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New Chiral Iminium Salt Catalysts for Asymmetric Epoxidation

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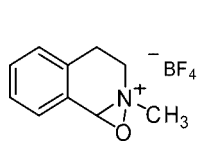
A range of enantiomerically pure 4-substituted 5-amino-1,3-dioxanes has been condensed with 2-(2-bromoethyl)benzaldehyde to produce chiral dihydroisoquinolinium salts, which are effective asymmetric catalysts for the epoxidation of simple alkenes, giving *ee*s of up to 71%.

Introduction

In 1976 Lusinchi reported the preparation of the first oxaziridinium salt, in a steroidal skeleton,[1] and showed that it behaved as an electrophilic oxygen transfer reagent towards nucleophiles. It was, however, not until some eleven years later that a second, racemic, oxaziridinium salt **1**, derived from dihydroisoquinoline, was reported;[2] it was shown to oxidize sulfides, amines, imines and alkenes. The first enantiomerically pure chiral oxaziridinium salt **2** was subsequently prepared by the quaternization of a chiral oxaziridine, derived from (1*S*,2*R*)-(+)-norephedrine.[3] The corresponding iminium salt induced catalytic epoxidation of *trans*-stilbene in 33% *ee* in the presence of oxone as stoichiometric oxidant. Complete retention of stereochemistry was observed, suggesting a single-step oxygen transfer process. Rozwadowska has reported a related system **3**, derived from thiomicamine **4**.[4] Biphenyl- and binaphthalene-derived iminium salts have also been reported to catalyse the asymmetric epoxidation of simple alkenes under similar conditions.[5,6] Armstrong has shown that even acyclic iminium salts can mediate epoxidation by oxone.[7] Komatsu[8] and Yang[9] have independently reported acyclic iminium salt catalysts for asymmetric epoxidation.

We have described a new type of chiral cyclic iminium salt epoxidation catalyst, in which the enantiocontrolling asymmetric centres are located in the exocyclic substituent at the nitrogen atom.[10,11] We have successfully employed these iminium salts in the catalytic asymmetric epoxidation of simple alkenes, giving *ee*s of up to 97% when employing catalysts **5**[12] and **6**.[13] Herein we report the design, synthesis and use as epoxidation catalysts of several new dihydroisoquinolinium salts **7**–**12** based upon the dioxane-containing catalyst **6**, in which the aryl substituent present in the acetal moiety of **6** has been replaced by other groups. We have also reported that the related biphenyl-derived dibenzazepinium salt **13** is a much more reactive epoxidation catalyst than is the corresponding dihydroisoquinolinium species.[14] We also report here three new dibenzazepinium salts **14**–**16**, similarly related to **13**, and their use as epoxidation catalysts.



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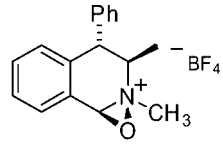

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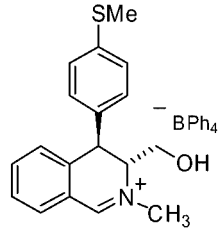

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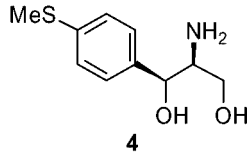

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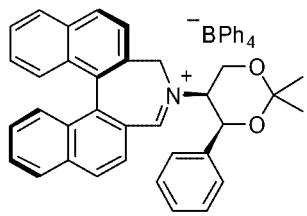

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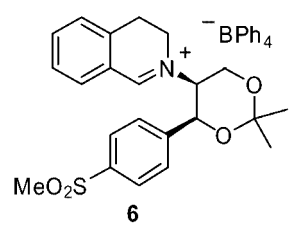

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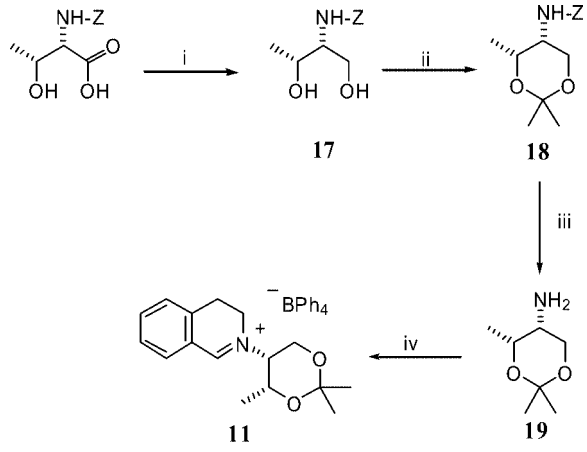
Results and Discussion

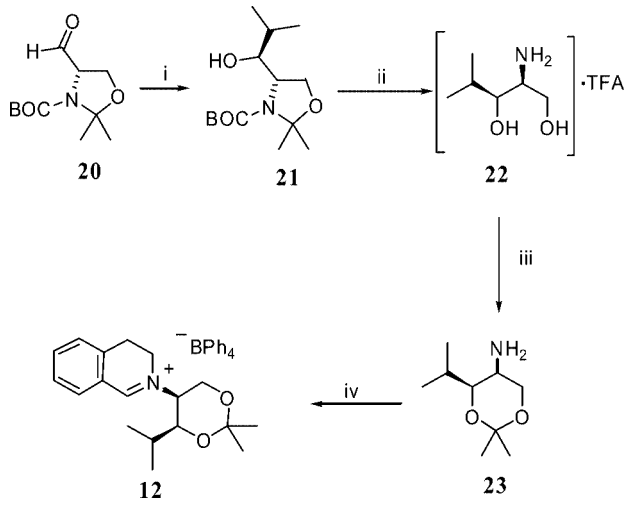
Generation of catalyst **11**, in which the aryl substituent of **6** has been replaced with a methyl group, was accomplished by acetonide formation from the (L)-threonine-derived diol **17**, and removal of the *N*-Cbz group from the resulting acetal **18** to afford the primary amine **19** required for cyclocondensation with 2-(2-bromoethyl)benzaldehyde under our usual conditions (Scheme 1).



Scheme 1. Reagents and conditions: i: a) NMM, *i*Bu–O–CO–Cl, DME, –15 °C, 1 min; b) $NaBH_4$, H_2O, –15 °C, 1 min, 70%; ii: 2,2-DMP, acetone, *p*TsOH, room temp., 8 h, 85%; iii: Pd/C, H_2, ethanol, room temp., 8 h, 90%; iv: 2-(2-bromoethyl)benzaldehyde, $NaBPh_4$, ethanol, room temp., 24 h, 66%.

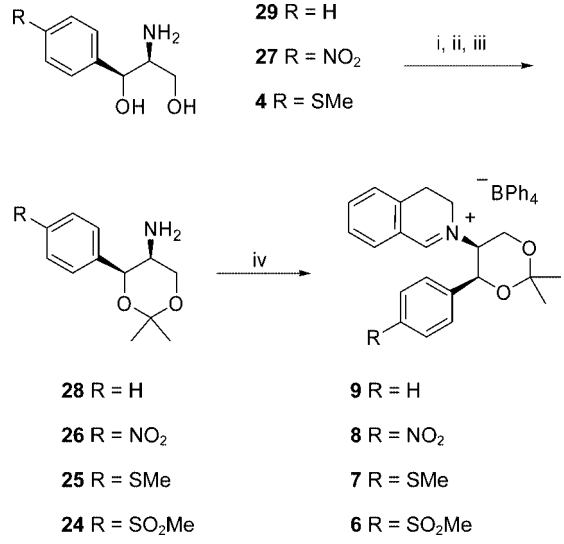
The corresponding isopropyl-substituted catalyst **12** was prepared from Garner's aldehyde **20** as shown in Scheme 2.[15] Reaction of Garner's aldehyde with isopropylmagnesium chloride at –78 °C under the conditions described by Joullé[16] gave the addition product **21** with high diastereoselectivity (>14:1) and in 73% yield. Global removal of the *N*-BOC and acetonide protecting groups with trifluoroacetic acid gave the amino diol as its trifluoroacetic acid salt **22**, which was treated directly with 2,2-dimethoxypropane in the presence of *p*-toluenesulfonic acid. The resulting acetonide **23** was cyclocondensed with 2-(2-bromoethyl)benzaldehyde to give **12**.

The primary amines **24**, **25**, and **26** required for the preparation of catalysts **6**, **7**, and **8** were prepared in good yields from the commercially available amino diols (+)-thiomicamine (**4**) and **27**, using a method similar to that developed by Nordin and Thomas for the synthesis of the simpler analogue (+)-acetonamine **28** from the amino diol **29**.[17] Acetonamine **28** was itself used to prepare the phenyl-substituted catalyst **9**.[11] Treatment of each amino diol with methyl formate and subsequent acetal formation with 2,2-dimethoxypropane afforded the formate-protected acetonide, which was deprotected to give the amino acetals **24**, **25**, **26**, **28** in 60–80% overall yield by heating with hydrazine hydrate. In the case of amine **24**, oxidation of the sulfide to the sulfone was accomplished in 85% yield at the formate-protected stage with *m*CPBA in dichloromethane at 0 °C. Cyclocondensation of the amino acetals **24**, **25**, **26**, **28** with



Scheme 2. Reagents and conditions: i: *i*PrMgCl, THF, –78 °C, 2 h, 73%; ii: TFA, DCM, –78 °C to room temp., 3 h; iii: 2,2-DMP, acetone, *p*TsOH, room temp., 8 h, 70%: iv: 2-(2-bromoethyl)benzaldehyde, $NaBPh_4$, ethanol, room temp., 24 h, 70%.

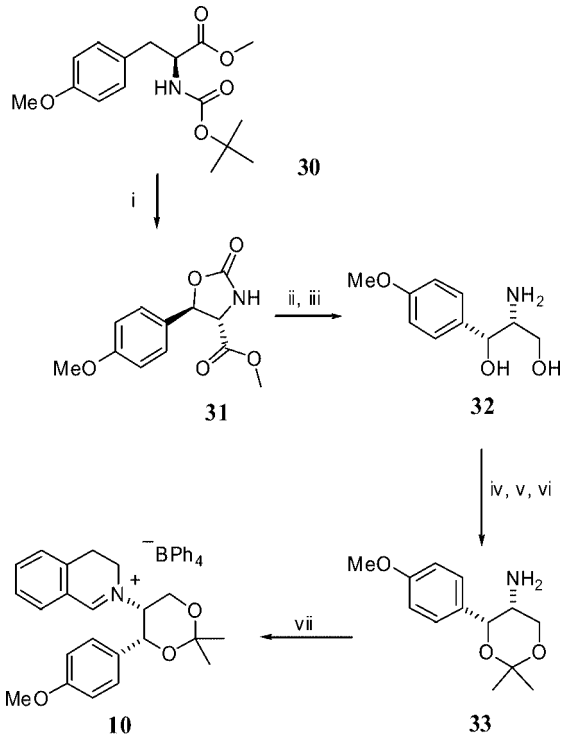
2-(2-bromoethyl)benzaldehyde proceeded smoothly, generating the corresponding iminium salt catalysts **6**–**9**, with the 4*S*,5*S* absolute configuration, having a tetraphenylborate anion, typically in >70% yields (Scheme 3).



Scheme 3. Reagents and conditions: i: MeOCHO, MeOH, room temp.; ii: $(Me)_2C(MeO)_2$, acetone, CSA, room temp. (**24**–**26**) *or* $(Me)_2C(MeO)_2$, acetone, HBr (1.0 M, cat.), 0 °C, 2.5 h (**28**); iii: $H_2NNH_2 \cdot H_2O$, Δ; iv: 2-(2-bromoethyl)benzaldehyde, EtOH, $NaBPh_4$, room temp.

The 4-methoxy-substituted catalyst **10**, with the opposite 4*R*,5*R* absolute configuration, was prepared from the (L)-tyrosine derivative **30** following the work of Ohfune,[18] whereby a benzylic cation is generated by treatment with potassium persulfate ($K_2S_2O_8$) and copper, and trapped by an oxygen atom of the BOC group in an intramolecular and highly diastereoselective manner to form the oxazolidinone **31** (≥ 98% *R* at C3) (Scheme 4). Reduction of the methyl ester was initially achieved with lithium aluminium

hydride (77%), but sodium borohydride provided a superior yield of 91%. Hydrolysis of the oxazolidinone with 1 M sodium hydroxide produced the *syn*-(1*R*,2*R*)-amino diol **32**.



Scheme 4. Reagents and conditions: i: $K_2S_2O_8$, $CuSO_4$, H_2O/MeCN (1:1), 70 °C, 3 h, 52%; ii: $NaBH_4$, EtOH, 0 °C to room temp. 45 min, 91%, iii: 1 M NaOH, Δ, 20 min, 93%; iv: MeOCHO, MeOH, room temp. 1 h; v: $(Me)_2C(MeO)_2$, acetone, $BF_3{\cdot}Et_2O$, room temp. 45 min, 81%; vi: $H_2NNH_2{\cdot}H_2O$, Δ, 2.5 h, 95%; vii: 2-(2-bromoethyl)benzaldehyde, EtOH, $NaBPh_4$, room temp., 71%.

The amino diol **32** was then subjected to the synthetic procedure outlined in Scheme 4. However, attempted acetalization of the formate-protected diol to the 1,3-dioxane did not proceed smoothly with (±)-10-camphorsulfonic acid. Catalytic boron trifluoride–diethyl ether was thus used instead, and the desired six-membered ring dioxane was produced exclusively. Subsequent deprotection afforded the primary amine **33**, which was cyclocondensed to form the desired iminium salt catalyst **10** in 71% yield.

Catalytic Asymmetric Epoxidation

With the syntheses of catalysts **6**–**12** complete, we were able to test their efficiency in the catalytic asymmetric epoxidation of several unfunctionalized alkenes (Table 1), using 10 mol-% of catalyst in acetonitrile/water (1:1), at 0 °C with oxone (2 equiv.) as stoichiometric oxidant and sodium carbonate (4 equiv.) as base.

The catalysts **11** and **12**, containing alkyl group substituents in the acetal moiety, while inducing efficient epoxidation, gave less than 5% *ee* in the epoxidation of 1-phenylcyclohexene. These results, not included in Table 1, suggest that the aromatic nature of the C4 substituent of **6** is vital for catalyst enantioselectivity, perhaps due to interactions of the aryl substituent with the dihydroisoquinolinium unit and/or with the substrate.

The 4-nitro substituted salt **8** gave the worst results, giving at best 42% *ee* for 1-phenyl-3,4-dihydronaphthalene oxide (Entry 3). The sulfide **7** gave similar *ee* values to the sulfone-based catalyst **6**, and catalyst **7** also gave the poorest epoxide conversions, we believe due at least in part to the susceptibility of the thiomethyl group to undergo oxidation giving **6** during the reaction, and so consuming oxidant; it is well known that oxone can oxidize sulfides to sulfoxides or sulfones.[19] Analysis of the catalyst by ^1H NMR spectroscopy after it had been subjected to the reaction conditions showed, the proton signal for the thiomethyl group had shifted from δ = 2.42 to δ = 3.0, and comparison of the spectrum with that of catalyst **6** confirmed that **7** had indeed been oxidized to the sulfone under the epoxidation reaction conditions. No sulfoxide was observed. Iminium salt **8**, containing the strongly electron-withdrawing 4-nitro group, generally gave lower conversions than did catalysts **6**, **9** and **10**, all of which gave similar conversions to epoxide. By far the most active catalysts were **9** and **10**, both of which induced complete conversion of 1-phenylcyclohexene into the epoxide in less than 3 minutes. One interesting point to note is that catalysts with an electron-withdrawing group at the 4-position (**6** and **8**) epoxidize *trans*-stilbene with very poor enantioselectivity.

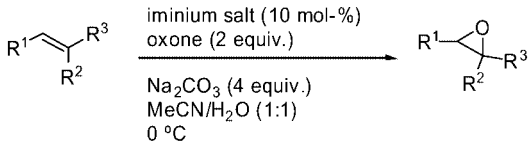
Undoubtedly the best catalyst for epoxidation of the range of alkenes tested here, when using oxone as the primary oxidant, was the 4-methoxy-substituted salt **10**. It imparted the highest enantioselectivity of this group of catalysts, giving triphenylethylene oxide with 71% *ee* in 60% yield in only 30 minutes. Even *trans*-stilbene was epoxidized with 35% *ee*.

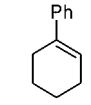
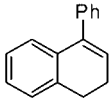
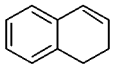
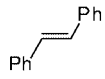
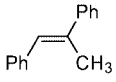
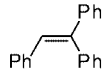
We have also recently reported the preparation and use of the related catalyst **13**, in which the dihydroisoquinolinium moiety has been replaced by a biphenyl structure fused to a seven-membered azepinium salt.[14] Lacour has recently reported related catalysts containing the interesting chiral TRISPHAT counterion.[6] We report here several new members of this family of catalysts **14**–**16**, generated from the substituted amino acetals described above.

Cyclocondensation of the amines **24**, **26**, **28**, and **33**, chosen from the more effective catalysts of the dihydroisoquinolinium salt series, with the bromoaldehyde **34**, prepared from 2,2′-bis(hydroxymethyl)biphenyl,[12] afforded the corresponding dibenzazepinium salts **13**–**16** in good yields (Scheme 5). These catalysts were tested in the asymmetric epoxidation of three alkene substrates: 1-phenylcyclohexene, α-methylstilbene and triphenylethylene (Table 2).

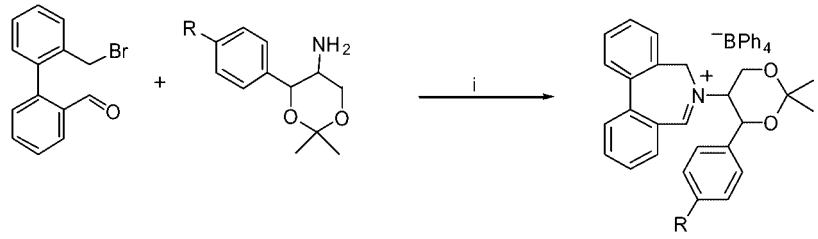
These new catalysts in general induced slightly poorer *ee*s than did their six-membered ring dihydroisoquinolinium counterparts. Methoxy-substituted catalyst **16**, however, gave 1-phenylcyclohexene oxide with 63% *ee* (compared to 45% *ee* for six-membered ring catalyst **10**). Disappointingly, for reasons that at this moment remain unclear, triphenylethylene proved to be a poor substrate with catalysts **14** (11% *ee*), **15** (10% *ee*), and **16** (26% *ee*); we have previously reported a 59% *ee* for triphenylethylene oxide when catalyst

Table 1. Catalytic asymmetric epoxidation of alkenes using dihydroisoquinolinium salts.[a]



	Catalyst[b]	**9**	**8**	**7**	**6**	**10**
Entry	Alkene	In all cases: *ee* (%)[c] / Conv. (%)[d] / Configuration[e]				
1		41 / 55[f] / (–)-(1*S*,2*S*)	15 / 82 / (–)-(1*S*,2*S*)	31 / 78 / (–)-(1*S*,2*S*)	39 / 100 / (–)-(1*S*,2*S*)	45 / 54[f] / (+)-(1*R*,2*R*)
2		49 / 64[f] / (–)-(1*S*,2*R*)	42 / 100 / (–)-(1*S*,2*R*)	49 / 100 / (–)-(1*S*,2*R*)	47 / 100 / (–)-(1*S*,2*R*)	63 / 62[f] / (+)-(1*R*,2*S*)
3		40 / 92 / (–)-(1*S*,2*R*)	41 / 52 / (–)-(1*S*,2*R*)	35 / 82 / (–)-(1*S*,2*R*)	45 / 61 / (–)-(1*S*,2*R*)	46 / 83 / (+)-(1*R*,2*S*)
4		15 / 56[f] / (–)-(*S*,*S*)	<5 / 100 / –	<5 / 85 / –	<5 / 100 / –	35 / 54[f] / (+)-(*R*,*R*)
5		52 / 52[f] / (–)-(1*S*,2*R*)	35 / 100 / (–)-(1*S*,2*R*)	42 / 85 / (–)-(1*S*,2*R*)	32 / 100 / (–)-(1*S*,2*R*)	60 / 55[f] / (+)-(1*R*,2*S*)
6		59 / 54[f] / (+)-(*S*)	33 / 100 / (+)-(*S*)	51 / 67 / (+)-(*S*)	50 / 100 / (+)-(*S*)	71 / 60[f] / (–)-(*R*)
7		20 / 64[f] / (+)-(*R*)	<5 / 62[f] / –	9 / 56[f] / (+)-(*R*)	4 / 64[f] / (+)-(*R*)	6 / 59[f] / (–)-(*S*)

[a] Epoxidation conditions: Iminium salt (10 mol-%), oxone (2 equiv.), Na_2CO_3 (4 equiv.), $MeCN/H_2O$ (1:1), 0 °C, 2 h. [b] Catalyst **6**–**9** configuration (4*S*,5*S*); Catalyst **10** configuration (4*R*,5*R*). [c] Enantiomeric excesses were determined by ^1H NMR spectroscopy in the presence of (+)-Eu(hfc)$_3$ (0.1 mol equiv.) or by chiral HPLC on a Chiracel OD column. [d] Conversions were evaluated from the ^1H NMR spectra by integration of alkene and epoxide signals. [e] The absolute configurations of the major enantiomers were determined by comparison of optical rotations with those reported in the literature. [f] Isolated yields.



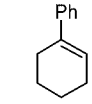
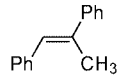
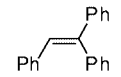
34

28 *R* = H (4*S*,5*S*)
26 *R* = NO_2 (4*S*,5*S*)
24 *R* = SO_2Me (4*S*,5*S*)
33 *R* = OMe (4*R*,5*R*)

13 *R* = H (4*S*,5*S*) 68%
14 *R* = NO_2 (4*S*,5*S*) 60%
15 *R* = SO_2Me (4*S*,5*S*) 66%
16 *R* = OMe (4*R*,5*R*) 64%

Scheme 5. i: a) EtOH, room temp., 12 h; b) $NaBPh_4$.

Table 2. Catalytic asymmetric epoxidation of unfunctionalized alkenes using azepinium salts.[a]

	Catalyst[b]			
	13	**14**	**15**	**16**
Alkene	In each case: *ee* (%)[c] / Conv. (%)[d] / Configuration[e]			
	60 / 100 / (–)-(1*S*,2*S*)	38 / 48 / (–)-(1*S*,2*S*)	47 / 56 / (–)-(1*S*,2*S*)	63 / 50[f] / (+)-(1*R*,2*R*)
	37 / 95 / (–)-(1*S*,2*S*)	17 / 30 / (–)-(1*S*,2*S*)	21 / 100 / (–)-(1*S*,2*S*)	50 / 61[f] / (+)-(1*R*,2*R*)
	59 / 90 / (+)-(*S*)	11 / 22 / (+)-(*S*)	10 / 55 / (+)-(*S*)	26 / 63[f] / (–)-(*R*)

[a] Epoxidation conditions: Iminium salt (5 mol-%), oxone (2 equiv.), Na_2CO_3 (4 equiv.), MeCN/H_2O (1:1), 0 °C, 2 h. [b] Catalyst **13**–**15** configuration (4*S*,5*S*); Catalyst **16** configuration (4*R*,5*R*). [c] Enantiomeric excesses were determined by ^{1}H NMR spectroscopy in the presence of (+)-Eu(hfc)$_3$ (0.1 mol equiv.). [d] Conversions were evaluated from the ^{1}H NMR spectra by integration of alkene and epoxide signals. [e] The absolute configurations of the major enantiomers were determined by comparison of optical rotations with those reported in the literature. [f] Isolated yields.

13 is employed. These seven-membered ring catalysts, however, provide dramatically faster reactions, providing complete consumption of alkene substrates in five to ten minutes, as opposed to around one hour for the six-membered ring systems under the same conditions.

Conclusions

We have discovered that the aromatic substituent present in the acetal moiety of our catalysts is vital for asymmetric induction during the epoxidation reaction. The new 4-methoxy-substituted catalyst **10** provides promising enantioselectivity in the group of alkenes tested, using oxone as the primary oxidant. The corresponding series of catalysts based around a dibenzazepinium nucleus is highly reactive, and all the catalysts described can be easily synthesized in good yields. We continue to develop this catalyst motif in order to achieve higher degrees of enantiocontrol.

Experimental Section

General: Acronyms: CSA = (±)-10-camphorsulfonic acid, DCM = dichloromethane, *m*CPBA = *m*-chloroperbenzoic acid, 2,2-DMP = 2,2-dimethoxypropane, NMM = *N*-methylmorpholine. All infrared spectra were obtained with a Perkin–Elmer Paragon 1000 FT-IR spectrophotometer; thin film spectra were acquired using sodium chloride plates. All ^{1}H and ^{13}C NMR spectra were measured at 250.13 and 62.86 MHz with a Bruker AC 250 MHz spectrometer or at 400.13 and 100.62 MHz with a Bruker DPX 400 MHz spectrometer, in deuteriochloroform solution unless otherwise stated, using TMS (tetramethylsilane) as the internal reference. Mass spectra were recorded with a Jeol-SX102 instrument utilizing electron-impact (EI), fast atom bombardment (FAB), and by the EPSRC national mass spectrometry service at the University of Wales, Swansea, utilising electrospray (ES.). Analysis by GCMS utilized a Fisons GC 8000 series (AS, 800), using a 15 m × 0.25 mm DB-5 column and an electron-impact low resolution mass spectrometer. Melting points were recorded using an Electrothermal-IA 9100 melting point instrument and are uncorrected. Optical rotation values were measured with an Optical Activity-polAAar 2001 instrument, operating at λ = 589 nm, corresponding to the sodium D line, at the temperatures indicated. Microanalyses were performed on a Perkin–Elmer Elemental Analyser 2400 CHN. All chromatographic manipulations used silica gel as the adsorbent. Reactions were monitored using thin-layer chromatography (TLC) on aluminium-backed plates coated with Merck Kieselgel 60 F254 silica gel. TLC plates were visualised by UV radiation at a wavelength of 254 nm, or stained by exposure to an ethanolic solution of phosphomolybdic acid (acidified with concentrated sulfuric acid), followed by charring where appropriate. Reactions requiring anhydrous conditions were carried out using glassware dried overnight at 150 °C, under nitrogen unless otherwise stated. Reaction solvents were used as obtained commercially unless otherwise stated. Light petroleum (b.p. 40–60 °C) was distilled from calcium chloride prior to use. Ethyl acetate was distilled from over calcium sulfate or chloride. Dichloromethane was distilled from over calcium hydride. Tetrahydrofuran was distilled under nitrogen from the sodium/benzophenone ketyl radical or from lithium aluminium hydride. Enantiomeric excesses were determined either by proton nuclear magnetic resonance spectroscopy in the presence of europium(III) tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate] as the chiral shift reagent, or by chiral HPLC using a Chiracel OD column on a TSP Thermo-Separating-Products Spectra Series P200 instrument, with a TSP Spectra Series UV100 ultra-violet absorption detector set at 254 nm and a Chromojet integrator.

(2*R*,3*R*)-2-(Benzyloxycarbonylamino)butane-1,3-diol (17): *N*-Methylmorpholine (2.20 mL, 19.8 mmol) and isobutyl chloroformate (2.50 mL, 19.8 mmol) were successively added to a cooled (–15 °C)

solution of (2*S*,3*R*)-*N*-benzyloxycarbonyl-L-threonine (5.00 g, 19.8 mmol) in 1,2-dimethoxyethane (20 mL). After 1 min the white precipitate was removed by filtration, washed with 1,2-dimethoxyethane (2×5 mL), and the filtrate cooled using an ice/salt bath. A solution of $NaBH_4$ (1.13 g, 29.6 mmol) in water (50 mL) was added in one portion. After the evolution of gas subsided, water (250 mL) was added. The reaction mixture was extracted with ethyl acetate (3×75 mL), the combined organic layers were washed with brine (2×50 mL) and dried ($MgSO_4$), and the solvents removed under reduced pressure to give **17** as a colourless oil (3.30 g, 70%). $[\alpha]_D$ = –15.0 (*c* = 1.12, $CHCl_3$). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 3334, 2971, 2360, 1698, 1522, 1456, 1251, 1069. ^1H NMR (250 MHz, $CDCl_3$, ppm): δ = 1.20 (d, *J* = 6.4 Hz, 3 H), 2.74 (br. s, 2 H), 3.51–3.61 (m, 1 H), 3.81 (br. s, 2 H), 4.05–4.20 (m, 1 H), 5.11 (s, 2 H), 5.54 (d, *J* = 8.6 Hz, 1 H), 7.25–7.47 (m, 5 H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 20.2, 56.3, 64.4, 67.0, 128.1, 128.2, 128.6, 136.3, 157.2. MS: *m*/*z* = 239.1152. $C_{12}H_{17}NO_4$ [M^+] requires 239.1158.

(4*R*,5*R*)-5-(Benzyloxycarbonylamino)-2,2,4-trimethyl-1,3-dioxane (18): (2*R*,3*R*)-2-(benzyloxycarbonylamino)butane-1,3-diol (**17**) (0.20 g, 0.87 mmol) was dissolved in acetone (20.0 mL) and 2,2-dimethoxypropane (1.10 mL, 8.70 mmol). A catalytic amount of *p*-toluenesulfonic acid (10 mol-%, 0.016 g, 0.09 mmol) was added and the reaction stirred overnight at room temperature. The solvent was evaporated under reduced pressure. The residue was dissolved in ethyl acetate, and the solution washed with sodium hydrogen carbonate (50%) (2×20 mL) and brine (2×20 mL). The organic layers were combined, dried (Mg_2SO_4), and the solvents removed under reduced pressure to give **18** as a colourless oil (0.24 g, 85%), $[\alpha]_D$ = –8.2 (*c* = 1.04, $CHCl_3$). $C_{15}H_{21}NO_4$ (279.33): calcd. C 64.50, H 7.58, N 5.01; found C 64.27, H 7.46, 4.61. IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 2360, 1716, 1505, 1455, 1381. ^1H NMR (400 MHz, $CDCl_3$, ppm): δ = 1.60 (d, *J* = 6.3 Hz, 3 H), 1.40 (s, 3 H), 1.48 (s, 3 H), 3.53 (dq, *J* = 9.8, 1.9 Hz, 1 H), 3.78 (dd, *J* = 12.0, 1.8 Hz, 1 H), 4.09 (dd, *J* = 12.0, 2.0 Hz, 1 H), 4.15 (ddd, *J* = 6.3, 1.9 Hz, 1 H), 5.16 (s, 2 H), 5.58 (d, *J* = 9.8 Hz, 1 H), 7.27–7.44 (m, 5 H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 18.2, 18.9, 30.1, 50.0, 65.3, 67.2, 67.4, 99.4, 127.3, 128.5, 128.9, 136.9, 156.8. MS: *m*/*z* = 279.1471. $C_{15}H_{21}NO_4$ [M^+] requires 279.1471.

(4*R*,5*R*)-5-Amino-2,2,4-trimethyl-1,3-dioxane (19): (4*R*,5*R*)-5-(Benzyloxycarbonylamino)-2,2,4-trimethyl-1,3-dioxane (**18**) (1.30 g, 4.7 mmol) was dissolved in ethanol under a slight positive pressure of hydrogen. Palladium (10% on carbon) (0.10 g) was added. The mixture was stirred at room temperature for 12 h, filtered through a pad of celite, and the ethanol removed under reduced pressure to give **19** as a colourless oil (0.61 g, 90%), $[\alpha]_D$ = –26.7 (*c* = 1.05, $CHCl_3$). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 3580, 2959, 1605, 1473, 1262, 1140. ^1H NMR (250 MHz, $CDCl_3$, ppm): δ = 1.16 (d, *J* = 6.4 Hz, 3 H), 1.41 (s, 3 H), 1.46 (s, 3 H), 1.60 (br. s, 2 H), 2.42 (q, *J* = 4.0, 2.0 Hz, 1 H), 3.72 (dd, *J* = 11.8, 2.0 Hz, 1 H), 4.11 (dd, *J* = 11.8, 2.0 Hz, 1 H), 4.09 (m, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 18.3, 19.0, 30.1, 49.2, 67.4, 68.0, 99.1. MS: *m*/*z* = 145.1100. $C_7H_{15}NO_2$ [M^+] requires 145.1103.

(4*S*)-*N*-*tert*-Butoxycarbonyl-4-[(1*S*)-hydroxy-2-methylpropyl]-2,2-dimethyloxazolidine (21): A solution of isopropylmagnesium chloride (2 M in THF, 8.60 mL, 17.2 mmol) was added dropwise over 30 min to a pre-cooled solution of Garner's aldehyde, (4*S*)-*N*-*tert*-butoxycarbonyl-2,2-dimethyloxazolidine-4-carbaldehyde (**20**) (1.20 g, 5.2 mmol) in tetrahydrofuran (50 mL) at –78 °C, under a stream of nitrogen. The resulting dark yellow solution was stirred for an additional 2 h at –78 °C, and warmed to 0 °C. The reaction mixture was diluted with diethyl ether (50 mL), and saturated aqueous ammonium chloride (10 mL) added. The organic layer was washed with brine, dried (Na_2SO_4), filtered, and the solvents removed under reduced pressure to give a yellow solid. Column chromatography, eluting with ethyl acetate/light petroleum (1:8), and recrystallization (ethyl acetate/light petroleum) gave **21** as a colourless crystalline solid (1.2 g, 73%); m.p. 77–79 °C (ref.[16] m.p. 78–80 °C). $[\alpha]_D^{20}$ = –52.2 (*c* = 1.06, $CHCl_3$) (ref.[16] $[\alpha]_D$ = –54.3)]. $C_{14}H_{27}NO_4$ (273.37): calcd. C 61.51, H 9.96, N 5.12; found C 61.92, H 9.93, N 4.96. IR (film, cm^{-1}): $\tilde{\nu}_{max}$ 3582, 3396, 1702, 1670, 1459, 1377, 1366, 1174. ^1H NMR (250 MHz, $CDCl_3$, ppm): δ = 0.90 (d, *J* = 6.7 Hz, 3 H), 0.98 (d, *J* = 6.8 Hz, 3 H), 1.44 (s, 9 H), 1.51 (s, 3 H) 1.60 (s, 3 H), 1.63–1.70 (m, 1 H), 3.45–3.49 (m, 1 H), 3.70–3.96 (m, 1 H), 3.98–4.10 (m, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 14.3, 20.4, 24.4, 27.3, 28.4, 31.0, 60.6, 65.3, 78.5, 81.4, 94.1, 155.7. MS: *m*/*z* = 273.1944. $C_{14}H_{27}NO_4$ [M^+] requires 273.1940.

(4*S*,5*S*)-2,2-Dimethyl-4-(1-methylethyl)-1,3-dioxan-5-amine (23): (4*S*)-*N*-*tert*-Butoxycarbonyl-4-[(1*S*)-hydroxy-2-methylpropyl]-2,2-dimethyloxazolidine (**21**) (0.10 g, 0.37 mmol) was dissolved in dichloromethane (1 mL), and the solution cooled using an ice bath. Trifluroacetic acid (0.50 mL, 6.50 mmol) was added dropwise. The mixture was stirred for 1.5 hours in an ice bath; the ice bath was removed, and the mixture stirred for a further 1.5 hours while reaching room temperature. The solvents were removed under reduced pressure and the residue dissolved in acetone (25 mL) and 2,2-dimethoxypropane (0.45 mL, 3.70 mmol), together with a catalytic amount of *p*-toluenesulfonic acid. The mixture was stirred overnight at room temperature. The solvents were removed under reduced pressure, and the dark oil dissolved in dichloromethane. The solution was washed with saturated aqueous sodium hydrogen carbonate, dried ($MgSO_4$), and the solvents removed under reduced pressure to give **23** as a pale yellow oil (0.045 g, 70%). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ 3583, 2966, 2361, 2306, 1675, 1471, 1265, 1138. $[\alpha]_D^{20}$ = +32.2 (*c* = 1.02, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$, ppm): δ = 0.86 (d, *J* = 6.7 Hz, 3 H), 0.95 (d, *J* = 6.5 Hz, 3 H), 1.41 (s, 3 H), 1.42 (s, 3 H), 1.69–1.87 (m, 1 H), 2.20 (br. s, 2 H), 2.65 (dd, *J* = 3.8, 2.0 Hz, 1 H), 3.32 (dd, *J* = 9.6, 1.6 Hz, 1 H), 3.72 (dd, *J* = 11.9, 2.0 Hz, 1 H), 4.06 (dd, *J* = 11.8, 2.1 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 19.0, 19.1, 27.6, 28.1, 32.5, 63.1, 64.3, 84.1, 94.6. MS: *m*/*z* = 173.1419. $C_9H_{19}NO_2$ [M^+] requires 173.1416.

General Procedure for the Formation of 5-Amino-1,3-dioxanes from Amino Diols: The amino diol (1.0 equiv.) was dissolved in methanol (10 mL/g), and methyl formate (1.1 equiv.) added together with sodium methoxide (10 mol-%). The mixture was stirred for 3.5 h and the solvent removed under reduced pressure. The crude yellow oil was dissolved in acetone (50 mL/g), and CSA (10 mol-%) and 2,2-dimethoxypropane (10.0 equiv.) added. The mixture was stirred for up to 4 h and monitored by TLC. Upon completion, the solvents were removed under reduced pressure and the residue redissolved in ethyl acetate. The solution was washed with saturated aqueous sodium hydrogen carbonate, dried ($MgSO_4$), and the solvents removed under reduced pressure to give the formate-protected 1,3-dioxane, which was dissolved in aqueous hydrazine hydrate (85%) (20 mL/g) and the solution heated under reflux for 2.5 h. The solution was cooled to room temperature and extracted with ethyl acetate (3×20 mL/g). The combined organic solutions were washed with water (2×20 mL/g), dried ($MgSO_4$), and the solvents removed under reduced pressure.

(4*S*,5*S*)-5-Formylamino-2,2-dimethyl-4-[4-(methylsulfonyl)phenyl]-1,3-dioxane: (4*S*,5*S*)-5-formylamino-2,2-dimethyl-4-[4-(methylthio)-phenyl]-1,3-dioxane (4.00 g, 14.2 mmol) was dissolved in dichloromethane (100 mL) and the solution cooled to 0 °C. A solution of *m*CPBA (2.2 equiv., 7.03 g, 31.0 mmol) in chloroform (20 mL) was

added dropwise over 10 min. The reaction was then stirred for 2 h, washed with saturated aqueous sodium hydrogen carbonate (2×40 mL) and brine (2×40 mL), and dried ($MgSO_4$). The solvents were removed under reduced pressure to give a colourless oil. Crystallization from chloroform/diethyl ether gave the product as a colourless crystalline solid (3.80 g, 85%); m.p. 146–147 °C. $[a]_D$ = –11.6 (c = 1.21, $CHCl_3$). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ 3054, 2993, 1675, 1516, 1382, 1300, 1239, 1202, 1149, 1086, 948. $C_{14}H_{19}NO_5S$ (313.37): calcd. C 53.66, H 6.11, N 4.47; found C 52.68, H 6.12, N 4.33. ^1H NMR (400 MHz, $CDCl_3$, ppm): δ = 1.54 (s, 3 H), 1.57 (s, 3 H), 3.01 (s, 3 H), 3.82 (dd, J = 12.0, 2.0 Hz, 1 H), 4.33 (dd, J = 12.0, 1.6 Hz, 1 H), 4.37 (dd, J = 10.0, 1.6 Hz, 1 H), 5.25 (s, 1 H), 6.51 (d, J = 9.2 Hz, 1 H), 7.52 (d, J = 8.0 Hz, 2 H), 7.85 (d, J = 8.0 Hz, 2 H), 7.89 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 18.9, 29.9, 44.8, 45.4, 64.9, 71.9, 100.4, 127.0, 127.5, 140.0, 145.0, 160.9. MS: m/z = 314.1058. $C_{14}H_{19}NO_5S$ [M^+ + H] requires 314.1062.

(4*S*,5*S*)-5-Amino-2,2-dimethyl-4-[4-(methylsulfonyl)phenyl]-1,3-dioxane (24): Prepared according to the general procedure from (4*S*,5*S*)-5-formylamino-2,2-dimethyl-4-[4-(methylsulfonyl)phenyl]-1,3-dioxane (1.80 g, 5.8 mmol), isolated as a colourless oil, and crystallized from diethyl ether/ethyl acetate. Colourless crystals (1.59 g, 96%); m.p. 120–122 °C. $[a]_D^{20}$ = +50.0 (c = 1.00, $CHCl_3$). $C_{13}H_{19}NO_4S$ (285.36): calcd. C 54.72, H 6.71, N 4.91; found C 54.64, H 6.69, N 4.83. IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 3372, 2991, 1601, 1380, 1198, 1077, 949. ^1H NMR (400 MHz, $CDCl_3$, ppm): δ = 1.56 (s, 6 H), 2.82–3.00 (m, 1 H), 3.06 (s, 3 H), 3.88 (dd, J = 11.6, 2.0 Hz, 1 H), 3.24 (dd, J = 11.6, 2.4 Hz, 1 H), 5.10–5.19 (m, 1 H), 7.55 (d, J = 8.0 Hz, 2 H), 7.95 (d, J = 8.0 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 19.0, 30.0, 44.9, 49.8, 66.8, 73.9, 99.9, 127.2, 127.9, 139.9, 146.6. MS: m/z = 285.1028. $C_{13}H_{19}NO_4S$ [M^+] requires 285.1035.

(4*S*,5*S*)-5-Formylamino-2,2-dimethyl-4-[4-(methylthio)phenyl]-1,3-dioxane: Prepared according to the general procedure from (1*S*,2*S*)-(+)-2-amino-1-(4-methylthiophenyl)-1,3-propandiol (5.00 g, 23.4 mmol). Colourless oil (5.50 g, 84%). $[a]_D$ = +1.3 (c = 1.27, $CHCl_3$). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 3315, 2988, 2362, 1667, 1494, 1380, 1197, 1084, 947. ^1H NMR (250 MHz, $CDCl_3$, ppm): δ = 1.54 (s, 3 H), 1.58 (s, 3 H), 2.45 (s, 3 H), 3.87 (dd, J = 7.5, 1.0 Hz, 1 H), 4.24 (dd, J = 7.5, 1.0 Hz, 1 H), 4.21–4.33 (m, 1 H), 5.16 (d, J = 1.3 Hz, 1 H), 6.27 (d, J = 5.8 Hz, 1 H), 7.20 (s, 4 H), 7.97 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 15.8, 18.5, 29.7, 45.3, 64.6, 71.4, 99.7, 125.8, 126.6, 135.0, 137.8, 160.5. MS: m/z = 281.1081. $C_{14}H_{19}NO_3S$ [M^+] requires 281.1085.

(4*S*,5*S*)-5-Amino-2,2-dimethyl-4-[4-(methylthio)phenyl]-1,3-dioxane (25): Prepared according to the general procedure from (4*S*,5*S*)-5-formylamino-2,2-dimethyl-4-[4-(methylthio)phenyl]-1,3-dioxane (1.50 g, 5.34 mmol). Colourless oil (1.28 g, 95%). $[a]_D^{20}$ = +44.7 (c = 1.20, $CHCl_3$). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 3369, 2990, 1599, 1495, 1379, 1198, 1076, 947. ^1H NMR (400 MHz, $CDCl_3$, ppm): δ = 1.53 (s, 3 H), 1.54 (s, 3 H), 2.47 (s, 3 H), 2.72 (q, J = 2.0 Hz, 1 H), 3.88 (dd, J = 12.0, 2.0 Hz, 1 H), 4.27 (dd, J = 12.0, 2.4 Hz, 1 H), 5.05 (d, J = 1.6 Hz, 1 H), 7.23–7.28 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 16.0, 18.6, 29.7, 49.6, 66.1, 73.5, 99.2, 126.4, 126.8, 136.6, 137.4. MS: m/z = 253.1137. $C_{13}H_{19}NO_2S$ [M^+] requires 253.1137.

(4*S*,5*S*)-5-Formylmino-2,2-dimethyl-4-(4-nitrophenyl)-1,3-dioxane: Prepared according to the general procedure from (1*S*,2*S*)-(+)-2-amino-1-(4-nitrophenyl)-1,3-propandiol (**27**) (1.00 g, 4.71 mmol). Colourless oil (1.12 g, 85%). $[a]_D$ = +3.5 (c = 1.02, $CHCl_3$). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 1674, 1520, 1346, 856. ^1H NMR (250 MHz, $CDCl_3$, ppm): δ = 1.55 (s, 3 H), 1.59 (s, 3 H), 3.83 (dd, J = 12.1, 1.7 Hz, 1 H), 4.24 (dd, J = 12.1, 1.8 Hz, 1 H), 4.34–4.44 (m, 1 H), 5.26 (d, J = 1.0 Hz, 1 H), 7.50 (d, J = 8.9 Hz, 2 H), 7.91 (s, 1 H), 8.15 (d, J = 8.9 Hz, 2 H). ^{13}C NMR (62.5 MHz, $CDCl_3$, ppm): δ = 18.8, 29.3, 45.4, 64.9, 71.9, 100.7, 123.7, 126.8, 145.8, 147.8, 160.6. MS: m/z = 298.1399. $C_{13}H_{16}N_2O_5$ [M^+ + NH_4] requires 298.1403.

(4*S*,5*S*)-5-Amino-2,2-dimethyl-4-(4-nitrophenyl)-1,3-dioxane (26): Prepared according to the general procedure from (4*S*,5*S*)-5-formylamino-2,2-dimethyl-4-(4-nitrophenyl)-1,3-dioxane (4.00 g, 14.9 mmol), and purified by chromatography, eluting with ethyl acetate. Pale yellow plates (2.80 g, 78%); m.p. 117–119 °C. $[a]_D^{20}$ = +66.2 (c = 1.13, $CHCl_3$). $C_{12}H_{16}N_2O_4$ (252.27): calcd. C 57.13, H 6.39, N 11.10; found C 57.05, H 6.51, N 10.77. IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 1605, 1520, 1350, 1196, 1080, 941, 856. ^1H NMR (250 MHz, $CDCl_3$, ppm): δ = 1.56 (s, 6 H), 2.84 (q, J = 1.9 Hz, 1 H), 3.86 (dd, J = 11.8, 1.9 Hz, 1 H), 4.31 (dd, J = 11.8, 2.3 Hz, 1 H), 5.17 (d, J = 0.7 Hz, 1 H), 7.49 (d, J = 7.5 Hz, 2 H), 8.22 (d, J = 7.5 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 18.6, 29.7, 49.4, 66.3, 73.4, 99.6, 123.6, 126.7, 147.2, 147.3. MS: m/z = 253.1191. $C_{12}H_{16}N_2O_4$ [M + H] requires 253.1188.

(4*R*,5*R*)-5-Formylamino-2,2-dimethyl-4-(4-methoxyphenyl)-1,3-dioxane: (1*R*,2*R*)-(–)-2-Amino-1-(4-methoxyphenyl)-1,3-propanediol (1.20 g, 6.1 mmol) was dissolved in methanol (25 mL), and methyl formate (0.45 mL, 7.3 mmol) added together with sodium methoxide (0.1 mL). The mixture was stirred for 3.5 h, and the solvent removed under reduced pressure. The crude yellow oil was dissolved in acetone (60 mL) and 2,2-dimethoxypropane (10 equiv.), and boron trifluoride–diethyl ether added until pale yellow colour persisted (ca. 0.2 mL). The reaction was then stirred for 45 min. The solvents were removed under reduced pressure and the residue dissolved in ethyl acetate. The solution was washed with saturated aqueous sodium hydrogen carbonate, dried ($MgSO_4$), and the solvents removed to give a pale yellow oil (1.21 g, 75%). $[a]_D$ = –2.7 (c = 1.20, $CHCl_3$). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 2992, 1668, 1515, 1381, 1248, 1199, 1084, 1032, 949. ^1H NMR (250 MHz, $CDCl_3$, ppm): δ = 1.54 (s, 3 H), 1.58 (s, 3 H), 3.78 (s, 3 H), 3.87 (dd, J = 12.25, 1.95 Hz, 1 H), 4.20–4.33 (m, 2 H), 5.16 (s, 1 H), 6.19 (d, J = 8.55 Hz, 1 H), 6.85 (d, J = 8.90 Hz, 2 H), 7.23 (d, J = 8.90 Hz, 2 H), 8.00 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 18.6, 29.6, 45.6, 55.3, 64.6, 71.4, 99.7, 113.7, 126.5, 130.1, 159.0, 160.5. MS: m/z = 266.1390. $C_{14}H_{19}NO_4$ [M + H] requires 266.1392.

(4*R*,5*R*)-5-Amino-2,2-dimethyl-4-(4-methoxyphenyl)-1,3-dioxane (33): Prepared according to the general procedure from (4*R*,5*R*)-5-formylamino-4-(4-methoxyphenyl)-2,2-dimethyl-1,3-dioxane (0.70 g, 2.6 mmol). Colourless oil. (0.59 g, 95%). $[a]_D^{20}$ = –28.9 (c = 1.08, $CHCl_3$). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 3050, 2991, 2925, 1612, 1515, 1458, 1380, 1249, 1199, 1129, 1079, 948, 850. ^1H NMR (250 MHz, $CDCl_3$, ppm): δ = 1.53 (s, 3 H), 1.55 (s, 3 H), 2.72 (q, 1 H, 2.0 Hz, 1 H), 3.81 (s, 3 H), 3.89 (dd, J = 13.4, 1.7 Hz, 1 H), 4.29 (dd, J = 11.7, 2.3 Hz, 1 H), 5.05 (d, J = 1.9 Hz, 1 H), 6.89 (d, J = 8.8 Hz, 1 H), 7.24 (d, J = 8.8 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 19.0, 30.1, 50.2, 55.7, 66.4, 73.9, 99.5, 114.3, 127.2, 132.1, 159.3. MS: m/z = 238.1443. $C_{13}H_{19}NO_3$ [M + H] requires 238.1443.

***N*-*tert*-Butoxycarbonyl-*O*-methyl-L-tyrosine Methyl Ester (30):** A solution of *N*-*tert*-butoxycarbonyl-L-tyrosine (8.00 g, 28.5 mmol) in dimethyl formamide (80 mL) was cooled using an ice bath, treated with freshly ground potassium hydroxide (1.72 g, 31.3 mmol), and a cooled solution of iodomethane (1.95 mL, 31.3 mmol) in dimethyl formamide (20 mL) added dropwise over 5 min. The mixture was stirred at room temperature for 30 min, cooled using an ice bath, and additional potassium hydroxide (1.72 g, 31.3 mmol) and a cooled solution of iodomethane (1.95 mL, 31.3 mmol) in di-

methyl formamide (20 mL) added. The mixture was stirred for 3 h, poured onto ice (150 mL), and extracted with ethyl acetate (3 × 75 mL). The organic layers were washed with water (3 × 50 mL), brine (2 × 50 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure to afford a colourless oil. Crystallization was achieved from ethyl acetate/light petroleum, to give **30** as colourless crystals (6.5 g, 74%); m.p. 52–53 °C. IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 2976, 1746, 1716, 1612, 1515, 1391, 1366, 1248, 1175, 1058, 1034. ^1H NMR (250 MHz, $CDCl_3$, ppm): δ = 1.42 (s, 9 H), 3.01–3.11 (m, 2 H), 3.71 (s, 3 H), 3.78 (s, 3 H), 4.53 (q, J = 5.7 Hz, 1 H), 5.00 (d, J = 6.7 Hz, 1 H), 6.82 (d, J = 8.7 Hz, 2 H), 7.03 (d, J = 8.7 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 28.3, 37.6, 52.7, 54.7, 55.3, 79.9, 114.1, 128.1, 130.3, 155.1, 158.8, 172.4. MS: m/z = 309.1578. $C_{16}H_{23}NO_5$ requires 309.1576.

Methyl (4*S*,5*R*)-5-(4-Methoxyphenyl)-2-oxo-1,3-oxazolidine-4-carboxylate (31): A solution of *N*-*tert*-butoxycarbonyl-*O*-methyl-L-tyrosine methyl ester (**30**) (5.00 g, 16.2 mmol) in CH_3CN (200 mL) was treated with a solution of $K_2S_2O_8$ (8.75 g, 32.4 mmol) in water (210 mL) and a solution of $CuSO_4$ (0.52 g, 3.2 mmol) in water (50 mL). The mixture was heated to 70 °C for 3 h under a blanket of N_2, cooled, and extracted with ethyl acetate (3 × 150 mL). The combined organic solutions were dried ($MgSO_4$) and concentrated under reduced pressure to give a dark yellow oil. Column chromatography, eluting with ethyl acetate/light petroleum (1:10 to 1:1), afforded a colourless solid, which was recrystallized from ethyl acetate/light petroleum to give **31** as a colourless crystalline solid (2.10 g, 52%); m.p. 94–96 °C. $[\alpha]_D^{20}$ = +83.5 (c = 1.15, $CHCl_3$). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 3316, 2956, 2362, 2337, 1762, 1613, 1515, 1382, 1250, 1224, 1026, 834, 763. ^1H NMR (400 MHz, $CDCl_3$, ppm): δ = 3.81 (s, 3 H), 3.83 (s, 3 H), 4.31 (d, J = 5.2 Hz, 1 H), 5.56 (d, J = 5.2 Hz, 1 H), 6.81 (s, 1 H), 6.93 (d, J = 4.8 Hz, 2 H), 7.33 (d, 2 H, 4.8 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 53.5, 55.7, 61.8, 79.9, 114.7, 127.5, 130.3, 158.6, 160.6, 170.7. MS: m/z = 251.0794. $C_{12}H_{13}NO_5$ [M^+] requires 251.0794.

(1*R*,2*R*)-(–)-2-Amino-1-(4-methoxyphenyl)propane-1,3-diol (32): Methyl (4*S*,5*R*)-5-[4-methoxyphenyl]-2-oxo-1,3-oxazolidine-4-carboxylate (**31**) (2.20 g, 8.8 mmol) was dissolved in ethanol (25 mL) and the solution cooled using an ice bath. A solution of $NaBH_4$ (0.70 g, 19.3 mmol) in ethanol (8 mL) was added dropwise with stirring. After the addition was complete the ice bath was removed and the mixture stirred for 45 min. The mixture was cooled to 0 °C and concd. HCl (1.5 mL) added, followed by water (15 mL). The ethanol was removed under reduced pressure and the remaining aqueous solution extracted with ethyl acetate (3 × 50 mL). The combined organic solutions were dried ($MgSO_4$), and the solvents removed to afford an off-white solid, which was recrystallized from ethyl acetate/light petroleum to give (4*R*,5*R*)-4-hydroxymethyl-5-(4-methoxyphenyl)-1,3-oxazolidin-2-one as a colourless crystalline solid (1.75 g, 90%); m.p. 140–142 °C. $[\alpha]_D^{20}$ = +74.8 (c = 1.08, CH_3COCH_3). IR (nujol, cm^{-1}): $\tilde{\nu}_{max}$ = 3239, 1725, 1614, 1514, 1459, 1376, 1251, 1174, 1062, 1016, 828. ^1H NMR (250 MHz; [D_6]-acetone, ppm): δ = 3.71–3.87 (m, 3 H), 3.86 (s, 3 H), 5.35 (d, J = 5.3 Hz, 1 H), 7.01 (d, J = 8.6 Hz, 2 H), 7.41 (d, J = 8.6 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 56.0, 63.1, 64.2, 80.4, 115.4, 128.7, 133.2, 159.6, 161.3. MS: m/z = 223.0842. $C_{11}H_{13}NO_4$ [M^+] requires 223.0845.

(4*R*,5*R*)-4-Hydroxymethyl-5-(4-methoxyphenyl)-1,3-oxazolidin-2-one (1.65 g, 7.4 mmol) was suspended in aqueous NaOH (1 M, 40 mL) and heated under reflux for 30 min. The mixture was cooled to room temperature and extracted with ethyl acetate (8 × 30 mL). The combined organic solutions were dried ($MgSO_4$), and the solvents removed to give **32** as a colourless solid, which was recrystallized from methanol/diethyl ether (1.33 g, 91%); m.p. 132–134 °C. $[\alpha]_D^{20}$ = –28.3 (c = 1.06, 2 M aq. HCl). $C_{10}H_{15}NO_3$ (197.23): calcd. C 60.90, H 7.67; N 7.10; found C 61.14, H 7.51; N 6.96. IR (nujol, cm^{-1}): $\tilde{\nu}_{max}$ = 3338, 1615, 1583, 1515, 1459, 1376, 1253, 1064, 873. ^1H NMR (400 MHz, CD_3OD, ppm): δ = 2.86–2.98 (m, 1 H), 3.32 (dd, J = 10.8, 4.4 Hz, 1 H), 3.42 (dd, J = 10.8, 4.4 Hz, 1 H), 3.80 (s, 3 H), 4.49 (d, J = 7.2 Hz, 1 H), 4.90 (br. s, 2 H), 6.90 (d, J = 8.8 Hz, 2 H), 7.29 (d, J = 8.8 Hz, 2 H). ^{13}C NMR (100 MHz, CD_3OD, ppm): δ = 56.1, 60.3, 64.4, 75.8, 115.2, 129.2, 136.4, 161.1. MS: m/z = 198.1125. $C_{10}H_{16}NO_3$ [M^+ + H] requires 198.1130.

General Procedure for the Preparation of Dihydroisoquinolinium Salts from 2-(2-Bromoethyl)benzaldehyde and Primary Amines: 2-(2-Bromoethyl)benzaldehyde (1.60 equiv., 1.10 if freshly distilled) was cooled using an ice bath, and a solution of the amine in ethanol (10 mL per g of amine) was added dropwise. After the addition was complete, the ice bath was removed and the reaction mixture stoppered to retain HBr and stirred overnight. A solution of sodium tetraphenylborate or other anion-exchanging salt (1.10 equiv.) in the minimum amount of acetonitrile was added in one portion to the reaction mixture. After stirring for 5 min, the organic solvents were removed under reduced pressure. Ethanol was added to the residue, followed by water. The resulting precipitate was collected by filtration and washed with additional ethanol followed by diethyl ether. If no solid materialized after the addition of the water, the mixture was allowed to settle and the ethanol/water phase was decanted. The gummy residue was triturated in hot ethanol or methanol, inducing precipitation of the organic salt immediately or upon slow cooling of the hot alcoholic solution. Small quantities of acetonitrile may be added during this process to aid solubility.

(+)-*N*-{(4*S*,5*S*)-2,2-Dimethyl-4-[4-(methylsulfonyl)phenyl]-1,3-dioxan-5-yl}-3,4-dihydroisoquinolinium Tetraphenylborate (6): Prepared according to the general procedure from (4*S*,5*S*)-5-amino-2,2-dimethyl-4-[4-(methylsulfonyl)phenyl]-1,3-dioxane (**24**) (0.75 g, 2.96 mmol), and purified by recrystallization from CH_2Cl_2/hexane to give **6** as yellow plates (1.55 g, 73%); m.p. 199–201 °C (dec.). $[\alpha]_D^{20}$ = +126.7 (c = 1.20, acetone). $C_{46}H_{46}BNO_4S{\cdot}0.5H_2O$ (anhydrate: 719.74): calcd. C 75.79, H 6.50, N 1.92; found C 75.62, H 6.32, N 1.84. IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 1636, 1603, 1572, 1478, 1383, 1314, 1266, 1202, 1150, 1076, 1032, 956. ^1H NMR (400 MHz; [D_6]acetone, ppm): δ = 1.69 (s, 3 H), 1.72 (s, 3 H), 2.60–2.69 (m, 1 H), 2.85–2.96 (m, 1 H), 3.00 (s, 3 H), 3.65–3.72 (m, 1 H), 4.12–4.20 (m, 1 H), 4.49 (d, J = 13.6 Hz, 1 H), 4.57 (m, 1 H), 4.77 (dd, J = 13.6, 2.8 Hz, 1 H), 6.05 (d, J = 2.8 Hz, 1 H), 6.80 (t, J = 7.2 Hz, 4 H), 6.92 (t, J = 7.2 Hz, 8 H), 7.33 (m, 8 H), 7.49 (t, J = 7.6 Hz, 1 H), 7.73–7.83 (m, 3 H), 7.82 (d, J = 8.2 Hz, 2 H), 7.95 (d, J = 8.2 Hz, 2 H), 9.28 (s, 1 H). ^{13}C NMR (100 MHz; [D_6]acetone, ppm): δ = 18.8, 25.4, 29.5, 44.3, 52.3 62.9, 66.1, 71.5, 101.7, 122.3, 125.3, 126.1, 127.6, 128.8, 129.3, 129.4, 135.4, 137.0, 137.0, 137.9, 142.4, 143.2, 165.0, 168.9. MS: m/z = 400.1586. $C_{22}H_{26}NO_4S$ (cation) requires 400.1583.

(+)-*N*-{(4*S*,5*S*)-2,2-Dimethyl-4-[4-(methylthio)phenyl]-1,3-dioxan-5-yl}-3,4-dihydroisoquinolinium Tetraphenylborate (7): Prepared according to the general procedure from (4*S*,5*S*)-5-amino-2,2-dimethyl-4-[4-(methylthio)phenyl]-1,3-dioxane (**25**) (0.50 g, 2.0 mmol), and purified by recrystallization from CH_2Cl_2/hexane to give **7** as yellow plates (1.00 g, 73%); m.p. 146–148 °C (dec.). $[\alpha]_D^{20}$ = +115.9 (c = 1.41, acetone). $C_{46}H_{46}BNO_2S{\cdot}0.5H_2O$ (anhydrate: 687.74): calcd. C 79.27, H 6.66, N 2.01; found C 79.05, H 6.59, N 1.93. IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 3053, 2996, 2360, 2341, 1634, 1603, 1571, 1478, 1265, 1201, 1162, 1108, 1075. ^1H NMR (250 MHz; [D_6]acetone, ppm): δ = 1.66 (s, 3 H), 1.72 (s, 3 H), 2.42 (s, 3 H),

2.66–2.84 (m, 1 H), 2.90–3.03 (m, 1 H), 3.62–3.74 (m, 1 H), 4.13–4.26 (m, 1 H), 4.53 (m, 2 H), 4.78 (dd, J = 13.8, 3.1 Hz, 1 H), 5.91 (d, J = 2.6 Hz, 1 H), 6.78 (t, J = 7.2 Hz, 4 H), 6.92 (t, J = 7.40 Hz, 8 H), 7.34 (m, 8 H), 7.40–7.56 (m, 6 H), 7.76–7.87 (m, 2 H), 9.30 (s, 1 H). ^{13}C NMR (100 MHz; [D$_6$]acetone, ppm): δ = 15.4, 18.8, 25.4, 30.0, 52.3, 62.7, 66.5, 71.5, 101.4, 122.3, 125.3, 126.1, 126.9, 127.4, 129.2, 129.3, 133.9, 135.2, 137.0, 137.8, 139.5, 140.5, 165.0, 168.5. MS: m/z = 368.1682. $C_{22}H_{26}NO_2S$ (cation) requires 368.1684.

(+)-*N*-[(4*S*,5*S*)-2,2-Dimethyl-4-(4-nitrophenyl)-1,3-dioxan-5-yl]-3,4-dihydroisoquinolinium Tetraphenylborate (8): Prepared according to the general procedure from (+)-(4*S*,5*S*)-5-amino-2,2-dimethyl-4-(4-nitrophenyl)-1,3-dioxane (**26**) (0.19 g, 0.8 mmol), and purified by recrystallization from CH_2Cl_2/hexane to give **8** as yellow plates (0.36 g, 74%); m.p. 176–178 °C (dec.). $[\alpha]_D^{20}$ = +107.7 (c = 1.30, acetone). $C_{45}H_{43}BN_2O_4 \cdot 0.5H_2O$ (anhydrate: 686.64): calcd. C 77.66, H 6.38, N 4.03; found C 77.73, H 6.23, N 4.00. IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 1635, 1604, 1571, 1524, 1478, 1384, 1202, 1163, 1107, 1032. ^{1}H NMR (400 MHz; [D$_6$]acetone, ppm): δ = 1.72 (s, 3 H, C*H*$_3$, C7), 1.76 (s, 3 H), 2.70–2.80 (m, 1 H), 2.88–2.96 (m, 1 H), 3.65–3.74 (m, 1 H), 4.19–4.23 (m, 1 H), 4.54 (d, J = 13.6 Hz, 1 H), 4.65 (m, 1 H), 4.82 (dd, J = 13.6, 2.8 Hz, 1 H), 6.11 (d, J = 2.4 Hz, 1 H), 6.80 (t, J = 6.8 Hz, 4 H), 6.94 (t, J = 7.2 Hz, 8 H), 7.36 (m, 8 H), 7.51 (t, J = 7.6 Hz, 1 H), 7.59–7.88 (m, 3 H), 7.85 (d, J = 8.4 Hz, 2 H), 7.95 (d, J = 8.8 Hz, 2 H), 9.28 (s, 1 H). ^{13}C NMR (100 MHz; [D$_6$]acetone, ppm): δ = 19.2, 25.9, 30.0, 52.8, 63.4, 66.4, 71.9, 102.2, 122.7, 125.3, 125.8, 126.4, 128.3, 129.7, 129.8, 135.9, 137.4, 138.4, 140.1, 145.0, 149.0, 165.0, 169.5. MS: m/z = 367.1658. $C_{21}H_{23}N_2O_4$ (cation) requires 367.1658.

(+)-*N*-[(4*S*,5*S*)-2,2-Dimethyl-4-phenyl-1,3-dioxan-5-yl]-3,4-dihydroisoquinolinium Tetraphenylborate (9):[11] Prepared according to the general procedure from (4*S*,5*S*)-5-amino-2,2-dimethyl-4-phenyl-1,3-dioxane **28** (3.00 g, 14.4 mmol), and purified by recrystallization from acetone/diethyl ether to give **9** as a yellow solid (6.93 g, 75%), m.p. 169–170 °C. $[\alpha]_D^{20}$ = +38.6 (c = 2.70, CH_3CN). IR (nujol, cm^{-1}): $\tilde{\nu}_{max}$ = 1637, 1603, 1571, 1480, 1266, 1202, 1166, 1108, 1073. ^{1}H NMR (250 MHz, CD_3CN, ppm): δ = 1.65 (s, 3 H), 1.94 (s, 3 H), 2.39–2.48 (m, 1 H), 2.70–2.82 (m, 1 H), 3.25–3.40 (m, 1 H), 3.81–3.97 (m, 1 H), 4.06 (m, 1 H), 4.30 (d, J = 13.7 Hz, 1 H), 4.58 (dd, J = 13.7, 3.1 Hz, 1 H), 5.70 (d, J = 2.8 Hz, 1 H), 6.81 (t, J = 7.2 Hz, 4 H), 7.35–7.40 (m, 6 H), 7.46 (t, J = 7.3 Hz, 1 H), 7.65–7.74 (m, 2 H), 8.92 (s, 1 H). ^{13}C NMR (62.50 MHz, CD_3CN, ppm): δ = 17.9, 24.1, 28.7, 51.6, 61.4, 65.5, 70.7, 104.9, 121.9, 124.3, 125.4, 125.7, 128.1, 128.5, 128.6, 128.0, 134.4, 135.8, 137.0, 137.7, 138.7, 163.5, 167.5. MS: m/z = 322.1809. $C_{21}H_{24}NO_2$ (cation) requires 322.1807.

(–)-*N*-[(4*R*,5*R*)-2,2-Dimethyl-4-(4-methoxyphenyl)-1,3-dioxan-5-yl]-3,4-dihydroisoquinolinium Tetraphenylborate (10): Prepared according to the general procedure from (–)-(4*R*,5*R*)-5-amino-4-(4-methoxyphenyl)-2,2-dimethyl-1,3-dioxane (**33**) (0.40 g, 1.7 mmol), and purified by recrystallization from CH_2Cl_2/hexane to give **10** as yellow plates (0.83 g, 74%); m.p. 171–173 °C (dec.). $[\alpha]_D^{20}$ –108.6 (c = 1.40, acetone). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 1639, 1604, 1573, 1514, 1382, 1254, 1202, 1107, 1031. $C_{46}H_{46}BNO_3 \cdot 0.5Et_2O$ (anhydrate: 671.67): calcd. C 77.92, H 6.54, N 1.98; found C 77.70, H 6.50, N 1.88. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 1.51 (s, 3 H), 1.52 (s, 3 H), 2.20–2.25 (m, 1 H), 2.31–2.35 (m, 1 H), 2.85–2.90 (m, 1 H), 3.00–3.10 (m, 1 H), 3.04 (m, 1 H), 3.56 (d, J = 14.4 Hz, 1 H), 3.72 (s, 3 H), 3.90 (dd, J = 14.0, 2.8 Hz, 1 H), 5.11 (d, J = 2.4 Hz, 1 H), 6.79 (d, J = 2.0 Hz, 2 H), 6.87 (m, 2 H), 7.02 (t, J = 7.6 Hz, 8 H), 7.23 (m, 2 H) 7.24 (m, 1 H), 7.41 (m, 8 H), 7.57 (m, 1 H), 8.25 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 18.4, 24.6, 29.4, 50.5, 55.4, 61.9, 64.9, 70.5, 100.4, 114.4, 122.2, 123.7, 125.9, 127.3, 127.9, 128.7, 129.5, 134.0, 134.7, 136.2, 138.8, 159.8, 163.8, 169.5. MS: m/z = 352.1915. $C_{22}H_{26}NO_3$ (cation) requires 352.1913.

(–)-*N*-[(4*R*,5*R*)-2,2,4-Trimethyl-1,3-dioxan-5-yl]-3,4-dihydroisoquinolinium Tetraphenylborate (11): Prepared according to the general procedure from (4*R*,5*R*)-5-amino-2,2,4-trimethyl-1,3-dioxane (**19**) (0.75 g, 2.96 mmol), and purified by recrystallization from DCM/hexane to give **11** as yellow plates (1.13 g, 66%); m.p. 164–165 °C (dec.). $[\alpha]_D^{20}$ –22.3 (c = 1.05, acetone). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 3054, 1636, 1604, 1576, 1477, 1268, 1201, 1180. ^{1}H NMR (400 MHz, CD_3CN, ppm): δ = 1.26 (d, J = 6.4 Hz, 3 H), 1.46 (s, 3 H), 1.55 (s, 3 H), 3.25 (t, J = 8.0 Hz, 2 H), 3.89 (t, 1 H, 2.4 Hz, 1 H), 4.23 (dd, J = 13.6, 0.8 Hz, 1 H), 4.27–4.36 (m, 2 H), 4.46 (dd, J = 14.0, 3.2 Hz, 1 H), 4.63 (dq, J = 6.4, 2.8 Hz, 1 H), 6.83 (t, J = 7.2 Hz, 4 H), 6.93 (t, J = 7.6 Hz, 8 H), 7.22–7.33 (m, 8 H), 7.45 (d, J = 7.6 Hz, 1 H), 7.53 (t, J = 7.6 Hz, 1 H), 7.80 (dt, J = 7.6, 1.2 Hz, 1 H), 7.86 (d, J = 7.6 Hz, 1 H), 9.05 (s, 1 H). ^{13}C NMR (100 MHz; [D$_6$]acetone, ppm): δ = 17.7, 18.7, 25.6, 51.7, 62.9, 66.1, 66.5, 100.6, 122.3, 125.7, 126.1, 129.3, 136.0, 137.0 138.2, 139.4, 164.9, 168.7. MS: m/z = 260.1655. $C_{16}H_{22}NO_2$ (cation) requires 260.1651.

(+)-*N*-[(4*S*,5*S*)-4-Isopropyl-2,2-dimethyl-1,3-dioxan-5-yl]-3,4-dihydroisoquinolinium Tetraphenylborate (12): Prepared according to the general procedure from (4*S*,5*S*)-5-amino-4-isopropyl-2,2-dimethyl-1,3-dioxane (**23**) (0.05 g, 0.29 mmol), and purified by recrystallization from acetone/diethyl ether to give **12** as yellow plates (0.120 g, 70%); m.p. 166–167 °C (dec.). $[\alpha]_D^{20}$ = +31.7 (c = 1.16, acetone). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 3055, 1637, 1604, 1574, 1479, 1265, 1202, 1152, 1088. ^{1}H NMR (400 MHz, CD_3CN, ppm): δ = 0.89 (d, J = 7.8 Hz, 3 H), 0.97 (d, J = 6.4 Hz, 3 H), 1.48 (s, 3 H), 1.51 (s, 3 H) 1.69–1.75 (m, 1 H), 3.14–3.22 (m, 2 H), 3.89 (m, 2 H), 4.06 (m, 2 H), 4.33 (m, 2 H), 6.84 (t, J = 7.1 Hz, 4 H), 6.99 (t, J = 7.4 Hz, 8 H), 7.23–7.29 (m, 8 H), 7.44 (d, J = 7.4 Hz, 1 H), 7.51 (t, J = 7.6 Hz, 1 H), 7.80 (m, 2 H), 9.13 (s, 1 H). ^{13}C NMR (100 MHz, CD_3CN, ppm): δ = 17.0, 17.4, 17.9, 24.5, 28.3, 28.6, 50.6, 62.0, 62.3, 74.8, 99.9, 121.5, 124.4, 125.3, 128.6, 129.2, 134.2, 135.4, 137.0, 138.4, 163.5, 167.8. MS: m/z = 288.1959. $C_{18}H_{26}NO_2$ (cation) requires 288.1964.

General Procedure for the Preparation of 5*H*-Dibenzo[*c*,*e*]azepinium Salts from 2-[2-(Bromomethyl)phenyl]benzaldehyde and Primary Amines: A solution of 2-[2-(bromomethyl)phenyl]benzaldehyde (1.10 equiv.) in ethanol (10 mL/g aldehyde) was cooled using an ice bath. A solution of the amine in ethanol (10 mL per g of amine, 1 equiv.) was added dropwise. After the addition was complete, the ice bath was removed and the reaction mixture stoppered to retain HBr and stirred overnight. A solution of sodium tetraphenylborate or other anion exchanging salt (1.10 equiv.) in the minimum amount of acetonitrile was added in one portion. After stirring for 5 min, the organic solvents were removed under reduced pressure. Ethanol was added to the residue, followed by water. The resulting solid was collected by filtration and washed with additional ethanol followed by diethyl ether. If no solid materialized after the addition of the water, the mixture was allowed to settle and the ethanol/water phase decanted. The gummy residue was triturated in hot ethanol or methanol, inducing precipitation of the organic salt immediately or upon slow cooling of the hot alcoholic solution. Small quantities of acetonitrile may be added during this process to aid solubility.

(–)-*N*-[(4*S*,5*S*)-2,2-Dimethyl-4-phenyl-1,3-dioxan-5-yl]-5*H*-dibenzo-[*c*,*e*]azepinium Tetraphenylborate (13): Prepared according to the general procedure from (+)-(4*S*,5*S*)-5-amino-2,2-dimethyl-4-phenyl-1,3-dioxane (**28**) (3.85 g, 18.8 mmol). The product was isolated as yellow plates (9.00 g, 68%); m.p. 187–188 °C (dec.). $[\alpha]_D^{20}$ = –44.0

(c = 1.01, CH_3CN). $C_{50}H_{46}BNO_2$ (703.72): calcd. C 85.34, H 6.59, N 1.99; found C 85.23, H 6.52, N 1.96. IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 3055, 3038, 2999, 1633, 1579, 1480, 1451, 1385, 1203, 1114, 848, 735, 706. ^1H NMR (400 MHz; [D$_6$]DMSO, 115 °C, ppm): δ = 1.71 (s, 3 H), 1.74 (s, 3 H), 4.32 (d, J = 21.8 Hz, 1 H), 4.49 (d, J = 21.6 Hz, 1 H), 4.68–4.77 (m, 1 H), 4.72 (dd, J = 5.2, 21.8 Hz, 1 H), 5.15 (d, J = 22.2 Hz, 1 H), 5.82 (d, J = 4.1 Hz, 1 H), 6.75 (t, J = 11.4 Hz, 4 H), 6.88 (t, J = 11.5 Hz, 8 H), 7.11–7.16 (m, 5 H), 7.20–7.25 (m, 8 H), 7.55–7.63 (m, 3 H), 7.64–7.69 (m, 3 H), 7.92–7.94 (m, 2 H), 9.03 (s, 1 H). ^{13}C NMR (100 MHz; [D$_6$]DMSO, 120 °C, ppm): δ = 18.1, 28.4, 55.8, 60.8, 66.1, 70.5, 99.9, 120.4, 124.1, 124.2, 124.2, 124.4, 127.3, 127.6, 127.7, 128.2, 128.3, 129.0, 129.3, 129.4, 132.6, 133.6, 135.0, 135.2, 140.5, 163.3, 170.1. MS: m/z = 384.1968. $C_{26}H_{26}NO_2$ (cation) requires 384.1964.

(–)-*N*-[(4*S*,5*S*)-2,2-Dimethyl-4-(4-nitrophenyl)-1,3-dioxan-5-yl]-5*H*-dibenzo[*c*,*e*]azepinium Tetraphenylborate (14): Prepared according to the general procedure from (+)-(4*S*,5*S*)-5-amino-2,2-dimethyl-4-(4-nitrophenyl)-1,3-dioxane (**26**) (0.30 g, 1.19 mmol). The product was isolated as yellow plates (0.57 g, 64%); m.p. 209–210 °C (dec.). $[\alpha]_D^{20}$ –68.0 (c = 1.17, acetone). $C_{50}H_{45}BN_2O_4$ (748.35): calcd. C 80.21, H 6.06, N 3.74; found C 80.43, H 6.09, N 3.72. IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 3055, 2998, 1633, 1600, 1579, 1523, 1480, 1451, 1385, 1349, 1204, 1106, 969, 852. ^1H NMR (400 MHz; [D$_6$]DMSO, 100 °C, ppm): δ = 1.67 (s, 3 H), 1.71 (s, 3 H), 4.35 (d, J = 13.2 Hz, 1 H), 4.49 (d, J = 12.8 Hz, 1 H), 4.66 (d, J = 13.2 Hz, 1 H), 4.82 (s, 1 H), 4.99 (d, J = 12.8 Hz, 1 H), 5.91 (s, 1 H), 6.71 (t, J = 6.8 Hz, 4 H), 6.85 (t, J = 6.8 Hz, 8 H), 7.17 (m, 8 H), 7.44 (m, 4 H), 7.56–7.75 (m, 4 H), 7.84 (d, J = 8.4 Hz, 2 H), 7.88 (m, 2 H), 9.19 (s, 1 H). ^{13}C NMR (100 MHz; [D$_6$]DMSO, 100 °C, ppm): δ = 19.7, 30.1, 58.0, 62.7, 67.1, 71.6, 101.8, 122.2, 124.2, 125.9, 126.9, 127.5, 129.5, 129.9, 130.0, 130.8, 130.9, 134.1, 135.8, 136.6, 137.1, 137.4, 142.1, 144.0, 164.6, 172.0. MS: m/z = 429.1815. $C_{26}H_{25}N_2O_4$ (cation) requires 429.1814.

(–)-*N*-{(4*S*,5*S*)-2,2-Dimethyl-4-[4-(methylsulfonyl)phenyl]-1,3-dioxan-5-yl}-5*H*-dibenzo[*c*,*e*]azepinium Tetraphenylborate (15): Prepared according to the general procedure from (+)-(4*S*,5*S*)-5-amino-2,2-dimethyl-4-[4-(methylsulfonyl)phenyl]-1,3-dioxane (**24**) (0.30 g, 1.05 mmol). The product was isolated as yellow plates (0.54 g, 66%); m.p. 162–165 °C (dec.). $[\alpha]_D^{20}$ = –50.3 (c = 1.09, acetone). $C_{51}H_{48}BNO_4S{\cdot}2.0H_2O$ (anhydrate: 781.81): calcd. C 74.87, H 6.29, N 1.71; found C 75.14, H 5.89, N 1.75. IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 3052, 2997, 1636, 1599, 1551, 1479, 1454, 1385, 1304, 1205, 1148, 1090, 947.6, 844. ^1H NMR (400 MHz; [D$_6$]DMSO, 100 °C, ppm): δ = 1.79 (s, 3 H), 2.01 (s, 3 H), 3.01 (s, 3 H), 4.40 (d, J = 13.6 Hz, 1 H), 4.56 (d, J = 13.2 Hz, 1 H), 4.66 (dd, J = 13.6 Hz, 1 H), 4.88 (br. s, 1 H), 5.15 (d, J = 12.8 Hz, 1 H), 5.91 (d, J = 2.8 Hz, 1 H), 6.79 (t, J = 6.8 Hz, 4 H), 6.92 (t, J = 7.6 Hz, 8 H), 7.17 (m, 8 H), 7.52–7.58 (m, 4 H), 7.65–7.74 (m, 4 H), 7.91–7.97 (m, 2 H), 9.16 (s, 1 H). ^{13}C NMR (100 MHz; [D$_6$]DMSO, 100 °C, ppm): δ = 19.3, 29.7, 44.2, 57.0, 62.1, 66.8, 71.4, 101.3, 121.8, 125.5, 126.4, 126.8, 127.4, 128.6, 129.0, 129.5, 129.6, 130.4, 130.6, 130.8, 135.1, 136.2, 136.7, 137.1, 141.5, 141.7, 142.0, 164.1, 171.6. MS: m/z = 462.1739. $C_{27}H_{28}NO_4S$ (cation) requires 462.1739.

(+)-*N*-[(4*S*,5*S*)-2,2-Dimethyl-4-(4-methoxyphenyl)-1,3-dioxan-5-yl]-5*H*-dibenzo[*c*,*e*]azepinium Tetraphenylborate (16): Prepared according to the general procedure from (–)-(4*R*,5*R*)-5-amino-4-(4-methoxyphenyl)-2,2-dimethyl-1,3-dioxane (**33**) (0.13 g, 0.48 mmol). The product was isolated as yellow plates (0.23 g, 64%); m.p. 207–209 °C (dec.). $[\alpha]_D^{20}$ = +37.8 (c = 1.09, acetone). $C_{51}H_{48}BNO_3{\cdot}3.5H_2O$ (anhydrate: 733.74): calcd. C 76.84, H 6.52, N 1.76; found C 76.58, H 6.02, N 1.84. IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 3055, 2998, 1633, 1613, 1579, 1557, 1514, 1480, 1384, 1253, 1202, 1031, 966. ^1H NMR (400 MHz; [D$_6$]DMSO, 100 °C, ppm): δ = 1.66 (s, 3 H), 1.68 (s, 3 H), 3.60 (s, 3 H), 4.28 (dd, J = 14.4, 2.0 Hz, 1 H), 4.43 (d, 1 H, 14.0 Hz, 1 H), 4.65 (m, 2 H), 5.02 (d, J = 14.0 Hz, 1 H), 5.70 (d, J = 2.8 Hz, 1 H), 6.63 (d, J = 8.6 Hz, 2 H), 6.72 (t, J = 7.4 Hz, 4 H), 6.86 (t, J = 7.4 Hz, 8 H), 7.08 (d, J = 8.6 Hz, 2 H), 7.18 (m, 8 H), 7.52 (m, 3 H), 7.65 (m, 3 H), 7.91 (m, 2 H), 9.00 (s, 1 H). ^{13}C NMR (100 MHz; [D$_6$]DMSO, 100 °C, ppm): δ = 18.3, 28.8, 54.8, 56.1, 60.9, 66.42, 70.5, 100.0, 113.8, 120.8, 124.6, 125.6, 125.9, 127.5, 128.0, 128.5, 128.5, 129.4, 129.6, 129.7, 132.9, 133.9, 135.2, 135.5, 136.2, 140.7, 158.7, 163.3, 170.2. MS: m/z = 414.2063. $C_{27}H_{28}NO_3$ (cation) requires 414.2069.

General Procedure for the Catalytic Asymmetric Epoxidation of Alkenes Mediated by Iminium Salts Using Oxone: Oxone (2 equiv. with respect to alkene) was added with stirring to an ice-cooled solution of sodium carbonate (4 equiv.) in water (12 mL per 1.50 g of sodium carbonate), and the resulting foaming solution was stirred for 5–10 minutes, until most of the initial effervescence subsided. A solution of the iminium salt (10 mol-% with respect to alkene) in acetonitrile (6 mL per 1.50 g of sodium carbonate used) was added, followed by a solution of the alkene substrate in acetonitrile (6 mL per 1.50 g of sodium carbonate used). The suspension was stirred with ice bath cooling until the substrate was completely consumed according to TLC. The reaction mixture was then diluted with ice-cooled diethyl ether (20 mL per 100 mg substrate) and the same volume of water added immediately. The aqueous phase was washed four times with diethyl ether and the combined organic solutions washed with brine and dried ($MgSO_4$). Filtration and removal of the solvents gave a yellow or light brown residue, which was purified by column chromatography, typically using ethyl acetate/light petroleum (1:99) to provide the pure epoxide.

General Procedure for the Formation of Racemic Epoxides: The alkene was dissolved in CH_2Cl_2 (10 mL/g) and the solution cooled using an ice bath. A solution of *m*CPBA (2 equiv.) in CH_2Cl_2 (10 mL/g, pre-dried with $MgSO_4$) was added. The reaction was allowed to attain ambient temperature and stirred until complete consumption of the substrate was observed by TLC. Saturated aqueous $NaHCO_3$ (10 mL/g) was added and the layers separated. The organic layer was washed with saturated aqueous NaOH (1.0 M, 10 mL/g) and dried ($MgSO_4$). The solvents were removed under reduced pressure, and the residue purified by column chromatography, typically eluting with ethyl acetate/light petroleum (1:99), to give pure epoxide.

α-Methylstyrene Oxide:[20] Colourless oil. IR (neat, cm^{-1}): $\tilde{\nu}_{max}$ = 3034, 2958, 2929, 2872, 1604, 1496, 1447, 1381, 1343, 1061, 1027, 860, 759, 699. ^1H NMR (250 MHz, $CDCl_3$, ppm): δ = 0.86 (d, J = 6.6 Hz, 3 H), 2.79 (dd, J = 0.8, 5.4 Hz, 1 H), 2.96 (d, J = 5.4 Hz, 1 H), 7.24–7.38 (m, 5 H). ^{13}C NMR (62.5 MHz, $CDCl_3$, ppm): δ = 21.7, 56.7, 56.9, 125.2, 127.4, 128.3, 129.0.

***trans*-α-Methylstilbene Oxide:**[21] Colourless oil. IR (neat, cm^{-1}): $\tilde{\nu}_{max}$ = 3061, 1602, 1495, 1449, 1381, 1279, 1157, 1118, 1065, 1027, 980. ^1H NMR (400 MHz, $CDCl_3$, ppm): δ = 1.46 (s, 3 H), 3.96 (s, 1 H), 7.30–7.46 (m, 10 H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 17.1, 63.5, 67.5, 125.6, 126.9, 127.7, 127.9, 128.6, 129.2, 136.4, 142.8.

Triphenylethylene Oxide:[22] Colourless oil which slowly solidified, m.p. 66–67 °C (ref. m.p. 75 °C). IR (neat, cm^{-1}): $\tilde{\nu}_{max}$ = 3062, 3030, 2957, 2925, 2856, 1605, 1596, 1499, 1471, 1448, 1262, 1221, 741, 698, 621. ^1H NMR (250 MHz, $CDCl_3$, ppm): δ = 4.40 (m, 1 H), 7.10–7.47 (m, 15 H). ^{13}C NMR (62.5 MHz, $CDCl_3$, ppm): δ = 68.0, 68.3, 126.3, 126.8, 127.5, 127.6, 127.7, 127.8 128.0, 128.2, 128.6, 135.4, 135.9, 141.1.

1-Phenylcyclohexene Oxide:[23] Colourless oil. IR (neat, cm^{-1}): $\tilde{\nu}_{max}$ = 3084, 1602, 1495, 1446, 1359, 1249, 1173, 1132, 1079, 1030, 993, 974. ^1H NMR (250 MHz, $CDCl_3$, ppm): δ = 1.22–1.35 (m, 1 H), 1.53–1.64 (3 H m), 1.99–2.06 (m, 2 H) 2.16–2.18 (m, 1 H), 2.26–2.32 (m, 1 H), 3.10 (t, J = 2.0 Hz, 1 H), 7.28–7.44 (m, 5 H). ^{13}C NMR (62.5 MHz, $CDCl_3$, ppm): δ = 19.8, 20.1, 24.7, 28.2, 60.1, 61.8, 125.3, 127.1, 128.2, 142.8.

1-Phenyl-3,4-dihydronaphthalene Oxide:[23] Pale yellow solid; m.p. 104–106 °C (ref.[24] m.p. 94–97 °C). IR (nujol, cm^{-1}): $\tilde{\nu}_{max}$ = 1602, 1486, 1307, 1155, 1074, 1042, 953. ^1H NMR (250 MHz, $CDCl_3$, ppm): δ = 2.10 (td, J = 5.8, 13.7 Hz, 1 H), 2.49–2.60 (m, 1 H), 2.77 (dd, J = 5.6, 15.5 Hz, 1 H), 2.98–3.06 (m, 1 H), 3.71 (d, J = 3.1 Hz, 1 H), 7.11–7.31 (m, 4 H), 7.45–7.61 (m, 5 H). ^{13}C NMR (62.5 MHz, $CDCl_3$, ppm): δ = 22.1, 25.4, 60.9, 63.0, 126.0, 127.7, 127.9, 128.1, 128.2, 128.6, 129.8, 135.0, 137.5, 138.8.

***trans*-Stilbene Oxide:**[25] Colourless solid; m.p. 66–67 °C (ref.[26] m.p. 61–63 °C). IR (neat, cm^{-1}): $\tilde{\nu}_{max}$ = 1601, 1492, 1284, 1176, 1157, 1094, 1072, 1025. ^1H NMR (400 MHz, $CDCl_3$, ppm): δ = 3.84 (s, 2 H), 7.28–7.37 (10 H m). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 63.3, 126.0, 128.6, 129.3, 137.6.

1,2-Dihydronaphthalene Oxide: Colourless oil. IR (neat, cm^{-1}): $\tilde{\nu}_{max}$ = 3059, 3028, 2930, 2850, 1602, 1493, 1316, 1129, 1088, 1030, 964. ^1H NMR (400 MHz, $CDCl_3$, ppm): δ = 1.67 (m, 1 H), 2.33 (m, 1 H), 2.45 (dd, J = 15.6, 5.6 Hz, 1 H), 2.67 (m, 1 H), 3.65 (t, J = 4.0 Hz, 1 H), 3.78 (d, J = 4.4 Hz, 1 H), 7.01 (d, J = 7.2 Hz, 1 H), 7.17 (m, 2 H), 7.33 (d, J = 7.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 22.2, 24.8, 55.2, 55.5, 126.5, 128.8, 128.8, 129.9, 132.9, 137.1.

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