[17] the reductive-amination of α-halo ketones,[5,18] the enzymatic resolution of racemic β-amino alcohols,[19] catalytic reduction of α-amino ketones,[20–24] and many others have been developed.[25–27] An attractive method for β-amino alcohol synthesis is the asymmetric transfer hydrogenation of α-functionalized ketones.[28–31] Asymmetric transfer hydrogenation (ATH) is established as an excellent reduction method due to its versatility, operational simplicity, avoidance of explosive hydrogen gas, catalyst robustness, and high stereoselectivity.[32–35]

In our previous asymmetric syntheses of benzofuryl β-amino alcohols, the transfer hydrogenation of α-halo ketones,[36] α-imino ketones,[37] and α-dialkylamino ketones[38] was a key step. Hereby, the corresponding β-amino alcohols possessing secondary and tertiary amine groups were obtained.

In continuation of our earlier efforts toward the preparation of chiral benzofuryl β-amino alcohols, we herein report the asymmetric transfer hydrogenation of α-sulfonyloxy, *N*-Cbz protected α-amino ketones, α-succinimido, and α-phthalimido ketones, and further transformations to afford β-amino alcohols with primary and secondary amine groups.

## 2. Results and discussion

### 2.1. Asymmetric transfer hydrogenation of benzofuryl α-sulfonyloxy ketones

The α-sulfonyloxy benzofuryl ketones **1**–**4** were readily prepared by sulfonyloxylation of the corresponding (benzofuran-2-yl)

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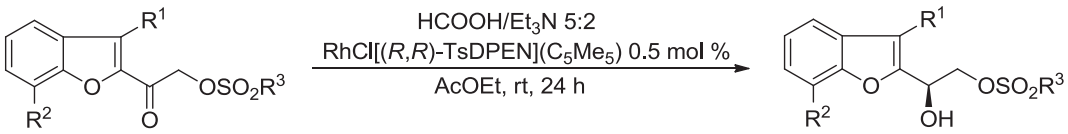
**Table 1**
Asymmetric transfer hydrogenation of benzofuryl α-sulfonyloxy ketones **1**–**4**.



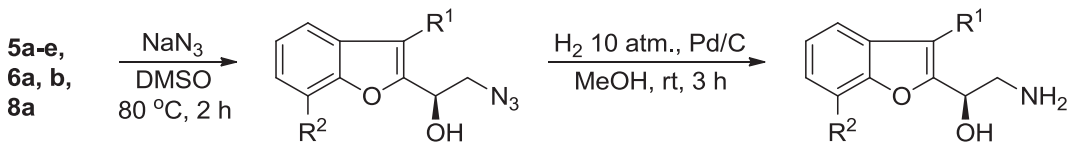

**1-4** **5-8**

| Ketone | $R^1$ | $R^2$ | $R^3$ | Alcohol | Yield[a] (%) | ee[b] (%) |
|---|---|---|---|---|---|---|
| **1a** | H | H | 4-Me-$C_6H_4$ | **5a** | 92 | 97 |
| **1b** | H | Et | 4-Me-$C_6H_4$ | **5b** | 93 | 90 |
| **1c** | Me | H | 4-Me-$C_6H_4$ | **5c** | 96 | 92 |
| **1d** | Me | Me | 4-Me-$C_6H_4$ | **5d** | 89 | 87 |
| **1e** | $Ph(CH_2)_2$ | H | 4-Me-$C_6H_4$ | **5e** | 95 | 93 |
| **2a** | H | H | 4-Cl-$C_6H_4$ | **6a** | 84 | 98[c] |
| **2b** | H | Et | 4-Cl-$C_6H_4$ | **6b** | 93 | 94[c] |
| **2c** | Me | H | 4-Cl-$C_6H_4$ | **6c** | 96 | 90 |
| **3a** | H | H | Ph | **7a** | 99 | 97 |
| **3b** | H | Et | Ph | **7b** | 93 | 94 |
| **3c** | Me | H | Ph | **7c** | 93 | 92 |
| **4a** | H | H | Me | **8a** | 95 | 99 |
| **4b** | H | Et | Me | **8b** | 93 | 95 |
| **4c** | Me | H | Me | **8c** | 93 | 93 |
| **4e** | $Ph(CH_2)_2$ | H | Me | **8e** | 96 | 93 |

[a] Isolated yield.
[b] Determined by HPLC analysis on a chiral column (Daicel Chiralcel OD-H, 250 × 4.6 mm, 5 μm).
[c] Separation was not possible. Assignments based on the ee of β-azido alcohols **9** and **10**, respectively.

ethanones with [hydroxy(tosyloxy)iodo]benzene (PhI(OH)OTs),[39] [hydroxy(mesyloxy)iodo]benzene (PhI(OH)OMs),[40] [hydroxy(4-chloroben-zenesulfonyloxy)iodo]benzene (PhI(OH)OCs),[39] and [hydroxy(benzenesulfonyloxy)-iodo]benzene (PhI(OH)$OSO_2$Ph).[39] The α-sulfonyloxylation reactions were carried out in acetonitrile at reflux for 3 h,[41] and products were separated in moderate to good yields (45–79%). In general, the reaction products of ketones with PhI(OH)OCs were formed with lower yields than in other cases (see Experimental section). Moreover, in contrast to Lee and co-workers,[41] no problems with mesyloxylation and tosyloxylation of 1-(7-ethylbenzofuran-2-yl)ethanone were noticed; appropriate products were obtained in 57% and 76% yields, respectively. The transfer hydrogenation of **1**–**4** was carried out with the formic acid/triethylamine azeotrope (5:2), catalyzed by RhCl[(*R*,*R*)-TsDPEN]($C_5Me_5$), in ethyl acetate at room temperature. All 1,2-diol monosulfonates **5**–**8** were formed in very high yields (84–99%) and with enantioselectivities over 90% (Table 1). Only one product, 2-tosyloxy-1-(3,7-dimethylbenzofuran-2-yl)ethanol (**5d**), was obtained with lower ee, 87%. There was no significant influence of the sulfonyl group type on the yield and enantioselectivity of the reduction. 2-Sulfonyloxy-1-(benzofuran-2-yl)ethanols (**5**–**8**)**a** differing in the substituent of the sulfonyl group, were afforded with excellent ee, 97–99%. Derivatives of 3-methylbenzofuran (**5**–**8**)**c** were isolated with 90–93% ee, and 2-tosyloxy-1-(3-

**Table 2**
Asymmetric synthesis of benzofuryl β-amino alcohols.




**9-13** **14-18**

| No. | $R^1$ | $R^2$ | No. | Yield[a] (%) | ee (%) | No. | Yield[a] (%) |
|---|---|---|---|---|---|---|---|
| **5a** | H | H | **9** | 84 | 97[b] | **14** | 99 |
| **5b** | H | Et | **10** | 72 | 90[c] | **15** | 97 |
| **5c** | Me | H | **11** | 62 | 92[c] | **16** | 96 |
| **5d** | Me | Me | **12** | 53 | 87[b] | **17** | 79 |
| **5e** | $Ph(CH_2)_2$ | H | **13** | 50 | 93[b] | **18** | 71 |
| **6a** | H | H | **9** | 77 | 98[b] | –[d] | – |
| **6b** | H | Et | **10** | 88 | 94[c] | –[d] | – |
| **8a** | H | H | **9** | 99 | 99[b] | –[d] | – |

[a] Isolated yield.
[b] Determined by HPLC analysis on a chiral column (Daicel Chiralcel OD-H, 250 × 4.6 mm, 5 μm).
[c] Determined by HPLC analysis on a chiral column (Daicel Chiralcel OJ, 250 × 4.6 mm, 10 μm).
[d] Not tested.

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phenethylbenzofuran-2-yl)ethanol (**5e**) and 2-mesyloxy-1-(3-phenethylbenzofuran-2-yl)ethanol (**8e**) with 93% ee. Minor differences in the reduction selectivity were found for the 7-ethylbenzofuran derivatives (**1**–**4**)**b**; the products were obtained with ee from 90 to 95%. In addition, we have no explanation, why 2-tosyloxy-1-(7-ethylbenzofuran-2-yl)ethanol (**5b**) and 2-mesyloxy-1-(7-ethylbenzofuran-2-yl)ethanol (**8b**) were formed with 90 and 95% ee, while (*S*)-**5b** and (*S*)-**8b** were reported as 95 and 97% ee, respectively.[41] It is noteworthy that Lee was unable to separate 2-tosyloxy-1-(benzofuran-2-yl)ethanol (**5a**) by chiral HPLC,[41] whereas we were successful. The enantioselectivity was determined to be 97% ee, using HPLC analysis on a Daicel Chiralcel OD-H column. However, determination of the enantiomeric excess of **6a** and **6b** was not possible, rather it was assigned based on HPLC separation of β-azido alcohols **9** and **10**, prepared in the next step (Table 2). The configuration of 1,2-diol monosulfonates **5**–**8** was (*R*), as established by comparing the sign of rotation with known (*S*)-**5a**, (*S*)-**5b**, and (*S*)-**8b**.[41]

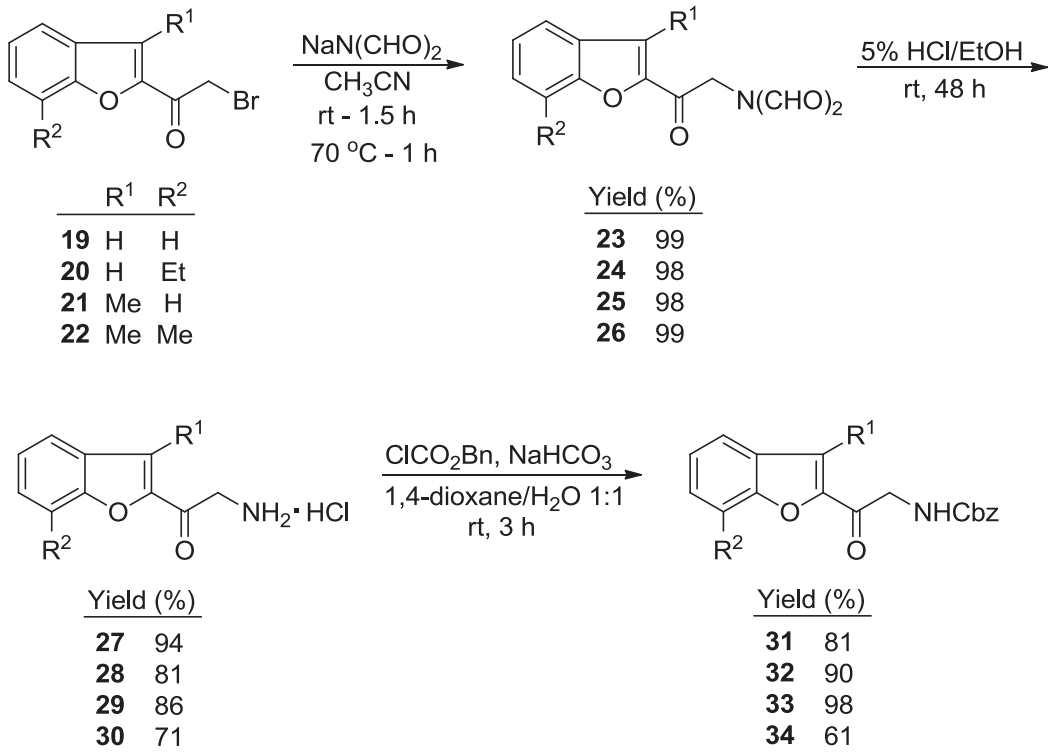
We were interested to apply the optically active benzofuryl 1,2-diol monosulfonates, obtained with high enantiomeric excesses, as precursors for the synthesis of β-amino alcohols. Although various aryl, heteroaryl, and alkyl β-sulfonyloxy alcohols have been used to obtain these target compounds,[42,43] there has been no report of the synthesis of chiral benzofuryl β-amino alcohols in this manner. To the best of our knowledge, no chiral benzofuryl β-amino alcohols possessing a primary amine group have been reported in the literature. Furthermore, derivatives of 2-amino-1-(benzofuran-2-yl)ethanol are an interesting group of compounds due to their anti-obesity, hypoglycemic, anti-inflammatory, and platelet-aggregation inhibiting activity.[44] Thus, following the known sequence: β-sulfonyloxy alcohol → β-azido alcohol → β-amino alcohol,[43] the new benzofuryl β-amino alcohols were prepared. For this purpose, tosylates **5a**–**e**, 4-chlorobenzenesulfonates **6a**, **6b**, and mesylate **8a** were selected for the aforementioned transformations. β-Sulfonyloxy alcohols were treated with an excess of sodium azide in DMSO to give β-azido alcohols **9**–**13** in good yields (50–99%). The results are summarized in Table 2.

The ee values were determined by HPLC analysis using Daicel Chiralcel OD-H or OJ columns. The results indicate that no racemization occurred during the azidation reaction. Next, the obtained β-azido alcohols were hydrogenated under 10 atm. pressure over 10% Pd/C to provide the benzofuryl β-amino alcohols **14**–**18** in high yields (71–99%). The exact enantiomeric excess of products could not be determined by chiral HPLC, hence we assumed that ee values were unchanged. The present work represents a convenient and highly enantioselective method for the synthesis of the benzofuryl β-amino alcohols in three steps from α-sulfonyloxy ketones.

### 2.2. Asymmetric transfer hydrogenation of benzofuryl N-Cbz α-amino ketones

The enantioselective reduction of α-amino ketones is a one-step transformation, which represents an attractive short synthetic pathway, and is an objective of ongoing interest.[45–48] The possibility of free α-amino ketone reduction is limited due to their poor availability and stability, because the primary and secondary amino group reacts with the carbonyl group.[49–51] However, their hydrochlorides are more stable and can be reduced, providing amino groups which remain in the hydrochloride form under the reducing conditions.[52,53] The benzofuryl α-amino ketones, as their hydrochloride salts **27**–**30**, were obtained in two steps from the appropriate α-bromo ketones **19**–**22**, following the reported procedure.[54] The reaction of **19**–**22** with sodium diformylamide[55] in acetonitrile led to the stable *N*,*N*-diformylamino ketones **23**–**26** in quantitative yields (Scheme 1). The formyl groups were easily removed by 5% hydrochloric acid in ethanol to afford the corresponding α-amino ketone hydrochlorides **27**–**30** in high yields.

Attempts at the transfer hydrogenation (HCOOH/$Et_3N$ 5:2 as a




| | $R^1$ | $R^2$ |
|---|---|---|
| **19** | H | H |
| **20** | H | Et |
| **21** | Me | H |
| **22** | Me | Me |

| | Yield (%) |
|---|---|
| **23** | 99 |
| **24** | 98 |
| **25** | 98 |
| **26** | 99 |

| | Yield (%) |
|---|---|
| **27** | 94 |
| **28** | 81 |
| **29** | 86 |
| **30** | 71 |

| | Yield (%) |
|---|---|
| **31** | 81 |
| **32** | 90 |
| **33** | 98 |
| **34** | 61 |

**Scheme 1.** Synthesis of benzofuryl *N*-Cbz protected α-amino ketones **31**–**34**.

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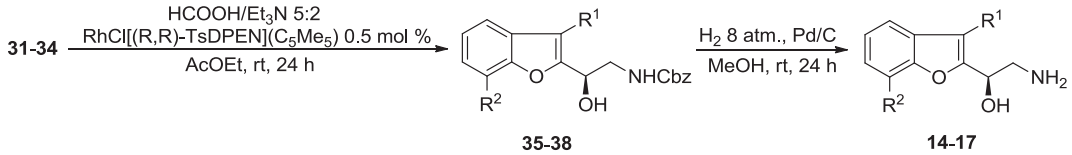
**Table 3**
Asymmetric transfer hydrogenation of **31**–**34** and deprotection of **35**–**38**.




35-38 14-17

| No. | $R^1$ | $R^2$ | No. | Yield[a] (%) | ee[b] (%) | No. | Yield[a] (%) |
|---|---|---|---|---|---|---|---|
| **31** | H | H | **35** | 81 | 99 | **14** | 99 |
| **32** | H | Et | **36** | 76 | 98 | **15** | 78 |
| **33** | Me | H | **37** | 94 | 95 | **16** | 75 |
| **34** | Me | Me | **38** | 95 | 97 | **17** | 80 |

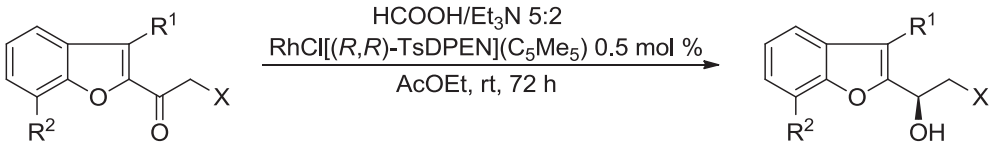
[a] Isolated yield.
[b] Determined by HPLC analysis on a chiral column (Daicel Chiralcel OD-H, 250 × 4.6 mm, 5 μm).

hydrogen source, RhCl[(*R*,*R*)-TsDPEN]($C_5Me_5$) as catalyst, AcOEt as a solvent) of the representative 2-amino-1-(benzofuran-2-yl)ethanone hydrochloride (**27**) failed. We presume that the catalyst containing an amine ligand undergoes deactivation by hydrogen chloride from the amino ketone hydrochloride. On the other hand, Wills and coworkers have reported the successful transfer hydrogenation of various *N*-Boc and *N*-Cbz protected α-amino ketones.[28,29,56] Therefore, we decided to protect the benzofuryl α-amino ketones prior to the reduction. Considering the possibility of removing the protecting group under neutral conditions (the benzofuryl derivatives are sensitive to strong acids), we chose the benzyloxycarbonyl group (Cbz) for protection of the amine. The reaction of the amino ketones hydrochlorides **27**–**30** with benzyl chloroformate, in a mixture of 1,4-dioxane/water (1:1) at room temperature, furnished benzyl (2-(benzofuran-2-yl)-2-oxoethyl) carbamates **31**–**34** in high yields (Scheme 1). Next, **31**–**34** were subjected to the transfer hydrogenation with formic acid/triethylamine (5:2), catalyzed by RhCl[(*R*,*R*)-TsDPEN]($C_5Me_5$), in ethyl acetate at room temperature (Table 3). The corresponding optically active β-amino alcohols **35**–**38** were obtained in high yields (76–95%), and excellent enantioselectivities (95–99%), as determined by chiral HPLC. Deprotection of the nitrogen group in **35**–**38**, under 8 atm. pressure of hydrogen over 10% Pd/C in methanol, gave benzofuryl β-amino alcohols **14**–**17** in high yields. The (*R*) configuration of compounds **35**–**38** was assigned based on comparison of the optical rotation signs of the final products **14**–**17** with those obtained earlier (Table 2). As can be seen from Table 3, benzofuryl *N*-Cbz protected α-amino ketones are excellent substrates for the asymmetric transfer hydrogenation, and hence benzofuryl β-primary amino alcohols are obtained with high yields and ees.

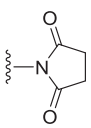
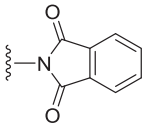
### 2.3. Asymmetric transfer hydrogenation of benzofuryl α-succinimido and α-phthalimido ketones

Succinimido and phthalimido ketones are alternative substrates for the synthesis of amino alcohols with easily removable protecting groups. There are several examples in the literature of the enantioselective catalytic reduction of various aromatic and aliphatic substituted α-phthalimido ketones under a high pressure of hydrogen and with diphosphine catalysts.[57–60] Very recently, Xu

**Table 4**
Asymmetric transfer hydrogenation of benzofuryl α-succinimido and α-phthalimido ketones **39**–**45**.




39-45 46-52

| No. | $R^1$ | $R^2$ | X | No. | Yield[a] (%) | ee (%) |
|---|---|---|---|---|---|---|
| **39** | H | H |  | **46** | 95 | 94[b] |
| **40** | H | Et | | **47** | 89 | 91[c] |
| **41** | Me | H | | **48** | 79 | 80[c] |
| **42** | Me | Me | | **49** | 76 | 79[c] |
| **43** | H | H |  | **50** | 98 | 91[c] |
| **44** | H | Et | | **51** | 76 | 89[c] |
| **45** | Me | H | | **52** | 92 | 84[c] |

[a] Isolated yield.
[b] Determined by HPLC analysis on a chiral column (Daicel Chiralcel OD-H, 250 × 4.6 mm, 5 μm).
[c] Determined by HPLC analysis on a chiral column (Daicel Chiralcel OJ, 250 × 4.6 mm, 10 μm).

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and co-workers reported the first asymmetric transfer hydrogenation of α-phthalimido ketones with the use of a chiral Ru(II)/TsDPEN complex and HCOOH as hydrogen resource.[30] On the other hand, only one example of the catalytic reduction of an α-succinimido ketone has been described.[61] Therefore, we decided to prepare the benzofuryl α-succinimido and α-phthalimido ketones, and submit them to the asymmetric transfer hydrogenation. The benzofuryl α-succinimido ketones **39**–**42** were synthesized by the reaction of α-bromo ketones **19**–**22** with freshly prepared potassium succinimide (see Experimental section).[61] Similarly, α-phthalimido ketones **43**–**45** were obtained in the reactions of **19**–**21** with commercially available potassium phthalimide. Under our ATH conditions (HCOOH/$Et_3N$ as a hydrogen source, RhCl[(*R*,*R*)-TsDPEN]($C_5Me_5$) as catalyst), the benzofuryl succinimido and phthalimido ketones were reduced to yield alcohols **46**–**52** in high yields and with good to high enantioselectivities (Table 4).

The transfer hydrogenation reactions were run at room temperature in ethyl acetate. The substrates **39**–**45** were sufficiently soluble in this solvent. However, longer reaction times were required (72 h); the reaction progress was monitored by TLC analysis. As shown in Table 4, the type of protecting group on nitrogen has no significant influence on enantioselectivity, in contrast to the substituents on the benzofuran ring. 3-Methylbenzofuryl ketones **41**, **42**, and **45** furnished the corresponding alcohols with lowered ees (79–84%) in comparison to other products (89–94%). The next step was deprotection of the succinimides and phthalimides to obtain β-amino alcohols with a primary amine group. Removal of the succinic acid group was accomplished by treating **46**–**49** with 20% aqueous sodium hydroxide in refluxing ethanol,[61] whilst phthalimides **50**–**51** were cleaved in the presence of hydrazine utilizing the classic Gabriel synthesis.[62] The optical rotation sign (+) of the obtained primary β-amino alcohols was the same as that of **14**–**17** prepared in the previous methods, hence the *R* configuration of compounds **46**–**52** was assigned.

## 3. Conclusion

In conclusion, we have described the highly efficient and enantioselective asymmetric transfer hydrogenation of benzofuryl α-functionalized ketones, catalyzed by RhCl[(*R*,*R*)-TsDPEN]($C_5Me_5$). The obtained chiral benzofuryl 1,2-diol monosulfonates represent useful substrates for three-step synthesis of β-amino alcohols with a primary amine group. Moreover, the 1,2-diol monosulfonates can be used as key intermediates in the direct synthesis of important β-amino alcohols possessing a secondary amine group. For example, (*S*)-2-mesyloxy-1-(7-ethylbenzofuran-2-yl)ethanol ((*S*)-**8b**) was reacted with *tert*-butylamine in ethanol providing (*S*)-bufuralol in 99% ee.[41] The simple deprotection of benzofuryl *N*-Cbz protected β-amino alcohols, obtained with 95–99% ee, led to β-amino alcohols with an $NH_2$ group. Furthermore, the chiral carbamate derivatives of β-amino alcohols, in turn, can be used in the synthesis of optically active aziridines.[28,29] Hence, our ongoing experiments are focused on the synthesis of new chiral benzofuryl compounds based on chiral β-amino alcohols.

## 4. Experimental

### 4.1. General

Experiments with air and moisture sensitive materials were carried out under a nitrogen atmosphere. Glassware was oven dried for several hours, assembled hot, and cooled in a stream of nitrogen. $^1H$ and $^{13}C$ spectra were recorded on Varian Gemini 200, Bruker AMX 300 MHz, Avance III 400 MHz, and Avance 700 MHz spectrometers. MS spectra were recorded on an AMD 604 spectrometer. Optical rotations were measured on an automatic polarimeter, PolAAr 3000, Optical Activity Ltd. HPLC analyses were performed on a Shimadzu LC-10AT chromatograph. IR analyses were recorded on a Perkin Elmer Spectrum RX I spectrometer. Melting points were determined in open glass capillaries and are uncorrected. Elemental analyses were performed on, a Vario MACRO CHN, ELEMENTAR Analysensysteme GmbH instrument.

### 4.2. Materials

Silica Gel 60, Merck 230–400 mesh, was used for preparative column chromatography. Analytical TLC was performed using Merck TLC Silica gel 60 $F_{254}$ 0.2 mm aluminium plates. THF was freshly distilled from sodium benzophenone ketyl. Acetonitrile was distilled from calcium hydride. Methanol was dried over 4 Å molecular sieves. Benzyl chloroformate and potassium phthalimide were commercial products. 1-(Benzofuran-2-yl)ethanone,[63] 1-(7-ethylbenzofuran-2-yl)ethanone,[64] 1-(3-phenethylbenzofuran-2-yl)ethanone,[64] 1-(benzofuran-2-yl)-2-bromoethanone,[65] 1-(3-methylbenzofuran-2-yl)ethanone,[66] 2-bromo-1-(7-ethyl-benzofuran-2-yl)ethanone,[64] 2-bromo-1-(3-methylbenzofuran-2-yl) ethanone,[66] [hydroxy(to-syloxy)iodo]benzene,[39] [hydroxy(mesyloxy)iodo]benzene,[40] [hydroxy(4-chlorobenzene-sulfonyloxy)iodo]benzene,[39] [hydroxy(benzenesulfonyloxy)iodo]benzene,[39] RhCl[(*R*,*R*)-TsDPEN]($C_5Me_5$),[38] sodium diformylamide,[55] and potassium succinimide[61] were prepared according to the literature procedures. 1-(3,7-Dimethylbenzofuran-2-yl)ethanone was prepared from 3,7-dimethylbenzofuran and acetic anhydride; 2-bromo-1-(3,7-dimethylbenzofuran-2-yl)ethanone from 1-(3,7-dimethylbenzofuran-2-yl)ethanone and pyridinium tribromide, according to the known protocols.[64] The formic acid/triethylamine (molar ratio 5:2) azeotrope was prepared by distillation of the mixture.[67]

The appropriate racemic compounds were also prepared and used as standards for ee determination.

### 4.3. General procedure for α-sulfonyloxylation of the benzofuryl ketones

To a solution of the corresponding benzofuryl ketone (7.5 mmol) in acetonitrile (50 mL) was added PhI(OH)$OSO_2R$ (R = 4-Me-$C_6H_4$, 4-Cl-$C_6H_4$, Ph, Me) (7.5 mmol) and stirred at reflux for 3 h. After cooling to rt, the reaction mixture was concentrated in vacuo. The residue was purified by column chromatography on silica gel or crystallized from ethanol.

#### 4.3.1. 2-Tosyloxy-1-(benzofuran-2-yl)ethanone ***1a***[41]

Crystallized from ethanol, 1.75 g, 70% yield, mp 115–116 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 2.47 (s, 3H, $CH_3$), 5.24 (s, 2H, $CH_2$), 7.34–7.40 (m, 3H), 7.54 (td, $J$ = 8.4, 1.2 Hz, 1H), 7.58 (ddd, $J$ = 8.4, 1.5, 0.8 Hz, 1H), 7.66 (d, $J$ = 1.2 Hz, 1H), 7.75 (dt, $J$ = 7.6, 1.2 Hz, 1H), 7.90–7.92 (m, 2H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 21.7 ($CH_3$), 69.7 ($CH_2$), 112.4 (CH), 114.7 (CH), 123.6 (CH), 124.3 (CH), 126.6 (C), 128.2 (2xCH), 129.1 (CH), 129.9 (2xCH), 132.5 (C), 145.4 (C), 149.7 (C), 155.6 (C), 181.5 (CO) ppm. Anal. calcd for $C_{17}H_{14}O_5S$: C, 61.81; H, 4.27. Found: C, 61.75; H, 4.25.

#### 4.3.2. 2-Tosyloxy-1-(7-ethylbenzofuran-2-yl)ethanone ***1b***[41,68]

Crystallized from ethanol, 1.88 g, 76% yield, mp 69–70 °C. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 1.35 (t, $J$ = 7.5 Hz, 3H, $CH_3$), 2.45 (s, 3H, $CH_3$), 2.96 (q, $J$ = 7.5 Hz, 2H, $CH_2$), 5.25 (s, 2H, $CH_2$), 7.24–7.29 (m, 1H), 7.33–7.38 (m, 3H), 7.54 (d, $J$ = 7.5 Hz, 1H), 7.63 (s, 1H),7.89 (d, $J$ = 8.1 Hz, 2H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 13.9 ($CH_3$), 21.7 ($CH_3$), 22.6 ($CH_2$), 69.6 ($CH_2$), 115.0 (CH), 120.9 (CH), 124.5 (CH), 126.2 (C), 128.0 (CH), 128.2 (2xCH), 128.9 (C), 129.9 (2xCH), 132.6 (C), 145.4

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(C), 149.5 (C), 154.4 (C), 181.4 (CO) ppm. Anal. calcd for $C_{19}H_{18}O_5S$: C, 63.67; H, 5.06. Found: C, 63.82; H, 5.15.

#### 4.3.3. 2-Tosyloxy-1-(3-methylbenzofuran-2-yl)ethanone **1c**

Crystallized from ethanol, 1.78 g, 75% yield, mp 126–127 °C. $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ = 2.45 (s, 3H, $CH_3$), 2.59 (s, 3H, $CH_3$), 5.31 (s, 2H, $CH_2$), 7.34–7.38 (m, 3H), 7.48–7.59 (m, 2H), 7.65 (d, $J$ = 10.0 Hz, 1H), 7.90 (d, $J$ = 8.2 Hz, 2H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 9.2 ($CH_3$), 21.6 ($CH_3$), 69.9 ($CH_2$), 112.2 (CH), 121.7 (CH), 123.6 (CH), 127.0 (C), 128.1 (2xCH), 128.7 (C), 129.0 (CH), 129.8 (2xCH), 132.9 (CH), 145.1(C), 145.4 (C), 154.2 (C), 182.7 (CO) ppm. Anal. calcd for $C_{18}H_{16}O_5S$: C, 62.78; H, 4.68. Found: C, 62.46; H, 4.79.

#### 4.3.4. 2-Tosyloxy-1-(3,7-dimethylbenzofuran-2-yl)ethanone **1d**

Crystallized from ethanol, 1.87 g, 76% yield, mp 146–148 °C. $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ = 2.45 (s, 3H, $CH_3$), 2.51 (s, 3H, $CH_3$), 2.57 (s, 3H, $CH_3$), 5.34 (s, 2H, $CH_2$), 7.18–7.39 (m, 4H), 7.48 (d, $J$ = 10.0 Hz, 1H), 7.90 (d, $J$ = 8.2 Hz, 2H) ppm. $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta$ = 9.4 ($CH_3$), 14.8 ($CH_3$), 21.6 ($CH_3$), 69.7 ($CH_2$), 119.0 (CH), 122.5 (C), 123.8 (CH), 127.5 (C), 128.1 (2xCH), 128.3 (C), 129.6 (CH), 129.8 (2xCH), 133.1 (C), 145.0 (C), 145.4 (C), 153.5 (C), 182.7 (CO) ppm. Anal. calcd for $C_{19}H_{18}O_5S$: C, 63.67; H, 5.06. Found: C, 62.63; H, 5.16.

#### 4.3.5. 2-Tosyloxy-1-(3-phenethylbenzofuran-2-yl)ethanone **1e**

Crystallized from ethanol, 1.92 g, 59% yield, mp 120–123 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 2.44 (s, 3H, $CH_3$), 2.88–2.93 (m, 2H), 3.31–3.36 (m, 2H), 5.31 (s, 2H, $CH_2$), 7.16–7.30 (m, 6H), 7.35–7.38 (m, 2H), 7.48 (d, $J$ = 1.2 Hz, 1H), 7.49 (dd, $J$ = 3.3, 1.2 Hz, 1H), 7.54 (dt, $J$ = 7.8, 0.9 Hz, 1H), 7.89–7.92 (m, 2H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 21.6 ($CH_3$), 26.2 ($CH_2$), 35.6 ($CH_2$), 69.9 ($CH_2$), 112.3 (CH), 121.8 (CH), 123.7 (CH), 126.2 (CH), 128.0 (C), 128.2 (2xCH), 128.4 (2xCH), 128.5 (2xCH), 128.9 (CH), 129.9 (2xCH), 130.9 (C), 132.9 (C), 140.9 (C), 145.1 (C), 145.3 (C), 154.3 (C), 182.5 (CO) ppm. Anal. calcd for $C_{25}H_{22}O_5S$: C, 69.11; H, 5.10. Found: C, 69.23; H, 5.36.

#### 4.3.6. 2-(4-Chlorobenzenesulfonyloxy)-1-(benzofuran-2-yl) ethanone **2a**

Purified by column chromatography on silica gel (hexane/ethyl acetate, 7:3), 1.23 g, 48% yield, mp 103–105 °C. $^1$H NMR (700 MHz, $CDCl_3$): $\delta$ = 5.35 (s, 2H, $CH_2$), 7.38 (ddd, $J$ = 7.7, 7.0, 0.7 Hz, 1H), 7.56 (td, $J$ = 7.0, 1.4 Hz, 1H), 7.58–7.61 (m, 3H), 7.67 (d, $J$ = 1.4 Hz, 1H), 7.77 (ddd, $J$ = 7.7, 1.4, 0.7 Hz, 1H),7.98 (dt, $J$ = 9.1, 2.1 Hz, 2H) ppm. $^{13}$C NMR (175 MHz, $CDCl_3$): $\delta$ = 70.9 ($CH_2$), 113.5 (CH), 115.6 (CH), 124.7 (CH), 125.4 (CH), 127.6 (C), 130.2 (CH), 130.6 (2xCH), 130.7 (2xCH), 135.3 (C), 142.0 (C), 150.7 (C), 156.7 (C), 182.3 (CO) ppm. IR, neat ($cm^{-1}$): 3007, 1698, 1382, 1172, 749. Anal. calcd for $C_{16}H_{11}ClO_5S$: C, 54.79; H, 3.16. Found: C, 54.75; H, 3.25.

#### 4.3.7. 2-(4-Chlorobenzenesulfonyloxy)-1-(7-ethylbenzofuran-2-yl) ethanone **2b**

Purified by column chromatography on silica gel (hexane/ethyl acetate, 9:1), 1.63 g, 56% yield, mp 82–85 °C. $^1$H NMR (700 MHz, $CDCl_3$): $\delta$ = 1.39 (t, $J$ = 7.7 Hz, 3H, $CH_3$), 3.00 (q, $J$ = 7.7 Hz, 2H, $CH_2$), 5.37 (s, 2H, $CH_2$), 7.31 (t, $J$ = 6.3 Hz, 1H), 7.37 (dq, $J$ = 7.0, 0.7 Hz, 1H), 7.57–7.59 (m, 3H), 7.65 (s, 1H).7.99 (dt, $J$ = 9.1, 2.1 Hz, 2H) ppm. $^{13}$C NMR (175 MHz, $CDCl_3$): $\delta$ = 14.9 ($CH_3$), 23.6 ($CH_2$), 70.8 ($CH_2$), 115.9 (CH), 120.0 (CH), 125.6 (CH), 127.3 (C), 129.1 (CH), 130.0 (C), 130.6 (2xCH), 130.7 (2xCH), 135.3 (C), 141.9 (C), 150.4 (C), 155.5 (C), 182.2 (CO) ppm. IR, neat ($cm^{-1}$): 2967, 1700, 1356, 1172, 979, 767. Anal. calcd for $C_{18}H_{15}ClO_5S$: C, 57.07; H, 3.99. Found: C, 56.95; H, 3.65.

#### 4.3.8. 2-(4-Chlorobenzenesulfonyloxy)-1-(3-methylbenzofuran-2-yl)ethanone **2c**

Purified by column chromatography on silica gel (hexane/ethyl acetate, 9:1), 1.37 g, 50% yield, mp 106–108 °C. $^1$H NMR (700 MHz, $CDCl_3$): $\delta$ = 2.63 (s, 3H, $CH_3$), 5.40 (s, 2H, $CH_2$), 7.37 (ddd, $J$ = 8.4, 7.0, 1.4 Hz, 1H), 7.51 (dt, $J$ = 8.4, 0.7 Hz, 1H), 7.55 (ddd, $J$ = 8.4, 7.0, 1.4 Hz, 1H), 7.58 (dt, $J$ = 8.1, 2.1 Hz, 2H), 7.70 (ddd, $J$ = 8.4, 1.4, 0.7 Hz, 1H),8.00 (dt, $J$ = 8.4, 2.1 Hz, 2H) ppm. $^{13}$C NMR (175 MHz, $CDCl_3$): $\delta$ = 10.3 ($CH_3$), 71.2 ($CH_2$), 113.2 (CH), 122.8 (CH), 124.8 (CH), 128.4 (C), 129.7 (C), 130.2 (CH), 130.6 (4xCH), 135.6 (C), 141.8 (C), 146.3 (C), 155.3 (C), 183.6 (CO) ppm. IR, neat ($cm^{-1}$): 3094, 2923, 1690, 1374, 1011, 814. Anal. calcd for $C_{17}H_{13}ClO_5S$: C, 55.97; H, 3.59. Found: C, 56.25; H, 3.35.

#### 4.3.9. 2-Benzenesulfonyloxy-1-(benzofuran-2-yl)ethanone **3a**

Purified by column chromatography on silica gel (hexane/ethyl acetate, 8:2), 1.48 g, 63% yield, mp 112–115 °C. $^1$H NMR (700 MHz, $CDCl_3$): $\delta$ = 5.30 (s, 2H, $CH_2$), 7.38 (ddd, $J$ = 8.4, 7.0, 0.7 Hz, 1H), 7.55 (ddd, $J$ = 8.4, 7.0, 1.4 Hz, 1H), 7.59 (dq, $J$ = 8.4, 1.4 Hz, 1H), 7.60–7.63 (m, 2H), 7.68 (d, $J$ = 1.4 Hz, 1H), 7.71–7.73 (m, 1H), 7.76 (ddd, $J$ = 8.4, 1.4, 0.7 Hz, 1H), 8.04–8.06 (m, 2H) ppm. $^{13}$C NMR (175 MHz, $CDCl_3$): $\delta$ = 70.8 ($CH_2$), 113.5 (CH), 115.7 (CH), 124.7 (CH), 125.4 (CH), 127.6 (C), 129.2 (2xCH), 130.2 (CH), 130.4 (2xCH), 135.3 (CH), 136.6 (C), 150.7 (C), 156.7 (C), 182.4 (CO) ppm. IR, neat ($cm^{-1}$): 2919, 1701, 1370, 1186, 919, 684. Anal. calcd for $C_{16}H_{12}O_5S$: C, 60.75; H, 3.82. Found: C, 60.53; H, 3.66.

#### 4.3.10. 2-Benzenesulfonyloxy-1-(7-ethylbenzofuran-2-yl)ethanone **3b**

Purified by column chromatography on silica gel (hexane/ethyl acetate, 9:1), 1.01 g, 76% yield, mp 62–64 °C. $^1$H NMR (700 MHz, $CDCl_3$): $\delta$ = 1.38 (t, $J$ = 7.7 Hz, 3H, $CH_3$), 2.99 (q, $J$ = 7.7 Hz, 2H, $CH_2$), 5.32 (s, 2H, $CH_2$), 7.29 (t, $J$ = 7.0 Hz, 1H), 7.36 (dq, $J$ = 7.7, 1.4 Hz, 1H), 7.57 (dd, $J$ = 7.7, 1.4 Hz, 1H), 7.59–7.62 (m, 2H), 7.65 (s, 1H), 7.71 (tt, $J$ = 7.0, 0.7 Hz, 1H), 8.04–8.06 (m, 2H) ppm. $^{13}$C NMR (175 MHz, $CDCl_3$): $\delta$ = 14.9 ($CH_3$), 23.6 ($CH_2$), 70.7 ($CH_2$), 116.0 (CH), 122.0 (CH), 125.6 (CH), 127.3 (C), 129.0 (CH), 129.2 (2xCH), 130.0 (C), 130.3 (2xCH), 135.2 (CH), 136.7 (C), 150.5 (C), 155.5 (C), 182.3 (CO) ppm. IR, neat ($cm^{-1}$): 2969, 1693, 1236, 1174, 923, 742. Anal. calcd for $C_{18}H_{16}O_5S$: C, 62.78; H, 4.68. Found: C, 62.24; H, 4.36.

#### 4.3.11. 2-Benzenesulfonyloxy-1-(3-methylbenzofuran-2-yl) ethanone **3c**

Purified by column chromatography on silica gel (hexane/ethyl acetate, 8:2), 1.72 g, 69% yield, mp 119–121 °C. $^1$H NMR (700 MHz, $CDCl_3$): $\delta$ = 2.62 (s, 3H, $CH_3$), 5.38 (s, 2H, $CH_2$), 7.36 (ddd, $J$ = 7.7, 7.0, 0.7 Hz, 1H), 7.51 (dt, $J$ = 8.4, 0.7 Hz, 1H), 7.54 (ddd, $J$ = 8.4, 7.0, 1.4 Hz, 1H), 7.60–7.63 (m, 2H), 7.69–7.72 (m, 2H), 8.06 (dt, $J$ = 9.8, 1.4 Hz, 2H) ppm. $^{13}$C NMR (175 MHz, $CDCl_3$): $\delta$ = 10.3 ($CH_3$), 71.1 ($CH_2$), 113.2 (CH), 122.7 (CH), 124.7 (CH), 128.2 (C), 129.1 (2xCH), 129.8 (C), 130.1 (CH), 130.3 (2xCH), 135.1 (CH), 137.0 (C), 146.4 (C), 155.3 (C), 183.7 (CO) ppm. IR, neat ($cm^{-1}$): 2923, 1695, 1356, 1172, 874, 740. Anal. calcd for $C_{17}H_{14}O_5S$: C, 61.81; H, 4.27. Found: C, 61.33; H, 4.47.

#### 4.3.12. 2-Mesyloxy-1-(benzofuran-2-yl)ethanone **4a**

Crystallized from ethanol, 1.51 g, 79% yield, mp 104–105 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 3.32 (s, 3H, $CH_3$), 5.51 (s, 2H, $CH_2$), 7.38 (ddd, $J$ = 8.0, 6.8, 1.2 Hz, 1H), 7.56 (td, $J$ = 8.4, 1.2 Hz, 1H), 7.61 (ddd, $J$ = 8.4, 1.5, 1.2 Hz, 1H), 7.67 (d, $J$ = 0.8 Hz, 1H), 7.77 (dt, $J$ = 8.0, 0.8 Hz, 1H) ppm. $^{13}$C NMR (175 MHz, $CDCl_3$): $\delta$ = 38.8 ($CH_3$), 69.5 ($CH_2$), 112.1 (CH), 113.9 (CH), 123.3 (CH), 124.1 (CH), 126.1 (C), 128.8 (CH), 149.2 (C), 155.4 (C), 182.1 (CO) ppm. IR, neat ($cm^{-1}$): 2949, 1682, 1339, 1115, 757. Anal. calcd for $C_{11}H_{10}O_5S$: C, 51.96; H, 3.96. Found: C, 51.73; H, 3.87.

#### 4.3.13. 2-Mesyloxy-1-(7-ethylbenzofuran-2-yl)ethanone **4b**[41]

Purified by column chromatography on silica gel (hexane/ethyl acetate, 8:2), 1.58 g, 75% yield, mp 56–59 °C. $^1$H NMR (700 MHz, $CDCl_3$): $\delta$ = 1.37 (t, $J$ = 7.7 Hz, 3H, $CH_3$), 2.98 (q, $J$ = 7.7 Hz, 2H, $CH_2$),

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3.31 (s, 3H, $CH_3$), 5.51 (s, 2H, $CH_2$), 7.28 (t, $J = 7.7$ Hz, 1H), 7.36 (dd, $J = 7.7$, 0.7 Hz, 1H), 7.57 (dd, $J = 7.7$, 0.7 Hz, 1H), 7.65 (s, 1H) ppm. $^{13}C$ NMR (175 MHz, $CDCl_3$): $\delta = 13.6$ ($CH_3$), 22.3 ($CH_2$), 38.8 ($CH_3$), 69.5 ($CH_2$), 114.3 (CH), 120.6 (CH), 124.3 (CH), 125.8 (C), 127.7 (CH), 128.6 (C), 148.9 (C), 154.2 (C), 182.1 (CO) ppm. IR, neat ($cm^{-1}$): 3023, 2931, 1685, 1305, 920, 765. Anal. calcd for $C_{13}H_{14}O_5S$: C, 55.31; H, 5.00. Found: C, 54.99; H, 4.67.

#### 4.3.14. 2-Mesyloxy-1-(3-methylbenzofuran-2-yl)ethanone **4c**

Purified by column chromatography on silica gel (hexane/ethyl acetate, 7:3), 1.27 g, 62% yield, mp 108–111 °C. $^1H$ NMR (700 MHz, $CDCl_3$): $\delta = 2.65$ (s, 3H, $CH_3$), 3.32 (s, 3H, $CH_3$), 5.53 (s, 2H, $CH_2$), 7.35 (ddd, $J = 7.7$, 7.0, 1.4 Hz, 1H), 7.51 (dq, $J = 8.4$, 0.7 Hz, 1H), 7.54 (ddd, $J = 8.4$, 7.0, 1.4 Hz, 1H), 7.69 (dq, $J = 7.7$, 0.7 Hz, 1H) ppm. $^{13}C$ NMR (175 MHz, $CDCl_3$): $\delta = 8.9$ ($CH_3$), 38.9 ($CH_3$), 70.2 ($CH_2$), 111.9 (CH), 121.4 (CH), 123.4 (CH), 127.1 (C), 128.3 (C), 128.9 (CH), 144.9 (C), 154.0 (C), 183.7 (CO) ppm. IR, neat ($cm^{-1}$): 3020, 2921, 1697, 1281, 960, 716. Anal. calcd for $C_{12}H_{12}O_5S$: C, 53.72; H, 4.51. Found: C, 53.73; H, 4.67.

#### 4.3.15. 2-Mesyloxy-1-(3-phenethylbenzofuran-2-yl)ethanone **4e**

Crystallized from ethanol, 1.71 g, 64% yield, mp 99–102 °C. $^1H$ NMR (700 MHz, $CDCl_3$): $\delta = 2.97–3.00$ (m, 2H, $CH_2$), 3.30 (s, 3H, $CH_3$), 3.40–3.42 (m, 2H, $CH_2$), 5.50 (s, 2H, $CH_2$), 7.19 (tt, $J = 7.0$, 1.4 Hz, H), 7.21–7.22 (m, 2H), 7.25–7.27 (m, 2H), 7.30 (ddd, $J = 8.4$, 5.6, 2.8 Hz, 1H), 7.51–7.52 (m, 2H), 7.56 (dt, $J = 7.7$, 0.7 Hz, 1H) ppm. $^{13}C$ NMR (175 MHz, $CDCl_3$): $\delta = 25.9$ ($CH_2$), 35.3 ($CH_2$), 38.9 ($CH_3$), 70.1 ($CH_2$), 111.9 (CH), 121.5 (CH), 123.4 (CH), 125.9 (CH), 127.6 (C), 128.0 (2xCH), 128.1 (2xCH), 128.8 (CH), 130.8 (C), 140.5 (C), 144.8 (C), 154.1 (C), 183.4 (CO) ppm. IR, neat ($cm^{-1}$): 3018, 2950, 1681, 1571, 1125, 875, 696. Anal. calcd for $C_{19}H_{18}O_5S$: C, 63.67; H, 5.06. Found: C, 63.51; H, 5.00.

### 4.4. General procedure for the asymmetric transfer hydrogenation of benzofuryl α-sulfonyloxy ketones

To a solution of α-sulfonyloxy ketone (1 mmol) in ethyl acetate (10 mL) was added RhCl[(*R*,*R*)-TsDPEN]($C_5Me_5$) (3.2 mg, 0.005 mmol) and HCOOH/$Et_3N$ (5:2, 0.3 mL), and the mixture was stirred at rt for 24 h. The solvent was removed under reduced pressure and the product isolated by column chromatography on silica gel (hexane/ethyl acetate, 7:3).

#### 4.4.1. (R)-2-Tosyloxy-1-(benzofuran-2-yl)ethanol **5a**[41]

White solid, 0.31 g, 92% yield, mp 78–80 °C, $[\alpha]_D^{26} = +33.50$ (*c* 2.00, $CHCl_3$), 97% ee, determined by HPLC analysis, Daicel Chiralcel OD-H column 250 × 4.6 mm, 5 μm, hexane/isopropanol 70:30, flow 0.6 mL/min, (*S*) 14.50 min, 1.57%, (*R*) 15.40 min, 98.43%. Lit.[41] for (*S*)-5a $[\alpha]_D^{27} = -28.98$ (*c* 0.98, $CHCl_3$). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta = 2.42$ (s, 3H, $CH_3$), 2.60 (d, $J = 5.7$ Hz, 1H, OH), 4.34 (dd $J = 10.5$, 6.9 Hz, 1H, $CH_2$), 4.42 (dd, $J = 10.5$, 3.9 Hz, 1H, $CH_2$), 5.11 (ddd, $J = 6.8$, 4.0, 0.8 Hz, 1H, CH), 6.71 (d, $J = 0.4$ Hz, 1H, CH), 7.22 (td, $J = 7.2$, 1.2 Hz, 1H), 7.24–7.31 (m, 3H), 7.38 (d, $J = 8.1$ Hz, 1H), 7.52–7.55 (m, 1H), 7.75 (dt, $J = 8.4$, 2.0 Hz, 2H) ppm. $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta = 21.7$ ($CH_3$), 66.7 (CH), 71.3 ($CH_2$), 104.7 (CH), 111.3 (CH), 121.3 (CH), 123.1 (CH), 124.6 (CH), 127.7 (C), 127.9 (2xCH), 129.9 (2xCH), 132.4 (C), 145.2 (C), 153.9 (C), 154.8 (C) ppm. IR, HCB ($cm^{-1}$): 3513, 3461, 1563, 1339, 1173, 980, 851. 794, 655. Anal. calcd for $C_{17}H_{16}O_5S$: C, 61.43; H, 4.85. Found: C, 61.49; H, 4.77.

#### 4.4.2. (R)-2-Tosyloxy-1-(7-ethylbenzofuran-2-yl)ethanol **5b**[41,69]

Yellow oil, 0.33 g, 93% yield, $[\alpha]_D^{25} = +31.42$ (*c* 1.22, $CHCl_3$), 90% ee, determined by HPLC analysis, Daicel Chiralcel OD-H column 250 × 4.6 mm, 5 μm, hexane/isopropanol 70:30, flow 0.6 mL/min, (*S*) 11.63 min, 5.13%, (*R*) 12.47 min, 94.87%. Lit.[41] for (*S*)-5b $[\alpha]_D^{20} = -33.1$ (*c* 0.66, $CHCl_3$); 94.67% ee. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta = 1.32$ (t, $J = 7.6$ Hz, 3H, $CH_3$), 2.42 (s, 3H, $CH_3$), 2.71 (d, $J = 5.4$ Hz, 1H, OH), 2.87 (q, $J = 7.6$ Hz, 2H, $CH_2$), 4.36 (dd, $J = 10.4$, 6.8 Hz, 1H, $CH_2$), 4.44 (dd, $J = 10.4$, 4.4 Hz, 1H, $CH_2$), 5.13 (dd, $J = 9.9$, 5.4 Hz, 1H, CH), 6.70 (t, $J = 0.4$ Hz, 1H), 7.24 (td, $J = 7.2$, 1.2 Hz, 1H), 7.27–7.29 (m, 3H), 7.39 (ddd, $J = 8.0$, 2.0, 0.8 Hz, 1H), 7.54 (ddd, $J = 7.6$, 1.6, 0.8 Hz, 1H), 7.76 (dt, $J = 8.4$, 2.0 Hz, 2H) ppm. $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta = 14.0$ ($CH_3$), 21.6 ($CH_3$), 22.7 ($CH_2$), 66.7 (CH), 71.4 ($CH_2$), 104.9 (CH), 118.7 (CH), 123.2 (CH), 123.8 (CH), 127.3 (C), 127.7 (C), 127.9 (2xCH), 129.9 (2xCH), 132.5 (C), 145.1 (C), 153.4 (C), 153.6 (C) ppm. IR, neat ($cm^{-1}$): 3500, 2963, 2931, 1598, 1455, 1362, 1290, 1177, 983, 814. 748, 665. Anal. calcd for $C_{19}H_{20}O_5S$: C, 63.32; H, 5.59. Found: C, 63.19; H, 5.35.

#### 4.4.3. (R)-2-Tosyloxy-1-(3-methylbenzofuran-2-yl)ethanol **5c**

Yellow solid, 0.36 g, 96% yield, mp 58–60 °C, $[\alpha]_D^{25} = +29.27$ (*c* 1.52, $CHCl_3$), 92% ee, determined by HPLC analysis, Daicel Chiralcel OD-H column 250 × 4.6 mm, 5 μm, hexane/isopropanol 70:30, flow 0.6 mL/min, (*S*) 12.34 min, 3.78%, (*R*) 13.59 min, 96.22%. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta = 2.24$ (s, 3H, $CH_3$), 2.42 (s, 3H, $CH_3$), 2.54 (bs, 1H, OH), 4.32 (dd, $J = 10.4$, 4.8 Hz, 1H, $CH_2$), 4.45 (dd, $J = 10.4$, 7.6 Hz, 1H, $CH_2$), 5.17 (t, $J = 6.0$ Hz, 1H, CH), 7.23–7.27 (m, 3H), 7.30 (td, $J = 8.4$, 1.2 Hz, 1H), 7.36 (ddd, $J = 8.0$, 1.2, 0.8 Hz, 1H), 7.49 (ddd, $J = 7.6$, 1.2, 0.8 Hz, 1H), 7.74 (dt, $J = 8.4$, 2.0 Hz, 2H) ppm. $^{13}C$ NMR (175 MHz, $CDCl_3$): $\delta = 7.4$ ($CH_3$), 21.3 ($CH_3$), 64.3 (CH), 70.7 ($CH_2$), 110.8 (CH), 113.9 (C), 119.3 (CH), 122.2 (CH), 124.5 (CH), 127.5 (2xCH), 129.0 (C), 129.5 (2xCH), 132.0 (C), 144.7 (C), 147.5 (C), 153.6 (C) ppm. Anal. calcd for $C_{18}H_{18}O_5S$: C, 62.41; H, 5.24. Found: C, 62.39; H, 5.26.

#### 4.4.4. (R)-2-Tosyloxy-1-(3,7-dimethylbenzofuran-2-yl)ethanol **5d**

Light yellow solid, 0.31 g, 89% yield, mp 64–66 °C, $[\alpha]_D^{25} = +15.33$ (*c* 1.26, $CHCl_3$), 87% ee, determined by HPLC analysis, Daicel Chiralcel OD-H column 250 × 4.6 mm, 5 μm, hexane/isopropanol 70:30, flow 0.6 mL/min, (*S*) 10.87 min, 6.39%, (*R*) 11.80 min, 93.61%. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta = 1.89$ (bs, 1H, OH), 2.21 (s, 3H, $CH_3$), 2.38 (s, 3H, $CH_3$), 2.41 (s, 3H, $CH_3$), 4.31 (dd, $J = 10.2$, 5.1 Hz, 1H, $CH_2$), 4.45 (dd, $J = 10.2$, 7.5 Hz, 1H, $CH_2$), 5.14 (dd, $J = 7.5$, 5.1 Hz, 1H, CH), 7.08 (ddd, $J = 7.2$, 1.5, 0.9 Hz, 1H), 7.14 (t, $J = 7.2$ Hz, 1H), 7.19–7.22 (m, 1H), 7.29 (ddd, $J = 7.5$, 1.5, 0.6 Hz, 1H), 7.70 (dt, $J = 8.4$, 1.8 Hz, 2H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta = 7.8$ ($CH_3$), 14.9 ($CH_3$), 21.6 ($CH_3$), 64.7 (CH), 71.1 ($CH_2$), 114.5 (C), 117.0 (CH), 121.4 (C), 122.6 (CH), 125.8 (CH), 127.8 (2xCH), 128.9 (C), 129.7 (2xCH), 132.5 (C), 144.9 (C), 147.6 (C), 153.0 (C) ppm. Anal. calcd for $C_{19}H_{20}O_5S$: C, 63.32; H, 5.59. Found: C, 62.98; H, 5.60.

#### 4.4.5. (R)-2-Tosyloxy-1-(3-phenethylbenzofuran-2-yl)ethanol **5e**

Light pink oil, 0.46 g, 95% yield, $[\alpha]_D^{25} = +18.71$ (*c* 1.28, $CHCl_3$), 93% ee, determined by HPLC analysis, Daicel Chiralcel OD-H column 250 × 4.6 mm, 5 μm, hexane/isopropanol 90:10, flow 0.7 mL/min, (*S*) 34.04 min, 3.67%, (*R*) 42.85 min, 96.33%. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta = 2.43$ (s, 3H, $CH_3$), 2.90–3.06 (m, 4H, 2x$CH_2$), 2.96 (bs, 1H, OH), 3.98 (dd, $J = 10.4$, 4.8 Hz, 1H, $CH_2$), 4.23 (dd, $J = 10.4$, 7.6 Hz, 1H, $CH_2$), 4.70 (dd, $J = 7.6$, 4.8 Hz, 1H, CH), 7.01–7.03 (m, 2H), 7.15–7.20 (m, 1H), 7.22–7.29 (m, 5H), 7.32 (td, $J = 8.0$, 1.6 Hz, 1H), 7.37 (ddd, $J = 8.0$, 2.0, 0.8 Hz, 1H), 7.56 (ddd, $J = 7.6$, 1.2, 0.8 Hz, 1H), 7.71 (dt, $J = 8.0$, 2.0 Hz, 2H) ppm. $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta = 21.6$ ($CH_3$), 25.6 ($CH_2$), 35.6 ($CH_2$), 64.3 (CH), 70.7 ($CH_2$), 111.5 (CH), 117.4 (C), 119.7 (CH), 122.7 (CH), 124.9 (CH), 126.4 (CH), 127.9 (2xCH), 128.3 (C), 128.5 (2xCH), 128.8 (2xCH), 129.8 (2xCH), 132.6 (C), 141.2 (C), 144.9 (C), 149.1 (C), 154.3 (C) ppm. IR, neat ($cm^{-1}$): 3518 3028, 2926, 1598, 1495, 1455, 1360, 1252, 1178, 983, 814. 750, 655. Anal. calcd for $C_{25}H_{24}O_5S$: C, 68.79; H, 5.54. Found: C, 68.50; H, 5.42.

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*4.4.6. (R)-2-(4-Chlorobenzenesulfonyloxy)-1-(benzofuran-2-yl) ethanol* ***6a***

Light brown solid, 0.29 g, 84% yield, mp 58–61 °C, $[\alpha]_D^{27} = +77.50$ (*c* 0.80, $CHCl_3$). $^1H$ NMR (700 MHz, $CDCl_3$): $\delta = 2.64$ (bs, 1H, OH), 4.41 (dd, $J = 10.5$, 7.0 Hz, 1H, $CH_2$), 4.47 (dd, $J = 10.5$, 4.2 Hz, 1H, $CH_2$), 5.15 (ddd, $J = 6.3$, 1.5, 0.7 Hz, 1H, CH), 6.74 (t, $J = 0.7$ Hz, 1H), 7.27 (ddd, $J = 7.7$, 7.0, 1.4 Hz, 1H), 7.32 (ddd, $J = 9.8$, 7.7, 1.7 Hz, 1H), 7.40 (dq, $J = 8.4$, 0.7 Hz, 1H), 7.44 (dt, $J = 8.4$, 2.1 Hz, 2H), 7.56 (dq, $J = 7.7$, 0.7 Hz, 1H), 7.79 (dt, $J = 8.4$, 0.9 Hz, 2H) ppm. $^{13}C$ NMR (175 MHz, $CDCl_3$): $\delta = 67.5$ (CH), 72.6 ($CH_2$), 105.9 (CH), 112.3 (CH), 122.3 (CH), 124.1 (CH), 125.8 (CH), 128.6 (C), 130.3 (2xCH), 130.6 (2xCH), 134.9 (C), 141.7 (C), 154.9 (C), 155.8 (C) ppm. IR, neat ($cm^{-1}$): 3505, 3094, 1341, 1172, 942, 750. Anal. calcd for $C_{16}H_{13}ClO_5S$: C, 54.47; H, 3.71. Found: C, 54.30; H, 3.62.

*4.4.7. (R)-2-(4-Chlorobenzenesulfonyloxy)-1-(7-ethylbenzofuran-2-yl)ethanol* ***6b***

Light brown solid, 0.36 g, 93% yield, mp 36–39 °C, $[\alpha]_D^{27} = +67.27$ (*c* 1.10, $CHCl_3$). $^1H$ NMR (700 MHz, $CDCl_3$): $\delta = 1.33$ (t, $J = 7.7$ Hz, 3H, $CH_3$), 2.61 (bs, 1H, OH), 2.87 (q, $J = 7.7$ Hz, 2H, $CH_2$), 4.42 (dd, $J = 10.5$, 6.3 Hz, 1H, $CH_2$), 4.49 (dd, $J = 10.5$, 3.0 Hz, 1H, $CH_2$), 5.15 (ddd, $J = 7.0$, 4.2, 0.7 Hz, 1H, CH), 6.72 (d, $J = 0.7$ Hz, 1H), 7.15 (dt, $J = 7.7$, 0.7 Hz, 1H), 7.20 (t, $J = 7.0$ Hz, 1H), 7.40 (dd, $J = 7.7$, 0.7 Hz, 1H), 7.42 (dt, $J = 8.4$, 2.1 Hz, 1H), 7.79 (dt, $J = 8.4$, 2.1 Hz, 2H) ppm. $^{13}C$ NMR (175 MHz, $CDCl_3$): $\delta = 15.0$ ($CH_3$), 23.7 ($CH_2$), 67.6 (CH), 72.6 ($CH_2$), 106.0 (CH), 119.7 (CH), 124.3 (CH), 124.9 (CH), 128.1 (C), 128.3 (C), 128.7 (C), 130.3 (2xCH), 130.6 (2xCH), 134.9 (C), 141.7 (C), 154.4 (C) ppm. IR, neat ($cm^{-1}$): 3487, 2966, 1348, 1113, 975, 827, 746. Anal. calcd for $C_{18}H_{17}ClO_5S$: C, 56.77; H, 4.50. Found: C, 56.67; H, 4.40.

*4.4.8. (R)-2-(4-Chlorobenzenesulfonyloxy)-1-(3-methylbenzofuran-2-yl)ethanol* ***6c***

Yellow solid, 0.35 g, 96% yield, mp 65–68 °C, $[\alpha]_D^{27} = +53.68$ (*c* 1.90, $CHCl_3$), 90% ee, determined by HPLC analysis, Daicel Chiralcel OD-H column 250 × 4.6 mm, 5 μm, hexane/isopropanol 55:45, flow 0.4 mL/min, (*S*) 17.83 min, 4.94%, (*R*) 19.12 min, 95.06%. $^1H$ NMR (700 MHz, $CDCl_3$): $\delta = 2.26$ (s, 3H, $CH_3$), 2.65 (bs, 1H, OH), 4.36 (dd, $J = 10.5$, 4.2 Hz, 1H, CH), 4.49 (dd, $J = 10.5$, 7.0 Hz, 1H, CH), 5.19 (dd, $J = 7.0$, 4.9 Hz, 1H, CH), 7.28 (ddd, $J = 7.7$, 7.0, 1.4 Hz, 1H), 7.34 (td, $J = 7.0$, 1.4 Hz, 1H), 7.36 (ddd, $J = 8.4$, 1.4, 0.7 Hz, 1H), 7.41 (dt, $J = 9.1$, 2.1 Hz, 2H), 7.51 (ddd, $J = 8.4$, 1.4, 0.7 Hz. 1H), 7.77 (dt, $J = 8.4$, 2.1 Hz, 2H) ppm. $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta = 8.7$ ($CH_3$), 65.5 (CH), 72.4 ($CH_2$), 112.2 (CH), 115.4 (C), 120.7 (CH), 123.7 (CH), 126.1 (CH), 130.2 (2xCH), 130.3 (C), 130.5 (2xCH), 134.9 (C), 141.6 (C), 148.8 (C), 154.9 (C) ppm. IR, neat ($cm^{-1}$): 3518, 3096, 1356, 1181, 973, 742. Anal. calcd for $C_{17}H_{15}ClO_5S$: C, 55.67; H, 4.12. Found: C, 55.10; H, 3.80.

*4.4.9. (R)-2-Benzenesulfonyloxy-1-(benzofuran-2-yl)ethanol* ***7a***

Light brown oil, 0.31 g, 99% yield, $[\alpha]_D^{27} = +24.00$ (*c* 1.00, $CHCl_3$), 97% ee, determined by HPLC analysis, Daicel Chiralcel OD-H column 250 × 4.6 mm, 5 μm, hexane/isopropanol 55:45, flow 0.4 mL/min, (*S*) 17.30 min, 1.57%, (*R*) 18.21 min, 98.44%. $^1H$ NMR (700 MHz, $CDCl_3$): $\delta = 2.89$ (s, 1H, OH), 4.39 (dd, $J = 10.5$, 7.0 Hz, 1H, $CH_2$), 4.46 (dd, $J = 10.5$, 4.2 Hz, 1H, $CH_2$), 5.14 (dd, $J = 7.0$, 4.2 Hz, 1H, CH), 6.73 (t, $J = 0.7$ Hz, 1H), 7.25 (ddd, $J = 8.4$, 7.0, 0.7 Hz, 1H), 7.31 (ddd, $J = 8.4$, 7.0, 0.7 Hz, 1H), 7.41 (dq, $J = 8.4$, 1.4 Hz, 1H), 7.51–7.52 (m, 2H), 7.56 (dq, $J = 7.7$, 0.7 Hz, 1H), 7.63–7.66 (m, 1H), 7.89–7.91 (m, 2H) ppm. $^{13}C$ NMR (175 MHz, $CDCl_3$): $\delta = 67.6$ (CH), 72.4 ($CH_2$), 105.8 (CH), 112.3 (CH), 122.3 (CH), 124.1 (CH), 125.6 (CH), 128.7 (C), 128.9 (2xCH), 130.3 (2xCH), 135.0 (CH), 136.5 (C), 154.9 (C), 155.8 (C) ppm. IR, neat ($cm^{-1}$): 3509, 3065, 1356, 1173, 972, 750. Anal. calcd for $C_{16}H_{14}O_5S$: C, 60.37; H, 4.43. Found: C, 59.98; H, 4.12.

*4.4.10. (R)-2-Benzenesulfonyloxy-1-(7-ethylbenzofuran-2-yl) ethanol* ***7b***

Light brown oil, 0.32 g, 93%, $[\alpha]_D^{27} = +57.50$ (*c* 0.80, $CHCl_3$), 94% ee, determined by HPLC analysis, Daicel Chiralcel OD-H column 250 × 4.6 mm, 5 μm, hexane/isopropanol 55:45, flow 0.4 mL/min, (*S*) 14.51 min, 2.85%, (*R*) 15.65 min, 97.15%. $^1H$ NMR (700 MHz, $CDCl_3$): $\delta = 1.33$ (t, $J = 7.7$ Hz, 3H, $CH_3$), 2.62 (bs, 1H, OH), 2.88 (q, $J = 7.7$ Hz, 2H, $CH_2$), 4.41 (dd, $J = 10.5$, 6.3 Hz, 1H, $CH_2$), 4.90 (dd, $J = 10.5$, 4.2 Hz, 1H, $CH_2$), 5.16 (ddd, $J = 7.0$, 4.2, 0.7 Hz, 1H, CH), 6.73 (d, $J = 0.7$ Hz, 1H), 7.14 (dt, $J = 7.0$, 0.7 Hz, 1H), 7.19 (t, $J = 7.0$ Hz, 1H), 7.40 (dd, $J = 7.7$, 1.4 Hz, 1H), 7.50–7.53 (m, 2H), 7.65 (tt, $J = 7.7$, 1.4 Hz, 1H), 7.90–7.92 (m, 2H) ppm. $^{13}C$ NMR (175 MHz, $CDCl_3$): $\delta = 15.0$ ($CH_3$), 23.7 ($CH_2$), 67.7 (CH), 72.5 ($CH_2$), 105.9 (CH), 119.8 (CH), 124.2 (CH), 124.8 (CH), 128.4 (C), 128.8 (C), 128.9 (2xCH), 130.3 (2xCH), 134.9 (CH), 136.5 (C), 154.5 (C), 154.6 (C) ppm. IR, neat ($cm^{-1}$): 3500, 3063, 1357, 1175, 973, 748. Anal. calcd for $C_{18}H_{18}O_5S$: C, 62.41; H, 5.24. Found: C, 62.18; H, 5.02.

*4.4.11. (R)-2-Benzenesulfonyloxy-1-(3-methylbenzofuran-2-yl) ethanol* ***7c***

Light brown oil, 0.31 g, 93%, $[\alpha]_D^{27} = +38.75$ (*c* 0.80, $CHCl_3$), 92% ee, determined by HPLC analysis, Daicel Chiralcel OD-H column 250 × 4.6 mm, 5 μm, hexane/isopropanol 55:45, flow 0.4 mL/min, (*S*) 16.72 min, 4.21%, (*R*) 18.41 min, 95.79%. $^1H$ NMR (700 MHz, $CDCl_3$): $\delta = 2.26$ (s, 3H, $CH_3$), 2.49 (bs, 1H, OH), 4.36 (dd, $J = 10.5$, 4.9 Hz, 1H, $CH_2$), 4.49 (dd, $J = 10.5$, 7.0 Hz, 1H, $CH_2$), 5.20 (dd, $J = 7.0$, 4.9 Hz, 1H, CH), 7.27 (ddd, $J = 7.7$, 7.0, 0.7 Hz, 1H), 7.32 (ddd, $J = 8.4$, 7.0, 1.4 Hz, 1H), 7.38 (dt, $J = 7.7$, 0.7 Hz, 1H), 7.49–7.52 (m, 3H), 7.63 (tt, $J = 7.0$, 1.4 Hz, 1H), 7.88–7.90 (m, 2H) ppm. $^{13}C$ NMR (175 MHz, $CDCl_3$): $\delta = 8.7$ ($CH_3$), 65.6 (CH), 72.3 ($CH_2$), 112.2 (CH), 115.3 (C), 120.7 (CH), 123.6 (CH), 125.9 (CH), 128.8 (2xCH), 130.2 (2xCH), 130.4 (C), 134.9 (CH), 136.5 (C), 149.0 (C), 155.0 (C) ppm. IR, neat ($cm^{-1}$): 3518, 3064, 2922, 1359, 1185, 972, 744. Anal. calcd for $C_{17}H_{16}O_5S$: C, 61.43; H, 4.85. Found: C, 61.40; H, 4.72.

*4.4.12. (R)-2-Mesyloxy-1-(benzofuran-2-yl)ethanol* ***8a***

Green oil, 0.24 g, 95% yield, $[\alpha]_D^{24} = +37.69$ (*c* 1.30, $CHCl_3$), 99% ee, determined by HPLC analysis, Daicel Chiralcel OD-H column 250 × 4.6 mm, 5 μm, hexane/isopropanol 90:10, flow 0.7 mL/min, (*S*) 68.92 min, 0.46%, (*R*) 72.39 min, 99.54%. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta = 2.74$ (d, $J = 5.2$ Hz, 1H, OH), 3.09 (s, 3H, $CH_3$), 4.60 (dd, $J = 10.8$, 7.2 Hz, 1H, $CH_2$), 4.64 (dd, $J = 10.8$, 3.6 Hz, 1H, $CH_2$), 5.21 (dd, $J = 10.4$, 4.4 Hz, 1H, CH), 6.81 (t, $J = 0.8$ Hz, 1H), 7.26 (td, $J = 7.6$, 1.2 Hz, 1H), 7.33 (ddd, $J = 8.4$, 7.2, 1.6 Hz, 1H), 7.48 (ddd, $J = 8.4$, 1.6, 1.2 Hz, 1H), 7.59 (ddd, $J = 7.6$, 5.6, 0.8 Hz, 1H) ppm. $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta = 37.7$ ($CH_3$), 66.8 (CH), 71.1 ($CH_2$), 104.8 (CH), 111.3 (CH), 121.4 (CH), 123.2 (CH), 124.8 (CH), 127.7 (C), 153.9 (C), 154.9 (C) ppm. IR, neat ($cm^{-1}$): 3391, 3114, 1342, 1170, 957, 774. Anal. calcd for $C_{11}H_{12}O_5S$: C, 51.55; H, 4.72. Found: C, 51.45; H, 4.71.

*4.4.13. (R)-2-Mesyloxy-1-(7-ethylbenzofuran-2-yl)ethanol* ***8b***[41]

Yellow oil, 0.26 g, 93% yield, $[\alpha]_D^{26} = +44.50$ (*c* 2.00, $CHCl_3$), 95% ee, determined by HPLC analysis, Daicel Chiralcel OD-H column 250 × 4.6 mm, 5 μm, hexane/isopropanol 60:40, flow 0.7 mL/min, (*S*) 14.92 min, 2.49%, (*R*) 16.90 min, 97.51%. Lit.[41] for (*S*)-8b $[\alpha]_D^{20} = -45.15$ (*c* 1.11, $CHCl_3$); 97.32% ee. $^1H$ NMR (700 MHz, $CDCl_3$): $\delta = 1.34$ (t, $J = 7.0$ Hz, 3H, $CH_3$), 2.75 (bs, 1H, OH), 2.92 (q, $J = 7.0$ Hz, 2H, $CH_2$), 3.07 (s, 3H, $CH_3$), 4.58 (dd, $J = 11.2$, 7.0 Hz, 1H, $CH_2$), 4.62 (dd, $J = 11.2$, 4.2 Hz, 1H, $CH_2$), 5.20 (dd, $J = 5.6$, 2.8 Hz, 1H, CH), 6.78 (s, 1H), 7.13 (dt, $J = 7.7$, 0.7 Hz, 1H), 7.18 (t, $J = 7.0$ Hz, 1H), 7.40 (dd, $J = 7.0$, 1.4 Hz, 1H) ppm. $^{13}C$ NMR (175 MHz, $CDCl_3$): $\delta = 13.7$ ($CH_3$), 22.4 ($CH_2$), 37.3 ($CH_3$), 66.5 (CH), 70.7 ($CH_2$), 104.6 (CH), 118.4 (CH), 122.9 (CH), 123.6 (CH), 126.9 (C), 127.5 (C), 153.1 (C), 153.2 (C) ppm. IR, neat ($cm^{-1}$): 3501, 3028, 1347, 1169, 958, 816, 746. Anal. calcd for $C_{13}H_{16}O_5S$: C, 54.92; H, 5.67. Found: C, 54.87; H, 5.60.

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*4.4.14. (R)-2-Mesyloxy-1-(3-methylbenzofuran-2-yl)ethanol* ***8c***

Light green oil, 0.27 g, 93% yield, $[\alpha]_D^{26} = +22.00$ (*c* 1.50, $CHCl_3$), 93% ee, determined by HPLC analysis, Daicel Chiralcel OD-H column 250 × 4.6 mm, 5 μm, hexane/isopropanol 55:45, flow 0.45 mL/min, (*S*) 16.44 min, 3.58%, (*R*) 19.49 min, 96.42%. $^1$H NMR (700 MHz, $CDCl_3$): $\delta = 2.30$ (s, 3H, $CH_3$), 2.60 (bs, 1H, OH), 3.06 (s, 3H, $CH_3$), 4.47 (dd, $J = 11.2$, 4.2 Hz, 1H, $CH_2$), 4.67 (dd, $J = 11.2$, 8.4 Hz, 1H, $CH_2$), 5.24 (dd, $J = 7.7$, 4.2 Hz, 1H, CH),7.26 (td, $J = 7.7$, 0.7 Hz, 1H), 7.32 (ddd, $J = 8.4$, 7.0, 1.4 Hz, 1H), 7.43 (dt, $J = 8.4$, 0.7 Hz, 1H), 7.51 (dq, $J = 7.7$, 0.7 Hz, 1H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 7.8$ ($CH_3$), 37.7 ($CH_3$), 64.9 (CH), 71.0 ($CH_2$), 111.3 (CH), 114.4 (C), 119.8 (CH), 122.7 (CH), 125.1 (CH), 129.4 (C), 147.9 (C), 154.1 (C) ppm. IR, neat ($cm^{-1}$): 3502, 3028, 1346, 1081, 957, 745. Anal. calcd for $C_{12}H_{14}O_5S$: C, 53.32; H, 5.22. Found: C, 53.32; H, 5.25.

*4.4.15. (R)-2-Mesyloxy-1-(3-phenetylbenzofuran-2-yl)ethanol* ***8e***

Yellow oil, 0.30 g, 96% yield, $[\alpha]_D^{25} = +12.50$ (*c* 0.80, $CHCl_3$), 93% ee, determined by HPLC analysis, Daicel Chiralcel OD-H column 250 × 4.6 mm, 5 μm, hexane/isopropanol 55:45, flow 0.45 mL/min, (*R*) 21.58 min, 96.34%, (*S*) 23.99 min, 3.66%. $^1$H NMR (400 MHz, $CDCl_3$): $\delta = 1.51$ (d, $J = 4.0$ Hz, 1H, OH), 2.96–3.12 (m, 4H, 2x$CH_2$), 3.01 (s, 3H, $CH_3$), 4.05 (dd, $J = 10.8$, 4.0 Hz, 1H, $CH_2$), 4.42 (dd, $J = 10.8$, 8.0 Hz, 1H, $CH_2$), 4.72 (dt, $J = 8.4$, 4.0 Hz, 1H, CH), 7.00–7.04 (m, 2H), 7.21–7.30 (m, 3H), 7.32 (dd, $J = 7.6$, 1.2 Hz, 1H), 7.36 (td, $J = 7.6$, 1.2 Hz, 1H), 7.46 (ddd, $J = 8.0$, 1.2, 0.8 Hz, 1H), 7.62 (ddd, $J = 7.6$, 1.6, 0.8 Hz, 1H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 25.7 ($CH_2$), 35.5 ($CH_3$), 37.6 ($CH_2$), 64.4 (CH), 70.7 ($CH_2$), 111.6 (CH), 117.4 (C), 119.8 (CH), 122.8 (CH), 125.1 (CH), 126.5 (CH), 128.2 (C), 128.5 (2xCH), 128.9 (2xCH), 141.1 (C), 149.1 (C), 154.4 (C) ppm. IR, neat ($cm^{-1}$): 3512, 3025, 2933, 1251, 1172, 961, 750. Anal. calcd for $C_{19}H_{20}O_5S$: C, 63.32; H, 5.59. Found: C, 63.21; H, 5.73.

### *4.5. General procedure for the synthesis of benzofuryl β-azido alcohols*

A mixture of benzofuryl 1,2-diol monosulfonate (0.68 mmol) and sodium azide (0.88 mg, 1.36 mmol) in DMSO (5 mL) was heated at 80 °C for 2 h and then cooled to rt. To this was added water (10 mL) and the mixture was extracted with ethyl acetate (3 × 7 mL). The combined extract was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate/dichloromethane, 5:2:3).

*4.5.1. (R)-2-Azido-1-(benzofuran-2-yl)ethanol* ***9***

Prepared from **5a**: light yellow solid, 0.12 g, 84% yield, mp 35–36 °C, $[\alpha]_D^{26} = +90.50$ (*c* 2.00, $CHCl_3$), 97% ee, determined by HPLC analysis, Daicel Chiralcel OD-H column 250 × 4.6 mm, 5 μm, hexane/isopropanol 95:5, flow 0.7 mL/min, (*S*) 33.89 min, 1.17%, (*R*) 36.56 min, 98.83%. $^1$H NMR (700 MHz, $CDCl_3$): $\delta = 2.54$ (bs, 1H, OH), 3.75 (dd, $J = 12.6$, 4.2 Hz, 1H, $CH_2$), 3.80 (dd, $J = 12.6$, 7.0 Hz, 1H, $CH_2$), 5.06 (ddd, $J = 7.0$, 4.2, 0.7 Hz, 1H, CH), 6.78 (t, $J = 0.7$ Hz, 1H), 7.27 (ddd, $J = 8.4$, 7.0, 1.4 Hz, 1H), 7.33 (ddd, $J = 8.4$, 7.0, 1.4 Hz, 1H), 7.50 (dq, $J = 8.4$, 0.7 Hz, 1H), 7.60 (dq, $J = 7.7$, 0.7 Hz, 1H) ppm. $^{13}$C NMR (175 MHz, $CDCl_3$): $\delta = 56.0$ ($CH_2$), 68.7 (CH), 105.1 (CH), 112.3 (CH), 122.3 (CH), 124.1 (CH), 125.6 (CH), 128.9 (C), 155.9 (C), 156.8 (C) ppm. IR neat ($cm^{-1}$): 3400, 2106, 1454, 1304, 1173, 1092, 812, 751. Anal. calcd for $C_{10}H_9O_2N_3$: C, 59.11; H, 4.46; N, 20.68. Found: C, 58.96; H, 4.63; N, 20.37.

*4.5.2. (R)-2-Azido-1-(7-ethylbenzofuran-2-yl)ethanol* ***10***

Prepared from **5b**: orange oil, 0.11 g, 72% yield, $[\alpha]_D^{29} = +67.65$ (*c* 1.59, $CHCl_3$), 90% ee, determined by HPLC analysis, Daicel Chiralcel OJ column 250 × 4.6 mm, 10 μm, hexane/isopropanol 80:20, flow 0.7 mL/min, (*S*) 9.68 min, 5.06%, (*R*) 10.75 min, 94.94%. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 1.35$ (t, $J = 7.5$ Hz, 3H, $CH_3$), 2.62 (d, $J = 5.7$ Hz, 1H, OH), 2.92 (q, $J = 7.5$ Hz, 2H, $CH_2$), 3.70 (dd, $J = 12.6$, 4.5 Hz, 1H, $CH_2$), 3.76 (dd, $J = 12.6$, 6.9 Hz, 1H, $CH_2$), 5.04 (ddd, $J = 7.0$, 4.5, 0.9 Hz, 1H, CH), 6.73 (d, $J = 0.6$ Hz, 1H), 7.12 (ddd, $J = 7.2$, 1.5, 0.6 Hz, 1H), 7.18 (t, $J = 7.5$ Hz, 1H), 7.40 (dd, $J = 7.5$, 1.5 Hz, 1H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 14.1$ ($CH_3$), 22.7 ($CH_2$), 55.1 ($CH_2$), 67.8 (CH), 104.2 (CH), 118.7 (CH), 123.2 (CH), 123.8 (CH), 127.4 (C), 127.8 (C), 153.4 (C), 155.3 (C) ppm. IR, neat ($cm^{-1}$): 3401, 2969, 2106, 1427, 1277, 1182, 1092, 820, 747.

*4.5.3. (R)-2-Azido-1-(3-methylbenzofuran-2-yl)ethanol* ***11***

Prepared from **5c**: yellow oil, 91 mg, 62% yield, $[\alpha]_D^{25} = +48.90$ (*c* 0.73, $CHCl_3$), 92% ee, determined by HPLC analysis, Daicel Chiralcel OJ column 250 × 4.6 mm, 10 μm, hexane/isopropanol 90:10, flow 0.7 mL/min, (*S*) 26.05 min, 3.97%, (*R*) 28.34 min, 96.03%. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 2.29$ (s, 3H, $CH_3$), 2.30 (d, $J = 8.7$ Hz, 1H, OH), 3.59 (dd, $J = 12.6$, 4.8 Hz, 1H, $CH_2$), 3.83 (dd, $J = 12.6$, 7.8 Hz, 1H, $CH_2$), 5.07 (dd, $J = 7.8$, 4.8 Hz, 1H, CH), 7.25 (td, $J = 7.2$, 1.5 Hz, 1H), 7.31 (td, $J = 7.2$, 1.5 Hz, 1H), 7.44 (ddd, $J = 8.1$, 1.5, 0.9 Hz, 1H), 7.51 (ddd, $J = 7.2$, 1.5, 0.9 Hz, 1H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 7.8$ ($CH_3$), 54.9 ($CH_2$), 65.9 (CH), 111.2 (CH), 113.6 (C), 119.6 (CH), 122.6 (CH), 124.9 (CH), 129.5 (C), 149.4 (C), 154.0 (C) ppm.

*4.5.4. (R)-2-Azido-1-(3,7-dimethylbenzofuran-2-yl)ethanol* ***12***

Prepared from **5d**: yellow oil, 83 mg, 53% yield, $[\alpha]_D^{23} = +44.30$ (*c* 1.16, $CHCl_3$), 87% ee, determined by HPLC analysis, Daicel Chiralcel OD-H column 250 × 4.6 mm, 5 μm, hexane/isopropanol 90:10, flow 0.7 mL/min, (*S*) 11.67 min, 6.29%, (*R*) 13.11 min, 93.71%. $^1$H NMR (200 MHz, $CDCl_3$): $\delta = 2.20$ (bs, 1H, OH), 2.28 (s, 3H, $CH_3$), 2.51 (s, 3H, $CH_3$), 3.60 (dd, $J = 12.6$, 4.8 Hz, 1H, $CH_2$), 3.85 (dd, $J = 12.6$, 7.8 Hz, 1H, $CH_2$), 5.06 (dd, $J = 7.8$, 4.8 Hz, 1H, CH), 7.05–7.20 (m, 2H), 7.32–7.38 (m, 1H) ppm. $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta = 7.9$ ($CH_3$), 14.9 ($CH_3$), 54.9 ($CH_2$), 66.0 (CH), 113.9 (C), 117.0 (CH), 121.5 (C), 122.6 (CH), 125.8 (CH), 129.0 (C), 149.2 (C), 153.0 (C) ppm.

*4.5.5. (R)-2-Azido-1-(3-phenethylbenzofuran-2-yl)ethanol* ***13***

Prepared from **5e**: yellow oil, 0.10 g, 50% yield, $[\alpha]_D^{26} = +34.69$ (*c* 1.03, $CHCl_3$), 93% ee, determined by HPLC analysis, Daicel Chiralcel OD-H column 250 × 4.6 mm, 5 μm, hexane/isopropanol 90:10, flow 0.7 mL/min, (*S*) 16.55 min, 3.48%, (*R*) 42.85 min, 96.52%. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 1.47$ (bs, 1H, OH), 2.93–3.10 (m, 5H, 3x$CH_2$), 3.52 (dd, $J = 12.6$, 8.1 Hz, 1H, $CH_2$), 4.52 (dd, $J = 8.1$, 4.8 Hz, 1H, CH), 6.97–7.01 (m, 2H), 7.21–7.30 (m, 4H), 7.33 (td, $J = 7.2$, 1.5 Hz, 1H), 7.44–7.47 (m, 1H), 7.58–7.61 (m, 1H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 25.6$ ($CH_2$), 35.4 ($CH_2$), 54.2 ($CH_2$), 65.4 ($CH_2$), 111.5 (CH), 116.5 (C), 119.7 (CH), 122.7 (CH), 124.9 (CH), 126.4 (CH), 128.3 (C), 128.5 (2xCH), 128.9 (2xCH), 141.2 (C), 150.6 (C), 154.3 (C) ppm.

### *4.6. General procedure for the synthesis of benzofuryl β-amino alcohols from β-azido alcohols*

A mixture of benzofuryl β-azido alcohol (0.5 mmol) and 10% Pd/C (50 mg) in methanol (5 mL) was hydrogenated in an autoclave under 10 atm. pressure for 3 h at rt. The reaction mixture was filtered on a Celite pad and the filtrate was concentrated under reduced pressure to give white solid products.

*4.6.1. (R)-2-Amino-1-(benzofuran-2-yl)ethanol* ***14***

88 mg, 99% yield, mp 128–132 °C, $[\alpha]_D^{25} = +36.20$ (*c* 1.13, MeOH). $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta = 1.95$ (bs, 2H, $NH_2$), 2.79 (dd, $J = 13.2$, 7.2 Hz, 1H, $CH_2N$), 2.90 (dd, $J = 13.2$, 4.8 Hz, 1H, $CH_2N$), 4.57 (dd, $J = 6.9$, 4.8 Hz, 1H, CH), 5.60 (bs, 1H, $NH_2$), 6.72 (t, $J = 0.6$ Hz, 1H), 7.19 (td, $J = 7.2$, 1.5 Hz, 1H), 7.24 (td, $J = 7.2$, 1.5 Hz, 1H), 7.51 (ddd, $J = 7.2$, 1.5, 0.9 Hz, 1H), 7.57 (ddd, $J = 6.9$, 2.1, 0.6 Hz, 1H) ppm. $^{13}$C NMR (75 MHz, DMSO-$d_6$): $\delta = 46.7$ ($CH_2$), 68.9 (CH), 102.4 (CH),

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110.9 (CH), 120.8 (CH), 122.6 (CH), 123.6 (CH), 128.0 (C), 153.9 (C), 160.1 (C) ppm. IR, KBr ($cm^{-1}$): 3341, 3059, 1606, 1454, 1256, 940, 809, 737. Anal. calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.25; N, 7.90. Found: C, 67.66; H, 6.27; N, 7.48

*4.6.2. (R)-2-Amino-1-(7-ethylbenzofuran-2-yl)ethanol* ***15***

99 mg, 97% yield, mp 80–81 °C, $[\alpha]_D^{24} = +32.53$ (*c* 0.91, MeOH). $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta = 1.26$ (t, $J = 7.6$ Hz, 3H, $CH_3$), 1.65 (bs, 2H, $NH_2$), 2.78 (dd, $J = 12.6$, 7.6 Hz, 1H $CH_2N$), 2.84 (q, $J = 7.6$ Hz, 2H, $CH_2$), 2.90 (dd, $J = 12.6$, 4.6 Hz, 1H, $CH_2N$), 4.57 (dd, $J = 7.0$, 4.8 Hz, 1H, CH), 5.57 (bs, 1H, OH), 6.68 (d, $J = 0.8$ Hz, 1H), 7.06 (dd, $J = 7.4$, 0.8 Hz, 1H, 1H), 7.12 (t, $J = 7.2$ Hz, 1H), 7.38 (dd, $J = 7.0$, 2.0 Hz, 1H) ppm. $^{13}$C NMR (75 MHz, DMSO-$d_6$): $\delta = 14.1$ ($CH_3$), 22.3 ($CH_2$), 46.9 ($CH_2$), 69.0 (CH), 102.5 (CH), 118.4 (CH), 122.7 (CH), 122.8 (CH), 126.7 (C), 127.7 (C), 152.4 (C), 159.7 (C) ppm. IR, KBr ($cm^{-1}$): 3339, 2967, 1599, 1454, 1189, 1042, 995, 814, 740. Anal. calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.36; N, 6.82. Found: C, 70.35; H, 7.48; N, 6.94

*4.6.3. (R)-2-Amino-1-(3-methylbenzofuran-2-yl)ethanol* ***16***

92 mg, 96% yield, mp 95–98 °C, $[\alpha]_D^{25} = +14.14$ (*c* 0.45, MeOH). $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta = 1.68$ (bs, 2H, $NH_2$), 2.20 (s, 3H, $CH_3$), 2.79 (dd, $J = 12.6$, 6.0 Hz, 1H, $CH_2$), 2.88 (dd, $J = 12.6$, 7.2 Hz, 1H, $CH_2$), 4.65 (dd, $J = 7.2$, 6.0 Hz, 1H, CH), 5.40 (bs, 1H, OH), 7.17–7.27 (m, 2H), 7.45–7.48 (m, 1H), 7.51–7.56 (m, 1H) ppm. $^{13}$C NMR (75 MHz, DMSO-$d_6$): $\delta = 7.5$ ($CH_3$), 46.6 ($CH_2$), 67.4 (CH), 110.7 (CH), 111.1 (C), 119.2 (CH), 122.1 (CH), 123.8 (CH), 129.7 (C), 153.1 (C), 153.9 (C) ppm. IR, HCB ($cm^{-1}$): 3341, 2905, 1612, 1456, 1254, 1062, 740. Anal. calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.21; H, 6.80; N, 7.46.

*4.6.4. (R)-2-Amino-1-(3,7-dimethylbenzofuran-2-yl)ethanol* ***17***

81 mg, 79% yield, mp 127–130 °C, $[\alpha]_D^{25} = +13.03$ (*c* 0.44, MeOH). $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta = 1.43$ (bs, 2H, $NH_2$), 2.19 (s, 3H, $CH_3$), 2.41 (s, 3H, $CH_3$), 2.81 (dd, $J = 12.9$, 5.7 Hz, 1H, $CH_2$), 2.90 (dd, $J = 12.9$, 7.2 Hz, 1H, $CH_2$), 4.66 (dd, $J = 7.2$, 5.7 Hz, 1H, CH), 5.42 (bs, 1H, OH), 7.05 (ddd, $J = 7.2$, 1.8, 0.9 Hz, 1H), 7.10 (t, $J = 7.4$ Hz, 1H), 7.33 (ddd, $J = 7.2$, 1.5, 0.6 Hz, 1H) ppm. $^{13}$C NMR (75 MHz, DMSO-$d_6$): $\delta = 7.7$ ($CH_3$), 14.7 ($CH_3$), 46.4 ($CH_2$), 67.3 (CH), 111.3 (C), 116.7 (CH), 120.3 (C), 122.2 (CH), 124.7 (CH), 129.3 (C), 152.0 (C), 153.5 (C) ppm. IR, KBr, ($cm^{-1}$): 3277, 2922, 1586, 1451, 1258, 1035, 744. Anal. calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.36; N, 6.82. Found: C, 70.29; H, 7.58; N, 6.91.

*4.6.5. (R)-2-Amino-1-(3-phenethylbenzofuran-2-yl)ethanol* ***18***

100 mg, 71% yield, mp 107–109 °C, $[\alpha]_D^{23} = +99.50$ (*c* 0.81, MeOH). $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta = 1.65$ (bs, 2H, $NH_2$), 2.59 (dd, $J = 12.9$, 5.1 Hz, 1H, $CH_2N$), 2.79 (dd, $J = 12.9$, 7.5 Hz, 1H, $CH_2N$), 2.83–3.05 (m, 4H, 2x$CH_2$), 4.56 (dd, $J = 7.2$, 5.4 Hz, 1H, CH), 5.42 (bs, 1H, OH), 7.14–7.29 (m, 7H), 7.46–7.49 (m, 1H), 7.56–7.59 (m, 1H) ppm. $^{13}$C NMR (75 MHz, DMSO-$d_6$): $\delta = 25.0$ ($CH_2$), 35.8 ($CH_2$), 46.5 ($CH_2$), 67.3 (CH), 110.9 (CH), 115.2 (CH), 119.5 (CH), 122.2 (CH), 123.8 (CH), 125.9 (CH), 128.2 (2xCH), 128.4 (2xCH), 128.8 (C), 141.5 (C), 153.2 (C), 154.2 (C) ppm. Anal. calcd for $C_{18}H_{19}O_2N$: C, 76.84; H, 6.80; N, 4.98. Found: C, 76.48; H, 6.96; N, 4.92.

*4.7. General procedure for the synthesis of benzofuryl N,N-diformylamino ketones*

A mixture of the corresponding benzofuryl α-bromo ketone **19**–**22** (10.0 mmol) and sodium diformylamide (1.00 g, 10.5 mmol) in acetonitrile (50 mL) was stirred at rt for 1.5 h and then heated at 70 °C for 1 h. The hot mixture was filtered and the precipitated NaBr was washed with hot acetonitrile (20 mL). The combined filtrates were evaporated in vacuo and the product was crystallized from hexane/diethyl ether 1:1 to give a yellow solid.

*4.7.1. 2-N,N-Diformylamino-1-(benzofuran-2-yl)ethanone* ***23***

2.30 g, 99% yield, mp 122–123 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 5.11$ (s, 2H, $CH_2$), 7.35 (ddd, $J = 7.8$, 6.9, 1.2 Hz, 1H), 7.53 (ddd, $J = 8.4$, 6.9, 1.2 Hz, 1H), 7.60 (ddd, $J = 8.4$, 1.8, 0.9 Hz, 1H), 7.63 (d, $J = 0.9$ Hz, 1H), 7.74 (ddd, $J = 7.8$, 1.2, 0.9 Hz, 1H), 9.05 (s, 2H, 2xCHO) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 44.7$ ($CH_2$), 112.5 (CH), 113.8 (CH), 123.5 (CH), 124.3 (CH), 126.7 (C), 128.9 (CH), 150.5 (C), 155.7 (C), 163.1 (2xCHO), 181.4 (CO) ppm. Anal. calcd for $C_{12}H_9NO_4$: C, 62.34; H, 3.92; N, 6.05. Found: C, 62.34; H, 4.01; N, 6.14.

*4.7.2. 2-N,N-Diformylamino-1-(7-ethylbenzofuran-2-yl)ethanone* ***24***

2.52 g, 98% yield, mp 106–107 °C. $^1$H NMR (200 MHz, $CDCl_3$): $\delta = 1.37$ (t, $J = 7.5$ Hz, 3H, $CH_3$), 3.00 (q, $J = 7.5$ Hz, 2H, $CH_2$), 5.13 (s, 2H, $CH_2$), 7.27 (t, $J = 7.8$ Hz, 1H), 7.35 (ddt, $J = 7.2$ Hz, 1H), 7.56 (dd, $J = 7.8$, 1.5 Hz, 1H), 7.63 (s, 1H), 9.05 (s, 2H, 2xCHO) ppm. $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta = 13.9$ ($CH_3$), 22.6 ($CH_2$), 44.6 ($CH_2$), 114.1 (CH), 120.9 (CH), 124.4 (CH), 126.3 (C), 127.7 (CH), 128.9 (C), 150.1 (C), 154.4 (C), 163.4 (2xCHO), 184.5 (CO) ppm. Anal. calcd for $C_{14}H_{13}NO_4$: C, 64.86; H, 5.04; N, 5.40. Found: C, 64.58; H, 4.98; N, 5.27.

*4.7.3. 2-N,N-Diformylamino-1-(3-methylbenzofuran-2-yl) ethanone* ***25***

2.48 g, 98% yield, mp 145–147 °C. $^1$H NMR (200 MHz, $CDCl_3$): $\delta = 2.60$ (s, 3H, $CH_3$), 5.12 (s, 2H, $CH_2$), 7.34 (dt, $J = 7.9$, 3.7 Hz, 1H), 7.50–7.55 (m, 2H), 7.68 (dt, $J = 7.8$, 1.0 Hz, 1H), 9.10 (s, 2H, 2xCHO) ppm. $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta = 9.4$ ($CH_3$), 45.5 ($CH_2$), 112.2 (CH), 121.7 (CH), 123.6 (CH), 126.9 (C), 128.8 (C), 128.9 (CH), 146.1 (C), 154.4 (C), 163.3 (2xCHO), 182.9 (CO) ppm. IR, KBr ($cm^{-1}$): 3350, 2923, 1681, 1567, 1345, 1259, 1171, 983, 943, 852, 793, 655. Anal. calcd for $C_{13}H_{11}NO_4$: C, 63.67; H, 4.51; N, 5.71. Found: C, 63.58; H, 4.55; N, 5.77.

*4.7.4. 2-N,N-Diformylamino-1-(3,7-dimethylbenzofuran-2-yl) ethanone* ***26***

2.57 g, 99% yield, mp 104–108 °C. $^1$H NMR (200 MHz, $CDCl_3$): $\delta = 2.55$ (s, 3H, $CH_3$), 2.59 (s, 3H, $CH_3$), 5.15 (s, 2H, $CH_2$), 7.24 (t, $J = 7.2$ Hz, 1H), 7.32 (ddd, $J = 7.2$, 1.2, 0.9 Hz, 1H), 7.50 (ddd, $J = 7.8$, 1.2, 0.6 Hz, 1H), 9.06 (s, 2H, 2xCHO) ppm. $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta = 9.5$ ($CH_3$), 14.8 ($CH_3$), 45.4 ($CH_2$), 119.1 (CH), 122.5 (C), 123.7 (CH), 127.3 (C), 128.4 (C), 129.6 (CH), 146.0 (C), 153.5 (C), 163.4 (2xCHO), 182.2 (CO) ppm. Anal. calcd for $C_{14}H_{13}NO_4$: C, 64.86; H, 5.04; N, 5.40. Found: C, 64.76; H, 5.09; N, 5.32.

*4.8. General procedure for the synthesis of benzofuryl α-amino ketones hydrochlorides*

A mixture of benzofuryl *N,N*-diformylamino ketone **23**–**26** (10.0 mmol) and 5% HCl/EtOH (33 mL) was stirred at rt for 48 h. The precipitate was filtered and crystallized from isopropanol to give white solid products.

*4.8.1. 2-Amino-1-(benzofuran-2-yl)ethanone hydrochloride* ***27***

1.97 g, 94% yield, mp 211–212 °C. $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta = 4.51$ (s, 2H, $CH_2$), 7.41 (ddd, $J = 7.8$, 7.2, 0.9 Hz, 1H), 7.60 (ddd, $J = 8.4$, 7.2, 1.2 Hz, 1H), 7.77 (dd, $J = 8.4$, 0.9 Hz, 1H), 7.89 (dd, $J = 7.8$, 0.9 Hz, 1H), 8.12 (d, $J = 0.9$ Hz, 1H), 8.53 (s, 3H, $NH_2$xHCl) ppm. $^{13}$C NMR (75 MHz, DMSO-$d_6$): $\delta = 44.3$ ($CH_2$), 112.4 (CH), 115.9 (CH), 124.0 (CH), 124.4 (CH), 126.4 (C), 129.2 (CH), 149.5 (C), 155.1 (C), 183.2 (CO) ppm. IR, KBr ($cm^{-1}$): 3321, 3009, 1690, 1560, 1499, 1400, 991, 771. Anal. calcd for $C_{10}H_{10}NO_2Cl$: C, 56.75; H, 4.76; N, 6.62. Found: C, 56.58; H, 4.89; N, 6.87.

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*4.8.2. 2-Amino-1-(7-ethylbenzofuran-2-yl)ethanone hydrochloride* ***28***

1.92 g, 81% yield, mp 198–200 °C. $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ = 1.30 (t, $J$ = 7.5 Hz, 3H, $CH_3$), 2.92 (q, $J$ = 7.5 Hz, 2H, $CH_2$), 4.51 (s, 2H, $CH_2$), 7.32 (t, $J$ = 7.4 Hz, 1H), 7.43 (dd, $J$ = 7.3, 0.9 Hz, 1H), 7.70 (dd, $J$ = 7.5, 0.9 Hz, 1H), 8.11 (s, 1H), 8.46 (s, 3H, $NH_2$xHCl) ppm. $^{13}$C NMR (50 MHz, DMSO-$d_6$): $\delta$ = 13.9 ($CH_3$), 22.1 ($CH_2$), 44.2 ($CH_2$), 116.2 (CH), 121.4 (CH), 124.6 (CH), 126.2 (C), 128.0 (C), 128.2 (CH), 149.2 (C), 153.8 (C), 183.1 (CO) ppm. IR, KBr (cm$^{-1}$): 3424, 2957, 1677, 1554, 1297, 1179, 917, 743. Anal. calcd for $C_{12}H_{14}NO_2Cl$: C, 60.13; H, 5.88; N, 5.84. Found: C, 59.98; H, 5.89; N, 5.87.

*4.8.3. 2-Amino-1-(3-methylbenzofuran-2-yl)ethanone hydrochloride* ***29***

1.94 g, 86% yield, mp 217–218 °C. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ = 2.62 (s, 3H, $CH_3$), 4.47 (s, 2H, $CH_2$), 7.42 (ddd, $J$ = 8.0, 7.2, 0.8 Hz, 1H), 7.62 (ddd, $J$ = 8.4, 7.2, 1.2 Hz, 1H), 7.26 (d, $J$ = 8.4 Hz, 1H), 7.90 (d, $J$ = 8.0 Hz, 1H), 8.46 (s, 3H, $NH_2$xHCl) ppm. $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ = 9.6 ($CH_3$), 45.7 ($CH_2$), 112.7 (CH), 122.8 (CH), 124.4 (CH), 126.7 (C), 128.8 (C), 129.9 (CH), 145.9 (C), 154.2 (C), 185.4 (CO) ppm. IR, KBr (cm$^{-1}$): 3345, 2989, 1674, 1550, 1195, 969, 829, 761. Anal. calcd for $C_{11}H_{12}NO_2Cl$: C, 58.54; H, 5.36; N, 6.20. Found: C, 58.50; H, 5.49; N, 6.37.

*4.8.4. 2-Amino-1-(3,7-dimethylbenzofuran-2-yl)ethanone hydrochloride* ***30***

1.70 g, 71% yield, mp 188–192 °C. $^1$H NMR (200 MHz, DMSO-$d_6$): $\delta$ = 2.51 (s, 3H, $CH_3$), 2.59 (s, 3H, $CH_3$), 4.48 (s, 2H, $CH_2$), 7.30 (t, $J$ = 7.5 Hz, 1H), 7.43 (d, $J$ = 7.5 Hz, 1H), 7.69 (d, $J$ = 7.5 Hz, 1H), 8.37 (s, 3H, $NH_2$xHCl) ppm. $^{13}$C NMR (75 MHz, DMSO-$d_6$): $\delta$ = 9.3 ($CH_3$), 14.5 ($CH_3$), 45.0 ($CH_2$), 119.6 (CH), 121.9 (C), 123.9 (CH), 126.4 (C), 127.9 (C), 129.8 (CH), 145.3 (C), 152.8 (C), 184.8 (CO) ppm. IR, KBr, (cm$^{-1}$): 3432, 2925, 1692, 1582, 1511, 1373, 1272, 1131, 932, 792, 751. Anal. calcd for $C_{12}H_{14}NO_2Cl$: C, 60.13; H, 5.88; N, 5.84. Found: C, 60.25; H, 5.71; N, 5.67.

*4.9. General procedure for the synthesis of benzyl (2-(benzofuran-2-yl)-2-oxoethyl)carbamates*

To a solution of benzofuryl $\alpha$-amino ketone hydrochloride **27**–**30** (2.0 mmol) in 1,4-dioxane (8 mL) and water (8 mL) was added benzyl chloroformate (0.72 g, 4.2 mmol) and the mixture was stirred at rt for 3 h. The pH value of the reaction mixture was maintained basic by the addition of sat. aq. $NaHCO_3$. The resulting mixture was extracted with ethyl acetate (3 × 10 mL), the organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The product was crystallized from methanol to give yellow solid products.

*4.9.1. Benzyl (2-(benzofuran-2-yl)-2-oxoethyl)carbamate* ***31***

0.50 g, 81% yield, mp 93–95 °C. $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ = 4.73 (d, $J$ = 4.8 Hz, 2H, $CH_2$N), 5.17 (s, 2H, $CH_2$), 5.69 (bs, 1H, NH), 7.31–7.40 (m, 6H), 7.51 (ddd, $J$ = 8.2, 7.2, 1.2 Hz, 1H), 7.59 (ddd, $J$ = 8.2, 1.8, 0.9 Hz, 1H), 7.61 (s, 1H), 7.73 (ddd, $J$ = 7.2, 1.8, 0.9 Hz, 1H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 47.9 ($CH_2$), 67.2 ($CH_2$), 112.5 (CH), 113.6 (CH), 123.5 (CH), 124.2 (CH), 126.7 (C), 128.1 (2xCH), 128.2 (CH), 128.6 (2xCH), 128.8 (CH), 136.3 (C), 150.6 (C), 155.7 (C), 156.3 (CO), 185.5 (CO) ppm. IR, KBr (cm$^{-1}$): 3338, 1685, 1560, 1289, 1258, 1177, 984, 735. Anal. calcd for $C_{18}H_{15}NO_4$: C, 69.89; H, 4.88; N, 4.53. Found: C, 69.55; H, 4.50; N, 4.56.

*4.9.2. Benzyl (2-(7-ethylbenzofuran-2-yl)-2-oxoethyl)carbamate* ***32***

0.60 g, 90% yield, mp 81–82 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 1.36 (t, $J$ = 7.6 Hz, 3H, $CH_3$), 2.98 (q, $J$ = 7.6 Hz, 2H, $CH_2$), 4.75 (d, $J$ = 4.8 Hz, 2H, $CH_2$N), 5.17 (s, 2H, $CH_2$), 5.71 (bs, 1H, NH), 7.22–7.38 (m, 7H), 7.55 (dd, $J$ = 7.5, 1.2 Hz, 1H), 7.61 (s, 1H) ppm. $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta$ = 14.0 ($CH_3$), 22.7 ($CH_2$), 47.8 ($CH_2$), 67.1 ($CH_2$), 113.8 (CH), 120.8 (CH), 124.4 (CH), 126.4 (C), 127.7 (CH), 128.1 (2xCH), 128.2 (CH), 128.5 (2xCH), 129.0 (C), 136.2 (C), 150.3 (C), 154.4 (C), 156.3 (CO), 185.5 (CO) ppm. IR, KBr (cm$^{-1}$): 3303, 2977, 1681, 1544, 1282, 1261, 1175, 987, 743. Anal. calcd for $C_{20}H_{19}NO_4$: C, 71.20; H, 5.67; N, 4.15. Found: C, 71.36; H, 5.48; N, 4.23.

*4.9.3. Benzyl (2-(3-methylbenzofuran-2-yl)-2-oxoethyl)carbamate* ***33***

0.52 g, 98% yield, mp 76–77 °C. $^1$H NMR (700 MHz, $CDCl_3$): $\delta$ = 2.63 (s, 3H, $CH_3$), 4.75 (d, $J$ = 4.8 Hz, 2H, $CH_2$N), 5.17 (s, 2H, $CH_2$), 5.71 (bs, 1H, NH), 7.30–7.40 (m, 6H), 7.50–7.53 (m, 2H), 7.67 (dt, $J$ = 7.8, 1.5 Hz, 1H) ppm. $^{13}$C NMR (175 MHz, $CDCl_3$): $\delta$ = 9.3 ($CH_3$), 48.6 ($CH_2$), 67.0 ($CH_2$), 112.2 (CH), 121.6 (CH), 123.4 (CH), 126.2 (C), 128.0 (2xCH), 128.1 (CH), 128.5 (2xCH), 128.7 (CH), 128.9 (C), 136.3 (C), 146.1 (C), 154.3 (C), 156.2 (CO), 187.2 (CO) ppm. IR, KBr (cm$^{-1}$): 3331, 2939, 1679, 1625, 1570, 1185, 985, 741. Anal. calcd for $C_{19}H_{17}NO_4$: C, 70.58; H, 5.30; N, 4.33. Found: C, 70.42; H, 5.38; N, 4.47.

*4.9.4. Benzyl (2-(3,7-dimethylbenzofuran-2-yl)-2-oxoethyl) carbamate* ***34***

0.41 g, 61% yield, mp 85–89 °C. $^1$H NMR (700 MHz, $CDCl_3$): $\delta$ = 2.54 (s, 3H, $CH_3$), 2.61 (s, 3H, $CH_3$), 4.74 (d, $J$ = 4.8 Hz, 2H, $CH_2$N), 5.17 (s, 2H, $CH_2$), 5.76 (bs, 1H, NH), 7.22 (dd, $J$ = 7.5, 7.2 Hz, 1H), 7.25–7.45 (m, 6H), 7.49 (ddd, $J$ = 7.5, 1.2, 0.6 Hz, 1H) ppm. $^{13}$C NMR (175 MHz, $CDCl_3$): $\delta$ = 9.5 ($CH_3$), 14.8 ($CH_3$), 48.5 ($CH_2$), 66.9 ($CH_2$), 118.9 (CH), 122.6 (C), 123.6 (CH), 126.6 (C), 126.9 (CH), 127.5 (CH), 128.1 (CH), 128.5 (2xCH), 129.4 (CH), 136.4 (C), 140.9 (C), 145.9 (C), 153.4 (C), 156.3 (CO), 187.2 (CO) ppm. IR, KBr (cm$^{-1}$): 3318, 3060, 2919, 1689, 1545, 1258, 1124, 1047, 965, 929, 776, 744, 698. Anal. calcd for $C_{20}H_{19}NO_4$: C, 71.20; H, 5.67; N, 4.15. Found: C, 71.07; H, 5.75; N, 4.30.

*4.10. Benzyl (R)-(2-(benzofuran-2-yl)-2-hydroxyethyl)carbamate* ***35***

Prepared by transfer hydrogenation of **31** (0.43 g, 1.4 mmol) following the procedure described in **4.4**: yellow solid, 0.35 g, 81% yield, mp 107–108 °C, $[\alpha]_D^{20}$ = +27.08 (c 4.98, $CHCl_3$), 99% ee, determined by HPLC analysis, Daicel Chiralcel OD-H column 250 × 4.6 mm, 5 μm, hexane/isopropanol 70:30, flow 0.6 mL/min, (*R*) 15.44 min, 99.55%, (*S*) 17.44 min, 0.45%.

$^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 3.16 (d, $J$ = 5.1 Hz, 1H, OH), 3.61 (ddd, $J$ = 14.3, 6.9, 5.6 Hz, 1H, $CH_2$N), 3.80 (ddd, $J$ = 14.3, 6.7, 3.9 Hz, 1H, $CH_2$N), 4.96–4.99 (m, 1H, CH), 5.12 (s, 2H, $CH_2$), 5.18 (bs, 1H, NH), 6.70 (s, 1H), 7.22 (td, $J$ = 7.2, 1.2, Hz, 1H), 7.25–7.40 (m, 6H), 7.44 (ddd, $J$ = 7.5, 1.2, 0.9 Hz, 1H), 7.54 (ddd, $J$ = 7.2, 1.2, 0.6 Hz, 1H) ppm. $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta$ = 45.6 ($CH_2$), 67.1 ($CH_2$), 68.0 (CH), 103.7 (CH), 111.2 (CH), 121.1 (CH), 122.9 (CH), 124.3 (CH), 127.9 (C), 128.1 (CH), 128.2 (CH), 128.5 (3xCH), 136.1 (C), 154.8 (C), 156.6 (C), 157.3 (CO) ppm. IR, KBr (cm$^{-1}$): 3473, 3315, 3034, 2924, 1702, 1560, 1455, 1276, 1061, 742. Anal. calcd for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.49. Found: C, 69.47; H, 5.56; N, 4.52. MS EI: *m/z* 311 ($M^+$, 2), 91 (100), 147 (91), 77 (28), 79 (26), 65 (21), 176 (20), 131 (18), 89 (17), 51 (17), 203 (16), 108 (15), 39 (15), 63 (14), 160 (14), 92 (12), 107 (12).

*4.11. Benzyl (R)-(2-(7-ethylbenzofuran-2-yl)-2-hydroxyethyl) carbamate* ***36***

Prepared by transfer hydrogenation of **32** (0.74 g, 2.2 mmol) following the procedure described in **4.4**: light yellow oil, 0.56 g,

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76% yield, $[\alpha]_D^{20} = +19.77$ (c 10.62, $CHCl_3$), 98% ee, determined by HPLC analysis, Daicel Chiralcel OD-H column 250 × 4.6 mm, 5 μm, hexane/isopropanol 70:30, flow 0.7 mL/min, (*R*) 9.69 min, 98.99%, (*S*) 11.53 min, 1.01%.

$^1$H NMR (300 MHz, $CDCl_3$): $\delta = 1.32$ (t, $J = 7.6$ Hz, 3H, $CH_3$), 2.90 (q, $J = 7.6$ Hz, 2H, $CH_2$), 3.39 (bs, 1H, OH), 3.58 (ddd, $J = 14.1$, 6.8, 5.8 Hz, 1H, $CH_2N$), 3.78 (ddd, $J = 14.1$, 6.8, 4.0 Hz, 1H, $CH_2N$), 4.97 (dd, $J = 6.8$, 4.0 Hz, 1H, CH), 5.10 (s, 2H, $CH_2$), 5.30 (bs, 1H, NH), 6.67 (s, 1H), 7.10 (ddt, $J = 7.5$, 1.2, 0.6 Hz, 1H), 7.16 (t, $J = 7.5$ Hz, 1H), 7.33–7.39 (m, 5H), 7.37 (dd, $J = 7.5$, 1.5 Hz, 1H) ppm. $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta = 14.0$ ($CH_3$), 22.7 ($CH_2$), 45.6 ($CH_2$), 67.1 ($CH_2$), 68.0 (CH), 103.8 (CH), 118.6 (CH), 123.0 (CH), 123.5 (CH), 127.5 (C), 127.7 (C), 128.0 (CH), 128.1 (2xCH), 128.5 (2xCH), 136.2 (C), 153.4 (C), 156.3 (C), 157.3 (CO) ppm. IR, KBr ($cm^{-1}$): 3411, 2967, 2934, 1702, 1542, 1524, 1455, 1261, 747. Anal. calcd for $C_{20}H_{21}NO_4$: C, 70.78; H, 6.23; N, 4.13. Found: C, 70.75; H, 6.24; N, 4.25. MS EI: *m/z* 339 ($M^+$, 3), 175 (100), 91 (75), 79 (28), 77 (27), 231 (25), 159 (24), 188 (19), 108 (17), 115 (16), 51 (14), 204 (14), 65 (13), 176 (13), 107 (13), 131 (13), 187 (12), 39 (11).

### 4.12. Benzyl (R)-(2-(3-methylbenzofuran-2-yl)-2-hydroxyethyl) carbamate **37**

Prepared by transfer hydrogenation of **33** (0.53 g, 1.6 mmol) following the procedure described in **4.4**: light yellow solid, 0.50 g, 94% yield, mp 103–106 °C, $[\alpha]_D^{20} = -17.15$ (c 2.91, $CHCl_3$), 95% ee, determined by HPLC analysis, Daicel Chiralcel OD-H column 250 × 4.6 mm, 5 μm, hexane/isopropanol 70:30, flow 0.6 mL/min, (*R*) 16.65 min, 97.30%, (*S*) 18.97 min, 2.70%. $^1$H NMR (200 MHz, $CDCl_3$): $\delta = 2.24$ (s, 3H, $CH_3$), 2.68 (d, $J = 5.0$ Hz, 1H, OH), 3.67 (t, $J = 5.8$ Hz, 2H, $CH_2N$), 5.01–5.06 (m, 1H, CH), 5.12 (s, 2H, $CH_2$), 5.17 (bs, 1H, NH), 7.19–7.50 (m, 9H) ppm. $^{13}$C NMR (175 MHz, $CDCl_3$): $\delta = 7.7$ ($CH_3$), 45.5 ($CH_2$), 65.9 (CH), 67.0 ($CH_2$), 111.1 (CH), 113.2 (C), 119.5 (CH), 122.4 (CH), 124.6 (CH), 128.1 (2xCH), 128.2 (CH), 128.5 (2xCH), 129.6 (C), 136.2 (C), 150.4 (C), 153.9 (C), 157.0 (CO) ppm. IR, KBr ($cm^{-1}$): 3351, 3060, 2931, 1692, 1544, 1451, 1249, 1069, 1003, 749. Anal. calcd for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.88; N, 4.30. Found: C, 69.98; H, 5.77; N, 4.39. MS EI: *m/z* 325 ($M^+$, 2), 161 (100), 91 (60), 77 (24), 79 (21), 174 (19), 105 (19), 159 (16), 65 (13), 51 (12), 131 (11), 162 (11), 115 (11), 103 (11).

### 4.13. Benzyl (R)-(2-(3,7-dimethylbenzofuran-2-yl)-2-hydroxyethyl) carbamate **38**

Prepared by transfer hydrogenation of **34** (0.25 g, 0.7 mmol) following the procedure described in **4.4**: light yellow solid, 0.20 g, 95% yield, mp 88–92 °C, $[\alpha]_D^{20} = -15.06$ (c 3.34, $CHCl_3$), 97% ee, determined by HPLC analysis, Daicel Chiralcel OD-H column 250 × 4.6 mm, 5 μm, hexane/isopropanol 60:40, flow 0.6 mL/min, (*S*) 10.50 min, 1.70%, (*R*) 18.32 min, 98.30%. $^1$H NMR (700 MHz, $CDCl_3$): $\delta = 2.23$ (s, 3H, $CH_3$), 2.48 (s, 3H, $CH_3$), 2.68 (d, $J = 3.3$ Hz, 1H, OH), 3.61–3.64 (dd, $J = 13.8$, 6.0 Hz, 1H, $CH_2N$), 3.73 (dd, $J = 13.8$, 7.5 Hz, 1H, $CH_2N$), 5.05 (bs, 1H, CH), 5.12 (s, 2H, $CH_2$), 5.19 (bs, 1H, NH), 7.08 (ddt, $J = 7.5$, 1.5, 0.6 Hz, 1H), 7.15 (t, $J = 7.5$ Hz, 1H), 7.27–7.40 (m, 6H) ppm. $^{13}$C NMR (175 MHz, $CDCl_3$): $\delta = 7.8$ ($CH_3$), 14.9 ($CH_3$), 45.6 ($CH_2$), 65.9 (CH), 66.9 ($CH_2$), 113.4 (C), 116.9 (CH), 121.3 (C), 122.5 (CH), 125.5 (CH), 126.9 (CH), 127.6 (C), 128.0 (CH), 128.1 (CH), 128.5 (2xCH), 129.1 (C), 136.3 (C), 150.2 (C), 152.9 (CO) ppm. IR, KBr ($cm^{-1}$): 3370, 3259, 2922, 2851, 2342, 1707, 1656, 1554, 1457, 1274. Anal. calcd for $C_{20}H_{21}NO_4$: C, 70.78; H, 6.23; N, 4.13. Found: C, 70.85; H, 6.31; N, 4.28.

### 4.14. General procedure for deprotection of benzofuryl N-Cbz protected β-amino alcohols

A mixture of benzofuryl *N*-Cbz protected β-amino alcohol **35**–**38** (1.0 mmol) and 5% Pd/C (30 mg) in methanol (35 mL) was hydrogenated in an autoclave under 8 atm. pressure for 24 h at rt. The reaction mixture was filtered on a Celite pad and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate/dichloromethane/methanol, 6:4:1:0.5) to give white solid products.

#### 4.14.1. (R)-2-Amino-1-(benzofuran-2-yl)ethanol **14**

0.19 g, 99% yield, mp 129–133 °C, $[\alpha]_D^{28} = +43.23$ (*c* 2.23, MeOH). $^1$H and $^{13}$C NMR spectra were the same as described in 4.6.1.

#### 4.14.2. (R)-2-Amino-1-(7-ethylbenzofuran-2-yl)ethanol **15**

0.16 g, 78% yield, mp 85–86 °C, $[\alpha]_D^{27} = +36.56$ (*c* 10.75, MeOH). $^1$H and $^{13}$C NMR spectra were the same as described in 4.6.2.

#### 4.14.3. (R)-2-Amino-1-(3-methylbenzofuran-2-yl)ethanol **16**

0.08 g, 75% yield, mp 98–101 °C, $[\alpha]_D^{25} = +14.56$ (*c* 0.35, MeOH). $^1$H and $^{13}$C NMR spectra were the same as described in 4.6.3.

#### 4.14.4. (R)-2-Amino-1-(3,7-dimethylbenzofuran-2-yl)ethanol **17**

0.16 g, 80% yield, mp 136–139 °C, $[\alpha]_D^{25} = +14.26$ (*c* 0.43, MeOH). $^1$H and $^{13}$C NMR spectra were the same as described in 4.6.4.

### 4.15. General procedure for the synthesis of benzofuryl α-succinimido ketones

The suspension of succinimide (0.93 g, 9.4 mmol) in THF (9 mL) was stirred at 50 °C until the succinimide was dissolved. In a separate flask potassium *tert*-butoxide (1.12 g, 10.0 mmol) was suspended in THF (7 mL) and the suspension sonicated for 10 min to give a cloudy suspension which was added dropwise to the stirred succinimide solution at such a rate that the temperature remained below 20 °C. After the addition was completed, the mixture was sonicated for an additional 1 h. To this suspension was added dropwise a solution of benzofuryl α-bromo ketone **19**–**22** (10.0 mmol) in DMF (11 mL) and the reaction mixture was stirred at rt for 24 h. Water (90 mL) was added and the mixture was extracted with dichloromethane (3 × 20 mL). The combined extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate/dichloromethane/methanol, 5:3:1:0.5) and crystallized from ethanol to give white solid products.

#### 4.15.1. 1-(2-(Benzofuran-2-yl)-2-oxoethyl)pyrrolidine-2,5-dione **39**

1.04 g, 43% yield, mp 145–147 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 2.87$ (s, 4H, 2x$CH_2$), 4.96 (s, 2H, $CH_2$), 7.33 (ddd, $J = 7.8$, 6.9, 0.9 Hz, 1H), 7.51 (td, $J = 7.2$, 1.3 Hz, 1H), 7.58 (dt, $J = 9.3$, 0.9 Hz, 1H), 7.61 (d, $J = 0.9$ Hz, 1H), 7.72 (ddd, $J = 7.8$, 1.4, 0.9 Hz, 1H) ppm. $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta = 28.3$ (2x$CH_2$), 44.6 ($CH_2$), 112.5 (CH), 113.6 (CH), 123.5 (CH), 124.2 (CH), 126.7 (C), 128.8 (CH), 150.6 (C), 155.7 (C), 176.5 (2xCO), 181.8 (CO) ppm. IR, neat ($cm^{-1}$): 3282, 2930, 1771, 1693, 1419, 1392, 1170, 1006, 758, 616. Anal. calcd for $C_{14}H_{11}NO_4$: C, 65.39; H, 4.31; N, 5.44. Found: C, 65.09; H, 4.53; N, 5.86.

#### 4.15.2. 1-(2-(7-Ethylbenzofuran-2-yl)-2-oxoethyl)pyrrolidine-2,5-dione **40**

1.37 g, 51%, mp 146–147 °C. $^1$H NMR (200 MHz, $CDCl_3$): $\delta = 1.38$ (t, $J = 7.6$ Hz, 3H, $CH_3$), 2.88 (s, 4H, 2x$CH_2$), 2.99 (q, $J = 7.6$ Hz, 2H, $CH_2$), 4.99 (s, 2H, $CH_2$), 7.23–7.37 (m, 2H), 7.56 (dd, $J = 7.4$, 1.6 Hz,

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1H), 7.61 (s, 1H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 13.9 ($CH_3$), 22.7 ($CH_2$), 28.3 (2x$CH_2$), 44.7 ($CH_2$), 113.9 (CH), 120.9 (CH), 124.4 (CH), 126.4 (C), 127.7 (CH), 128.9 (C), 150.4 (C), 154.5 (C), 176.5 (2xCO), 181.8 (CO) ppm. IR, neat ($cm^{-1}$): 3311, 2932, 1765, 1714, 1410, 1392, 1314, 1009, 720, 530. Anal. calcd for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 66.97; H, 5.27; N, 5.15.

#### 4.15.3. 1-(2-(3-Methylbenzofuran-2-yl)-2-oxoethyl)pyrrolidine-2,5-dione **41**

1.40 g, 55% yield, mp 143–147 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 2.59 (s, 3H, $CH_3$), 2.87 (s, 4H, 2x$CH_2$), 4.98 (s, 2H, $CH_2$), 7.34 (ddd, $J$ = 7.8, 4.8, 3.3 Hz, 1H), 7.51 (dd, $J$ = 1.5, 0.9 Hz, 1H), 7.53 (d, $J$ = 1.2 Hz, 1H), 7.78 (dt, $J$ = 7.8, 0.9 Hz, 1H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 9.3 ($CH_3$), 28.3 (2x$CH_2$), 45.4 ($CH_2$), 112.2 (CH), 121.7 (CH), 123.5 (CH), 126.8 (C), 128.9 (CH), 146.1 (C), 154.4 (C), 176.7 (2xCO), 183.5 (CO) ppm. IR, neat ($cm^{-1}$): 3267, 2944, 1768, 1680, 1410, 1391, 1171, 1010, 769. Anal. calcd for $C_{15}H_{13}NO_4$: C, 66.41; H, 4.83; N, 5.16. Found: C, 66.62; H, 4.92; N, 5.04.

#### 4.15.4. 1-(2-(3,7-Dimethylbenzofuran-2-yl)-2-oxoethyl) pyrrolidine-2,5-dione **42**

1.29 g, 48%, mp 172–175 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 2.55 (s, 3H, $CH_3$), 2.59 (s, 3H, $CH_3$), 2.88 (s, 4H, 2x$CH_2$), 5.01 (s, 2H, $CH_2$), 7.21–7.23 (m, 1H), 7.31 (ddd, $J$ = 7.5, 1.5, 0.9 Hz, 1H), 7.50 (ddd, $J$ = 7.5, 1.5, 0.9 Hz, 1H) ppm. $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta$ = 9.4 ($CH_3$), 14.8 ($CH_3$), 28.3 (2x$CH_2$), 45.4 ($CH_2$), 119.1 (CH), 122.4 (C), 123.7 (CH), 127.2 (C), 128.4 (C), 129.5 (CH), 146.0 (C), 153.6 (C), 176.7 (2xCO), 183.4 (CO) ppm. IR, neat ($cm^{-1}$): 3276, 2942, 1769, 1682, 1418, 1392, 1171, 1005, 752, 642. Anal. calcd for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.41; H, 5.37; N, 4.78.

### 4.16. General procedure for the synthesis of benzofuryl α-phthalimido ketones

To a solution of benzofuryl α-bromo ketone **19**–**21** (10.0 mmol) in DMF (10 mL) was added potassium phthalimide (2.03 g, 11.0 mmol) and stirred at rt for 3 h. The reaction mixture was poured into water (50 mL) and extracted with chloroform (2 × 15 mL). The combined extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was crystallized from ethanol to give white solid products.

#### 4.16.1. 2-(2-(Benzofuran-2-yl)-2-oxoethyl)isoindoline-1,3-dione **43**

1.62 g, 53% yield, mp 201–203 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 5.15 (s, 2H, $CH_2$), 7.35 (dd, $J$ = 7.2, 0.9 Hz, 1H), 7.52 (dd, $J$ = 7.2, 1.2 Hz, 1H), 7.61 (dd, $J$ = 8.4, 0.9 Hz, 1H), 7.64 (d, $J$ = 0.9 Hz, 1H), 7.54 (dt, $J$ = 8.1, 0.9 Hz, 1H), 7.76 (dd, $J$ = 5.4, 3.0 Hz, 2H), 7.91 (dd, $J$ = 5.7, 3.0 Hz, 2H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 44.1 ($CH_2$), 112.5 (CH), 113.6 (CH), 123.5 (CH), 123.6 (2xCH), 124.2 (CH), 126.7 (C), 128.7 (CH), 132.1 (C), 134.1 (2xCH), 150.7 (C), 155.7 (C), 167.7 (CO), 182.6 (2xCO) ppm. IR, neat ($cm^{-1}$): 3315, 2936, 1774, 1710, 1683, 1415, 1392, 1160, 1100, 1003, 930, 753, 710. Anal. calcd for $C_{18}H_{11}NO_4$: C, 70.82; H, 3.63; N, 4.58. Found: C, 70.96; H, 3.72; N, 4.60.

#### 4.16.2. 2-(2-(7-Ethylbenzofuran-2-yl)-2-oxoethyl)isoindoline-1,3-dione **44**

2.30 g, 69%, mp 184–185 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 1.38 (t, $J$ = 7.5 Hz, 3H, $CH_3$). 2.99 (q, $J$ = 7.5 Hz, 2H, $CH_2$), 5.16 (s, 2H, $CH_2$), 7.27 (t, $J$ = 7.5 Hz, 1H), 7.34 (ddd, $J$ = 7.5, 1.5, 0.9 Hz, 1H), 7.56 (dd, $J$ = 7.8, 1.5 Hz, 1H), 7.64 (s, 1H), 7.76 (dd, $J$ = 5.4, 3.0 Hz, 2H), 7.91 (dd, $J$ = 5.7, 3.0 Hz, 2H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 13.9 ($CH_3$), 22.7 ($CH_2$), 44.2 ($CH_2$), 113.9 (CH), 120.9 (CH), 123.6 (2xCH), 124.4 (CH), 126.4 (C), 127.7 (CH), 128.9 (C), 132.1 (C), 134.1 (2xCH), 150.4 (C), 154.5 (C), 167.7 (CO), 182.6 (2xCO) ppm. IR, neat ($cm^{-1}$): 3309, 2938, 1775, 1714, 1681, 1416, 1391, 1155, 1009, 944, 754, 713. Anal. calcd for $C_{20}H_{15}NO_4$: C, 72.06; H, 4.53; N, 4.20. Found: C, 72.12; H, 4.48; N, 4.37.

#### 4.16.3. 2-(2-(3-Methylbenzofuran-2-yl)-2-oxoethyl)isoindoline-1,3-dione **45**

2.58 g, 81% yield, mp 210–212 °C. $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ = 2.60 (s, 3H, $CH_3$), 5.16 (s, 2H, $CH_2$), 7.34 (ddd, $J$ = 8.0, 7.2, 2.8 Hz, 1H), 7.53 (dd, $J$ = 2.6, 1.0 Hz, 1H), 7.55 (d, $J$ = 1.2 Hz, 1H), 7.69 (dt, $J$ = 7.6, 1.0 Hz, 1H), 7.76 (dd, $J$ = 5.6, 3.0 Hz, 2H), 7.91 (dd, $J$ = 5.4, 3.2 Hz, 2H) ppm. $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta$ = 9.3 ($CH_3$), 44.9 ($CH_2$), 112.2 (CH), 121.7 (CH), 123.5 (2xCH), 126.7 (C), 126.8 (CH), 128.9 (C), 132.2 (C), 134.1 (2xCH), 146.2 (C), 154.4 (C), 167.9 (CO), 184.3 (2xCO) ppm. IR, neat ($cm^{-1}$): 3299, 2929, 1776, 1712, 1693, 1426, 1390, 1159, 1010, 947, 754, 712. Anal. calcd for $C_{19}H_{13}NO_4$: C, 71.47; H, 4.10; N, 4.38. Found: C, 71.52; H, 4.29; N, 4.49.

### 4.17. (R)-1-(2-(Benzofuran-2-yl)-2-hydroxyethyl)pyrrolidine-2,5-dione **46**

Prepared by transfer hydrogenation of **39** (0.26 g, 1.0 mmol) following the procedure described in **4.4**: white solid, 0.24 g, 95% yield, mp 154–157 °C, $[\alpha]_D^{23}$ = +26.47 (c 0.34, $CHCl_3$), 94% ee, determined by HPLC analysis, Daicel Chiralcel OD-H column 250 × 4.6 mm, 5 μm, hexane/isopropanol 60:40, flow 0.5 mL/min, (*S*) 21.89 min, 3.11%, (*R*) 22.83 min, 96.88%. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 2.76 (s, 4H, 2x$CH_2$), 3.07 (d, $J$ = 7.5 Hz, 1H, OH), 3.99 (dd, $J$ = 14.1, 3.6 Hz, 1H, $CH_2$N), 4.12 (dd, $J$ = 14.1, 8.7 Hz, 1H, $CH_2$N), 5.10 (dd, $J$ = 8.4, 3.3 Hz, 1H, CH), 6.73 (t, $J$ = 0.9 Hz, 1H), 7.21 (td, $J$ = 7.2, 1.2 Hz, 1H), 7.28 (td, $J$ = 7.2, 1.5 Hz, 1H), 7.45–7.49 (m, 1H), 7.55 (ddd, $J$ = 7.2, 1.5, 0.6 Hz, 1H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 28.1 (2x$CH_2$), 43.7 ($CH_2$), 66.5 (CH), 103.8 (CH), 111.3 (CH), 121.2 (CH), 122.9 (CH), 124.5 (CH), 127.8 (CH), 154.9 (C), 155.9 (C), 177.7 (2xCO) ppm. IR, neat ($cm^{-1}$): 3331, 3270, 2926, 1776, 1715, 1683, 1415, 1391, 1157, 1012, 770, 743. Anal. calcd for $C_{14}H_{13}NO_4$: C, 64.86; H, 5.05; N, 5.40. Found: C, 64.75; H, 5.16; N, 5.75.

### 4.18. (R)-1-(2-(7-Ethylbenzofuran-2-yl)-2-hydroxyethyl) pyrrolidine-2,5-dione **47**

Prepared by transfer hydrogenation of **40** (0.28 g, 1.0 mmol) following the procedure described in **4.4**: white solid, 0.25 g, 89% yield, mp 152–154 °C, $[\alpha]_D^{25}$ = +44.90 (c 1.25, $CHCl_3$), 91% ee, determined by HPLC analysis, Daicel Chiralcel OJ column 250 × 4.6 mm, 10 μm, hexane/isopropanol 90:10, flow 0.8 mL/min, (*S*) 51.81 min, 4.34%, (*R*) 55.64 min, 95.66%. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 1.34 (t, $J$ = 7.5 Hz, 3H, $CH_3$), 1.59 (bs, 1H, OH), 2.75 (s, 4H, 2x$CH_2$), 2.93 (q, $J$ = 7.5 Hz, 2H, $CH_2$), 3.97 (dd, $J$ = 14.1, 3.6 Hz, 1H, $CH_2$N), 4.15 (dd, $J$ = 14.1, 8.7 Hz, 1H, $CH_2$N), 5.11 (dd, $J$ = 8.7, 3.6 Hz, 1H, CH), 6.72 (d, $J$ = 0.9 Hz, 1H), 7.11 (dd, $J$ = 7.5, 1.5 Hz, 1H), 7.16 (t, $J$ = 7.5 Hz, 1H), 7.37 (dd, $J$ = 7.5, 1.5 Hz, 1H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 14.1 ($CH_3$), 22.7 ($CH_2$), 28.1 (2x$CH_2$), 43.7 ($CH_2$), 66.6 (CH), 104.1 (CH), 118.7 (CH), 123.1 (CH), 123.7 (CH), 124.4 (C), 127.8 (C), 153.5 (C), 155.5 (C), 177.7 (2xCO) ppm. IR, neat ($cm^{-1}$): 3310, 3267, 2930, 1772, 1716, 1676, 1405, 1392, 1170, 1008, 755, 715. Anal. calcd for $C_{16}H_{17}NO_4$: C, 66.89; H, 5.96; N, 4.87. Found: C, 66.50; H, 5.76; N, 4.88.

### 4.19. (R)-1-(2-Hydroxy-2-(3-methylbenzofuran-2-yl)ethyl) pyrrolidine-2,5-dione **48**

Prepared by transfer hydrogenation of **41** (0.13 g, 0.5 mmol) following the procedure described in **4.4**: white solid, 0.11 g, 79% yield, mp 150–151 °C, $[\alpha]_D^{32}$ = +35.79 (c 0.95, $CHCl_3$), 80% ee, determined by HPLC analysis, Daicel Chiralcel OJ column

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250 × 4.6 mm, 10 μm, hexane/isopropanol 85:15, flow 0.8 mL/min, (*S*) 47.35 min, 10.10%, (*R*) 56.30 min, 89.90%. $^1$H NMR (200 MHz, $CDCl_3$): δ = 2.27 (s, 3H, $CH_3$), 2.76 (s, 4H, 2x$CH_2$), 2.80 (d, *J* = 8.0 Hz, 1H, OH), 3.83 (dd, *J* = 14.0, 3.6 Hz, 1H, $CH_2N$), 4.27 (dd, *J* = 14.0, 9.4 Hz, 1H, $CH_2N$), 5.15 (ddd, *J* = 9.2, 7.8, 3.6 Hz, 1H, CH), 7.23 (td, *J* = 6.0, 1.6 Hz, 1H), 7.29 (td, *J* = 6.6, 1.6 Hz, 1H), 7.41–7,51 (m, 2H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 1.0 ($CH_3$), 7.7 ($CH_3$). 28.2 (2x$CH_2$), 43.5 ($CH_2$), 64.3 (CH), 111.2 (CH), 113.1 (C), 119.6 (CH), 122.4 (CH), 124.7 (CH), 129.5 (C), 149.7 (C), 154.0 (C), 177.6 (2xCO) ppm. IR, neat ($cm^{-1}$): 3326, 3266, 2935, 1777, 1716, 1684, 1418, 1392, 1318, 1170, 1011, 772, 756. Anal. calcd for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.12. Found: C, 65.64; H, 5.66; N, 5.19.

### 4.20. (R)-1-(2-(3,7-Dimethylbenzofuran-2-yl)-2-hydroxyethyl) pyrrolidine-2,5-dione **49**

Prepared by transfer hydrogenation of **42** (0.14 g, 0.5 mmol) following the procedure described in **4.4**: white solid, 0.11 g, 76% yield, mp 175–177 °C, $[\alpha]_D^{25}$ = +36.49 (c 0.64, $CHCl_3$), 79% ee, determined by HPLC analysis, Daicel Chiralcel OJ column 250 × 4.6 mm, 10 μm, hexane/isopropanol 90:10, flow 0.8 mL/min, (*S*) 35.40 min, 10.59%, (*R*) 41.61 min, 89.41%. $^1$H NMR (300 MHz, $CDCl_3$): δ = 2.26 (s, 3H, $CH_3$), 2.50 (d, *J* = 7.5, 1H, OH), 2.51 (s, 3H, $CH_3$), 2.77 (s, 4H, 2x$CH_2$), 3.82 (dd, *J* = 14.1, 3.6 Hz, 1H, $CH_2N$), 4.25 (dd, *J* = 14.1, 9.6 Hz, 1H, $CH_2N$), 5.16 (dd, *J* = 9.6, 3.6 Hz, 1H, CH), 7.09 (ddd, *J* = 7.5, 1.5, 0.6 Hz, 1H), 7.14 (t, *J* = 7.2 Hz, 1H), 7.31 (ddd, *J* = 7.5, 1.5, 0.6 Hz, 1H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 7.8 ($CH_3$), 14.9 ($CH_3$). 28.1 (2x$CH_2$), 43.5 ($CH_2$), 64.3 (CH), 113.3 (C), 116.9 (CH), 121.4 (C), 122.5 (CH), 125.6 (CH), 128.9 (C), 149.4 (C), 153.0 (C), 177.6 (2xCO) ppm. IR, neat ($cm^{-1}$): 3320, 3287, 2933, 1776, 1710, 1686, 1415, 1390, 1165, 1004, 753, 712. Anal. calcd for $C_{16}H_{17}NO_4$: C, 66.89; H, 5.96; N, 4.87. Found: C, 66.35; H, 6.16; N, 4.89.

### 4.21. (R)-2-(2-(Benzofuran-2-yl)-2-hydroxyethyl)isoindoline-1,3-dione **50**

Prepared by transfer hydrogenation of **43** (50 mg, 0.16 mmol) following the procedure described in **4.4**: white solid, 48 mg, 98% yield, mp 158–160 °C, $[\alpha]_D^{23}$ = +28.74 (c 0.42, $CHCl_3$), 91% ee, determined by HPLC analysis, Daicel Chiralcel OJ column 250 × 4.6 mm, 10 μm, hexane/isopropanol 80:20, flow 0.7 mL/min, (*S*) 35.67 min, 4.62%, (*R*) 40.90 min, 95.38%. $^1$H NMR (300 MHz, $CDCl_3$): δ = 3.05 (d, *J* = 6.9 Hz, 1H, OH), 4.18 (dd, *J* = 14.4, 4.2 Hz, 1H, $CH_2N$), 4.27 (dd, *J* = 14.4, 8.1 Hz, 1H, $CH_2N$), 5.19 (tdd, *J* = 7.6, 4.2, 1.2 Hz, 1H, CH), 6.76 (t, *J* = 0.9 Hz, 1H), 7.21 (td, *J* = 7.2, 1.2 Hz, 1H), 7.28 (td, *J* = 7.2, 1.5 Hz, 1H), 7.46 (ddd, *J* = 8.4, 1.5, 0.9 Hz, 1H), 7.54 (ddd, *J* = 7.8, 1.5, 0.9 Hz, 1H), 7.74 (dd, *J* = 5.7, 3.0 Hz, 2H), 7.87 (dd, *J* = 5.4, 3.0 Hz, 2H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 42.9 ($CH_2$), 67.0 (CH), 103.9 (CH), 111.3 (CH), 121.2 (CH), 122.9 (CH), 123.6 (2xCH), 124.4 (CH), 127.8 (C), 131.8 (C), 134.2 (2xCH), 154.9 (C), 155.9 (C), 168.7 (2xCO) ppm. IR, neat ($cm^{-1}$): 3333, 2933, 1774, 1713, 1698, 1392, 1252, 1067, 1004, 942, 757, 708, 529. Anal. calcd for $C_{18}H_{13}NO_4$: C, 70.35; H, 4.26; N, 4.56. Found: C, 70.26; H, 4.35; N, 4.69.

### 4.22. (R)-2-(2-(7-Ethylbenzofuran-2-yl)-2-hydroxyethyl) isoindoline-1,3-dione **51**

Prepared by transfer hydrogenation of **44** (50 mg, 0.15 mmol) following the procedure described in **4.4**: white solid, 38 mg, 76% yield, $[\alpha]_D^{23}$ = +33.15 (c 0.83, $CHCl_3$), 89% ee, determined by HPLC analysis, Daicel Chiralcel OJ column 250 × 4.6 mm, 10 μm, hexane/isopropanol 90:10, flow 0.7 mL/min, (*S*) 40.16 min, 5.43%, (*R*) 44.30 min, 94.57%.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 1.28 (t, *J* = 7.5 Hz, 3H, $CH_3$), 1.59 (bs, 1H, OH), 2.87 (q, *J* = 7.5 Hz, 2H, $CH_2$), 4.17 (dd, *J* = 14.4, 4.2 Hz, 1H, $CH_2N$), 4.27 (dd, *J* = 14.4, 8.1 Hz, 1H, $CH_2N$), 5.21 (dd, *J* = 8.1, 4.2 Hz, 1H, CH), 6.74 (t, *J* = 0.6 Hz, 1H), 7.08–7.16 (m, 2H), 7.36 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.72 (dd, *J* = 5.7, 3.0 Hz, 2H), 7.86 (dd, *J* = 5.4, 3.0 Hz, 2H) ppm. $^{13}$C NMR (50 MHz, $CDCl_3$): δ = 14.0 ($CH_3$), 22.7 ($CH_2$), 43.1 ($CH_2$), 67.0 (CH), 104.1 (CH), 118.6 (CH), 123.0 (CH), 123.5 (2xCH), 123.6 (CH), 127.5 (C), 127.8 (C), 131.9 (C), 134.2 (2xCH), 155.7 (C), 168.6 (2xCO) ppm. IR, neat ($cm^{-1}$): 3345, 2937, 1777, 1715, 1695, 1392, 1283, 1076, 1003, 944, 754, 713, 529. Anal. calcd for $C_{20}H_{17}NO_4$: C, 71.63; H, 5.11; N, 4.18. Found: C, 71.42; H, 5.27; N, 4.19.

### 4.23. (R)-2-(2-Hydroxy-2-(3-methylbenzofuran-2-yl)ethyl) isoindoline-1,3-dione **52**

Prepared by transfer hydrogenation of **45** (51 mg, 0.16 mmol) following the procedure described in **4.4**: white solid, 47 mg, 92% yield, mp 130–133 °C, $[\alpha]_D^{25}$ = +25.15 (c 0.55, $CHCl_3$), 84% ee, determined by HPLC analysis, Daicel Chiralcel OJ column 250 × 4.6 mm, 10 μm, hexane/isopropanol 90:10, flow 0.8 mL/min, (*S*) 46.95 min, 8.20%, (*R*) 63.66 min, 91.80%. $^1$H NMR (300 MHz, $CDCl_3$): δ = 1.58 (bs, 1H, OH), 2.26 (s, 3H, $CH_3$), 4.03 (dd, *J* = 14.1, 3.9 Hz, 1H, $CH_2N$), 4.36 (dd, *J* = 14.1, 9.0 Hz, 1H, $CH_2N$), 5.24 (dd, *J* = 9.0, 4.2 Hz, 1H, CH), 7.23 (td, *J* = 7.2, 1.2 Hz, 1H), 7.29 (td, *J* = 7.2, 1.5 Hz, 1H), 7.42–7.49 (m, 2H), 7.72 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.87 (dd, *J* = 5.4, 3.0 Hz, 2H) ppm. $^{13}$C NMR (175 MHz, $CDCl_3$): δ = 8.8 ($CH_3$), 43.8 ($CH_2$), 65.9 (CH), 112.2 (CH), 120.6 (CH), 123.5 (CH), 124.5 (2xCH), 124.7 (C), 125.7 (CH), 132.9 (C), 135.1 (2xCH), 135.3 (C), 150.8 (C), 155.1 (C), 169.6 (2xCO) ppm. IR, neat ($cm^{-1}$): 3327, 2938, 1776, 1714, 1700, 1412, 1009, 947, 757, 714. Anal. calcd for $C_{19}H_{15}NO_4$: C, 71.02; H, 4.71; N, 4.36. Found: C, 70.86; H, 4.55; N, 4.44.

### 4.24. General procedure for deprotection of the succinimides

A mixture of the corresponding benzofuryl succinimido alcohol **46**–**49** (0.50 mmol) and 20% aqueous sodium hydroxide (2.4 mL) in 95% ethanol (15 mL) was stirred at reflux for 24 h. After cooling to rt, the precipitate was filtered off and the reaction mixture was concentrated in vacuo. The residue was refluxed with MTBE (8 mL) and methylene chloride (4 mL) for 1 h. Next, the reaction mixture was filtered on a Celite pad and the filtrate decolored by stirring with Norit for 2 h. After filtration the solvents were removed under reduced pressure to give white solid products.

#### 4.24.1. (R)-2-Amino-1-(benzofuran-2-yl)ethanol **14**

59 mg, 67% yield, mp 126–127 °C; $[\alpha]_D^{25}$ = +34.48 (*c* 0.93, MeOH). $^1$H and $^{13}$C NMR spectra were the same as described in 4.6.1.

#### 4.24.2. (R)-2-Amino-1-(7-ethylbenzofuran-2-yl)ethanol **15**

82 mg, 80% yield, mp 83–85 °C; $[\alpha]_D^{25}$ = +32.84 (*c* 0.70, MeOH). $^1$H and $^{13}$C NMR spectra were the same as described in 4.6.2.

#### 4.24.3. (R)-2-Amino-1-(3-methylbenzofuran-2-yl)ethanol **16**

79 mg, 83% yield, mp 84–86 °C; $[\alpha]_D^{25}$ = +11.04 (*c* 0.52, MeOH). $^1$H and $^{13}$C NMR spectra were the same as described in 4.6.3.

#### 4.24.4. (R)-2-Amino-1-(3,7-dimethylbenzofuran-2-yl)ethanol **17**

80 mg, 78% yield, mp 120–123 °C; $[\alpha]_D^{23}$ = +11.24 (*c* 0.30, MeOH). $^1$H and $^{13}$C NMR spectra were the same as described in 4.6.4.

### 4.25. General procedure for deprotection of the phthalimides

A mixture of the corresponding benzofuryl phthalimido alcohol **50**–**52** (0.30 mmol) and hydrazine hydrate (22.5 mg, 0.45 mmol) in 95% ethanol (5 mL) was stirred at reflux for 5 h. After addition of

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concd. HCl (0.04 mL) the resulting mixture was again refluxed for 1 h. After cooling to rt, the precipitate was filtered off and the filtrate was evaporated in vacuo. The residue was dissolved in water (8 mL) and aqueous potassium hydroxide (5 mL) was added. The mixture was extracted with dichloromethane (2 × 10 mL). The combined extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give white solid products.

*4.25.1. (R)-2-Amino-1-(benzofuran-2-yl)ethanol* ***14***

27 mg, 50% yield, mp 125–126 °C; $[\alpha]_D^{25} = +33.20$ (*c* 0.55, MeOH). $^1H$ and $^{13}C$ NMR spectra were the same as described in 4.6.1.

*4.25.2. (R)-2-Amino-1-(7-ethylbenzofuran-2-yl)ethanol* ***15***

27 mg, 44% yield, mp 82–84 °C; $[\alpha]_D^{25} = +31.00$ (*c* 0.84, MeOH). $^1H$ and $^{13}C$ NMR spectra were the same as described in 4.6.2.

*4.25.3. (R)-2-Amino-1-(3-methylbenzofuran-2-yl)ethanol* ***16***

28 mg, 48% yield, mp 90–93 °C; $[\alpha]_D^{25} = +12.62$ (*c* 0.47, MeOH). $^1H$ and $^{13}C$ NMR spectra were the same as described in 4.6.3.

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## Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2017.05.059.

## References

1. Cardillo Guiliana, Tomasini Claudia. *Chem Soc Rev*. 1996;25(2):117–128.
2. Juaristi E, Quintana D, Escalante J. *Aldrichim Acta*. 1994;27:3–11.
3. Ager DJ, Prakash I, Schaad DR. *Chem Rev*. 1996;96(2):835–876.
4. Morris DJ, Hayes AM, Wills M. *J Org Chem*. 2006;71(18):7035–7044.
5. Corey EJ, Helal CJ. *Angew Chem Int Ed Engl*. 1988;37:1986–2012.
6. Ohta Y, Shinkai I. *Bioorg Med Chem*. 1997;5:465–466.
7. Takeda Hideo, Tachinami Takeshi, Aburatani Masakazu, Takahashi Hisashi, Morimoto Toshiaki, Achiwa Kazuo. *Tetrahedron Lett*. 1989;30(3):363–366.
8. Nevagi RJ, Dighe SN, Dighe SN. *Eur J Med Chem*. 2015;97:561–581.
9. Ando K, Kawamura Y, Akai Y, et al. *Org Biomol Chem*. 2008;6(2):296–307.
10. Guo HF, Shao HY, Yang ZY, et al. *J Med Chem*. 2010;53(4):1819–1829.
11. Fothergill GA, Osbond JM, Wickens JC. *Arzneim*. 1977;27(5):978–981.
12. Weerawarna S Ananda, Guha-Biswas Michael, Nelson Wendel L. *J Heterocycl Chem*. 1991;28(5):1395–1403.
13. Narimatsu S, Takemi C, Kuramoto S, et al. *Chirality*. 2003;15(4):333–339.
14. Li DN, Pritchard MP, Hanlon SP, Burchell B, Wolf CR, Friedberg T. *J Pharmacol Exp Ther*. 1999;289(2):661–667.
15. Guengerich FP, Miller GP, Hanna IH, et al. *Biochemistry*. 2002;41(36):11025–11034.
16. Ecker G, Fleischhacker W, Helml T, et al. *Chirality*. 1994;6(4):329–336.
17. Bayer A. In: Jacobsen EN, Pflatz A, Yamamoto H, eds. *Comprehensive Asymmetric Catalysis, Supplement 2*. Springer: Berlin, Heidelberg; 2004:43–71.
18. Cho BT. *Aldrichim Acta*. 2002;35:3–16.
19. Klingler FD. *Accounts Chem Res*. 2007;40(12):1367–1376.
20. Devocelle Marc, Agbossou Francine, Mortreux André. *Synlett*. 1997;1997(11):1306–1308.
21. Ohkuma Takeshi, Ishii Dai, Takeno Hiroshi, Noyori Ryoji. *J Am Chem Soc*. 2000;122(27):6510–6511.
22. Takahashi H, Sakuraba S, Takeda H, Achiwa K. *J Am Chem Soc*. 1990;112:5876–5878.
23. Kitamura Masato, Ohkuma Takeshi, Inoue Shinichi, et al. *J Am Chem Soc*. 1988;110(2):629–631.
24. Klingler FD. *Accounts Chem Res*. 2007;40(12):1367–1376.
25. Baeza A, Nájera C, Sansano JM, Saá JM. *Chem (Weinheim der Bergstrasse, Ger*. 2005;11(13):3849–3862.
26. Xiong Y, Wang F, Huang X, Wen Y, Feng X. *Chem (Weinheim der Bergstrasse, Ger*. 2007;13(3):829–833.
27. Métro TX, Pardo DG, Cossy J. *J Org Chem*. 2007;72(17):6556–6561.
28. Kawamoto Aparecida, Wills Martin. *Tetrahedron Asym*. 2000;11(16):3257–3261.
29. Kawamoto Aparecida M, Wills Martin. *J Chem Soc Perkin Trans 1*. 2001;(16):1916–1928.
30. Xu Z, Li Y, Liu J, et al. *Org Biomol Chem*. 2015;13(27):7513–7516.
31. Lennon Ian C, Ramsden James A. *Org Process Res Dev*. 2005;9(1):110–112.
32. Farina V, Reeves JT, Senanayake CH, Song JJ. *Chem Rev*. 2006;106(7):2734–2793.
33. Palmer Matthew J, Wills Martin. *Tetrahedron Asym*. 1999;10(11):2045–2061.
34. Ohkuma T, Noyori R. In: Jacobsen EN, Pflatz A, Yamamoto H, eds. *Comprehensive Asymmetric Catalysis, Supplement 1*. Springer: Berlin, Heidelberg; 2004:1–41.
35. Wang F, Liu H, Cun L, Zhu J, Deng J, Jiang Y. *J Org Chem*. 2005;70(23):9424–9429.
36. Zaidlewicz Marek, Tafelska-Kaczmarek Agnieszka, Prewysz-Kwinto Andrzej. *Tetrahedron Asym*. 2005;16(19):3205–3210.
37. Tafelska-Kaczmarek Agnieszka, Prewysz-Kwinto Andrzej, Skowerski Krzysztof, Pietrasiak Katarzyna, Kozakiewicz Anna, Zaidlewicz Marek. *Tetrahedron Asym*. 2010;21(18):2244–2248.
38. Kosmalski Tomasz, Wojtczak Andrzej, Zaidlewicz Marek. *Tetrahedron Asym*. 2009;20(10):1138–1143.
39. Koser Gerald F, Wettach Richard H. *J Org Chem*. 1977;42(8):1476–1478.
40. Stang Peter J, Surber Bruce W, Chen Zhen Chu, Roberts Kenneth A, Anderson Albert G. *J Am Chem Soc*. 1987;109(1):228–235.
41. Kwak Se Hun, Lee Do-Min, Lee Kee-In. *Tetrahedron Asym*. 2009;20(22):2639–2645.
42. Cho BT, Kang SK, Shin SH. *Tetrahedron Asym*. 2002;13:1209–1217.
43. Lee D-M, Lee J-C, Jeong N, Lee K-I. *Tetrahedron Asym*. 2007;18:2662–2667.
44. Ferris, M. J. UK Pat. Appl. GB 2,084,577, 1984; Chem. Abstr. 1982, 97, 144754z.
45. Ager DJ, Prakash I, Schaad DR. *Chem Rev*. 1996;96(2):835–876.
46. Bergmeier Stephen C. *Tetrahedron*. 2000;56(17):2561–2576.
47. Hoffman RV, Maslouh N, Cervantes-Lee F. *J Org Chem*. 2002;67(4):1045–1056.
48. Fraser David S, Park Sheldon B, Chong J Michael. *Can J Chem*. 2004;82(2):87–101.
49. Burger Alfred, Deinet Adolph J. *J Am Chem Soc*. 1945;67(4):566–569.
50. Hyatt John A. *J Org Chem*. 1972;37(8):1254–1256.
51. Lown JW, Akhtar MH. *J Chem Soc, Perkin Trans I*. 1973:683–686.
52. McKay WR, Proctor GR. *J Chem Soc, Perkin Trans I*. 1981:2435–2442.
53. Nohara Fujio, Nishii Masahiro, Ogawa Kazuo, et al. *Tetrahedron Lett*. 1987;28(12):1287–1290.
54. Yinglin Han, Hongwen Hu. *Synthesis*. 1990;1990(07):615–618.
55. Yinglin Han, Hongwen Hu. *Synthesis*. 1990;1990(02):122–124.
56. Kenny Jennifer A, Palmer Matthew J, Smith Athene RC, Walsgrove Tim, Wills Martin. *Synlett*. 1999;1999(10):1615–1617.
57. Lei A, Wu S, He M, Zhang X. *J Am Chem Soc*. 2004;126(6):1626–1627.
58. Wang YQ, Lu SM, Zhou YG. *Org Lett*. 2005;7(15):3235–3238.
59. Hu A, Lin W. *Org Lett*. 2005;7(3):455–458.
60. Wang Changqing, Yang Guoqiang, Zhuang Jing, Zhang Wanbin. *Tetrahedron Lett*. 2010;51(15):2044–2047.
61. Tanielyan Setrak K, Marin Norman, Alvez Gabriela, Augustine Robert L. *Org Process Res Dev*. 2006;10(5):893–898.
62. Gibson MS, Bradshaw RW. *Angew Chem, Int Ed Engl*. 1968;7:919–930.
63. Buu-Hoï NP, Xuong ND, Bac NV. *J Chem Soc*. 1964;0(0):173–176.
64. Zaidlewicz Marek, Tafelska-Kaczmarek Agnieszka, Prewysz-Kwinto Andrzej, Chechłowska Aldona. *Tetrahedron Asym*. 2003;14(12):1659–1664.
65. Shriner RL, Anderson John. *J Am Chem Soc*. 1939;61(10):2705–2708.
66. Nielek B, Lesiak T. *Chem Ber*. 1982;115:1247–1251.
67. Narita K, Sekiya M. *Chem Pharm Bull*. 1977;25:135–140.
68. Johnston EV, Bogár K, Bäckvall JE. *J Org Chem*. 2010;75(13):4596–4599.
69. Nagy Botond, Dima Norbert, Paizs Csaba, Brem Jürgen, Irimie Florin Dan, Toşa Monica Ioana. *Tetrahedron Asym*. 2014;25(18-19):1316–1322.