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Aziridin-2-yl methanols as organocatalysts in Diels–Alder reactions and Friedel–Crafts alkylations of *N*-methyl-pyrrole and *N*-methyl-indole

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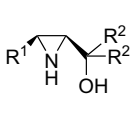
Abstract—A series of enantiomerically pure aziridin-2-yl methanols have been synthesized from aziridine-2-carboxylic esters and have been tested as organocatalysts in Diels–Alder reactions and Friedel–Crafts alkylations of *N*-methyl-pyrrole and *N*-methyl-indole using α,β-unsaturated aldehydes. Moderate to good ee's have been obtained. The coupling of *N*-methyl-pyrrole with crotonaldehyde and cinnamaldehyde using (2*S*,3*S*)-3-methylazirin-2-yl(diphenyl)methanol TFA salt as the catalyst gave the best results (ee 75%).

1. Introduction

Functionalized aziridines are highly valuable three-membered ring systems in modern synthetic chemistry, because of their widely recognized versatility as synthetic building blocks and their use in functional group transformations.[1] In synthetic transformations, their utility is mostly associated with stereo- and regio-controlled ring-opening reactions of the highly strained three-membered ring.[2] Moreover, chiral aziridines can serve as a source of chirality in stereocontrolled reactions and have been employed both as ligands and chiral auxiliaries in asymmetric synthesis.[2d,3] Aziridine-2-carbinols of type **1** have been used in the preparation of oxazaborolidines, which are mediating reagents in the enantioselective reduction of ketones.[4] It has been demonstrated that the *N*-trityl derivative[5] and a number of N-alkylated derivatives[6] of **1** are effective catalysts in the enantioselective addition of diethylzinc to aromatic and aliphatic aldehydes. *N*-Trityl-azirin-2-yl-(diphenyl)methanol **5a** turned out to be superior in this respect.[5,7] Aziridine alcohols have also been screened as chirality transfer reagents in the enantioselective addition of dialkylzincs to *N*-(diphenylphosphinoyl) imines.[8] Very recently, the acetate salt of **1** was tested in an intramolecular formal aza [3+3] cycloaddition reaction as an organocatalyst.[9] Although the aziridine salt was efficient in promoting the reaction, a very poor ee was obtained.



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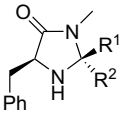

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In recent years there has been an increasing awareness that small organic molecules, in addition to metal complexes and biocatalysts, can serve as highly selective and efficient catalysts.[10] In particular, the use of chiral amines as organocatalysts has received considerable attention in enantioselective synthesis. Typical reactive intermediates are iminium ions formed by the reversible reaction of the amine catalyst with a carbonyl substrate. A pioneering example of iminium catalysis is MacMillan's enantioselective Diels–Alder reactions of α,β-unsaturated aldehydes[11] or ketones[12] using the chiral imidazolidinone catalyst of type **2**. This type of catalysis has been further extended to other reactions of α,β-unsaturated aldehydes, such as

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[3+2] cycloaddition with nitrones,[13] Friedel–Crafts alkylation with pyrroles,[14] indoles[15] and benzenes,[16] and the Mukaiyama–Michael reaction[17] achieving high yields and enantioselectivities.

The efficiency of chiral imidazolidinone as chiral catalysts, prompted us to investigate the possibility of using the three-membered ring aziridin-2-yl methanols **1** as organocatalysts. An intriguing additional question is whether the aziridinium ions, which will be the true chirality transferring species, will be sufficiently stable under these catalytic processes.

2. Results and discussion

2.1. Preparation of aziridine-2-carbinols 1

We prepared a series of compounds **1** with the aim of exploring their use as organocatalysts. Various approaches[18] for the preparation of optically active aziridine-2-carboxylic esters **3a** and **3b**, that are the precursors of the aziridine-2-carbinols **1**, have been described. We selected *N*-tritylmethylesters of L-serine and L-threonine as starting materials from which the compounds **3a** and **3b** could be prepared,[4,19] by a convenient multigram 'one-pot procedure' using methansulfonyl chloride and triethylamine. Aziridine esters **3a** and **3b** were next converted into the corresponding aziridine carbinols **1a–f** by reaction with a Grignard reagent[19] followed by detritylation with sulfuric acid in MeOH/THF[19,20] (Scheme 1). Compounds **4a** and **4b** were obtained by methylation[20] of **5a** and **5b** with methyl iodide in the presence of sodium hydride and subsequent detritylation.

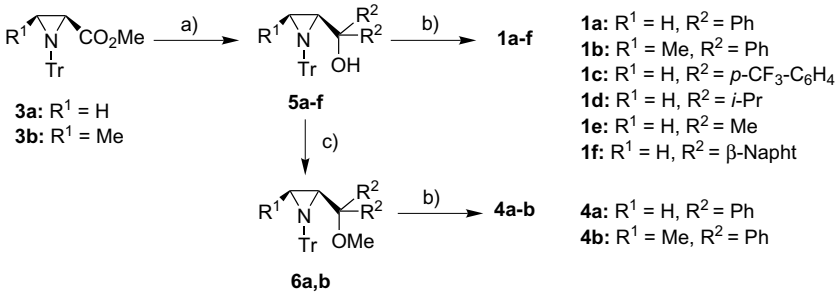
2.2. Enantioselective Diels–Alder reaction

The efficiency of the aziridinyl carbinol catalysts was first tested in the enantioselective catalytic Diels–Alder reaction of cyclopentadiene with (*E*)-cinnamaldehyde **7a** and (*E*)-crotonaldehyde **7b** (Scheme 2).

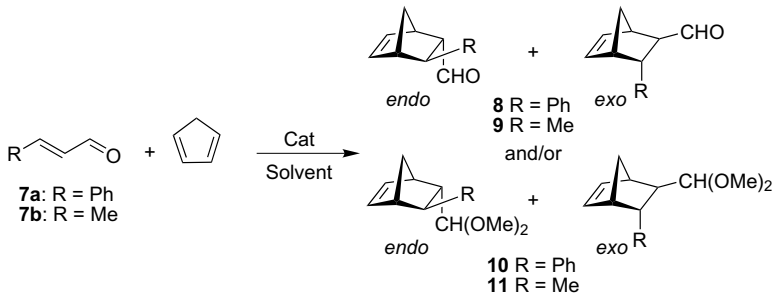
When the cycloaddition reaction was performed in MeOH/H_2O 95:5 (by volume) as the reaction medium, the final products were mixtures of aldehydes **8** (or **9**) and acetals **10** (or **11**). The final mixture was completely acetalized for the determination of the enantiomeric excess (ee) by ^1H NMR in the presence of Pirkle's alcohol. When the solvent was H_2O, the final products were the aldehydes **8** (or **9**) that were also transformed into the corresponding acetals **10** (or **11**) for the ee determination.

The aziridine carbinols **1a–f** and **4a** were used either as preformed HCl salts in 5 mol %, or as in situ prepared $HClO_4$ salts in 10 mol %. It is well known that the highly strained three-membered ring can undergo a nucleophilic ring-opening reaction when protonated. Surprisingly, the aziridine salts (HCl and $HClO_4$) were remarkably stable. The **1**-HCl salts were generally used in MeOH/H_2O while the **1**-$HClO_4$ salts were employed in H_2O (Table 1).

When using the preformed HCl salt of **1a** in the reaction with (*E*)-cinnamaldehyde **7a**, the Diels–Alder adducts were obtained in rather low yield (with the *exo*-isomer predominanting) and in modest enantiomeric excess (entry 1). A somewhat better result was obtained at lower temperature, but an attempted reaction at 0 °C did not produce any adduct. An increase in the amount of catalyst to 20% decreased both the yield and the ee. The use of a different



Scheme 1. Reagents and conditions: (a) R^2MgBr, THF, 3 h, reflux; (b) H_2SO_4, THF, MeOH, 18 h, rt; (c) NaH, MeI, DMF, 48 h, rt.



Scheme 2. Organocatalyzed Diels–Alder reaction.

Table 1. Organocatalyzed Diels–Alder reaction

Entry	Aldehyde	Catalyst	Time (h)	*T* (°C)	Yield[a] (%)	*endo:exo*[b]	*exo* ee[c] (%)	*endo* ee[c] (%)
1	**7a**	**1a**-HCl[d]	48	18	33	1.8:1	36	37
2	**7a**	**1a**-$HClO_4$[e]	48	18	74	1.7:1	66	57
3	**7a**	**1b**-HCl[d]	48	18	16	1.4:1	43	38
4	**7a**	**1b**-HCl[d]	48	30	35	1.4:1	51	48
5	**7a**	**1c**-HCl[d]	48	18	35	1.5:1	28	24
6	**7b**	**1a**-HCl[d]	24	18	85	1:1	24	22
7	**7b**	**1a**-$HClO_4$[e]	24	18	88	1:1.4	10	11
8	**7b**	**1b**-HCl[d]	24	18	83	1:1.6	37	25
9	**7b**	**1b**-HCl[d]	18	30	88	1:1	45	35

[a] Calculated after chromatography.
[b] Determined by ^{1}H NMR on the crude reaction mixture.
[c] Determined by ^{1}H NMR on the dimethylacetal in the presence of Pirkle's alcohol.
[d] As a preformed salt, using MeOH/H_2O 95:5 (by volume) as the reaction medium.
[e] Prepared in situ, using H_2O as solvent.

solvent (CH_2Cl_2/*i*-PrOH 85:15) in the absence of any water, had only a marginal effect.

Better results with (*E*)-cinnamaldehyde **7a** were obtained in terms of the yield of adducts and ee using the $HClO_4$ salt of **1a**, prepared in situ (entry 2). Under these conditions, the highest level of enantiofacial discrimination was achieved, with 66% ee for the *exo* adduct and 57% for the *endo* adduct.

Next, our attention was focused on the influence of a structural variation of the catalyst on the outcome of the asymmetric induction; thus the series of catalysts **1b–f** and **4a** was tested as a preformed HCl salt with (*E*)-cinnamaldehyde **7a**. The presence of a methyl group at the 3-position of the aziridine ring **1b** led to a very low yield of adduct, but to a slightly better ee (compare entries 1 and 3). Both the yield and the ee values were improved by performing the reaction at higher temperature (30 °C) (entry 4). The presence of an electron withdrawing substituent at the *para* position of the phenyl ring **1c** (entry 5), did not lead to better results when compared with **1a**. Both the yields and the enantioselectivities realized with catalysts **1d** and **1e** with R^2 = alkyls, with catalyst **1f** having the hindered β-naphthyl group and with catalyst **4a**, in which the hydroxy group of **1a** was replaced with a methoxy group, were very low. In this case, the use of HCl or $HClO_4$ as the acid component did not make much difference.

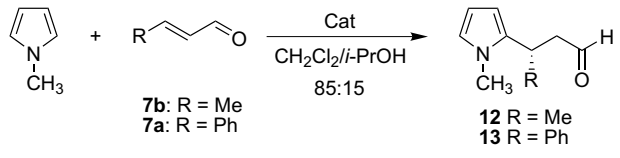
It is important to note that a reaction performed with (*E*)-cinnamaldehyde **7a** in the absence of the aziridine carbinols, but in the presence of 10 mol % of $HClO_4$ in H_2O or of 5 mol % of HCl in MeOH/H_2O 95:5 for 48 h afforded aldehydes **8** or acetals **10** in about 10% yield. This background reaction, probably due to the long reaction time, might contribute, with a detrimental effect, to the generally low ee's.

Variation in the steric effect of the olefin substrate was also examined. The reaction of (*E*)-crotonaldehyde **7b** and cyclopentadiene afforded the corresponding cycloadducts in better yields and in a shorter reaction time, when compared to (*E*)-cinnamaldehyde but with lower ee's (entries 6 and 7). The reaction proceeds also at 0 °C affording the cycloadducts in comparable yields after 72 h but with practically no asymmetric induction. Aziridine **1b** furnished the better ee (entry 8) that can be improved upon by conducting the reaction at 30 °C (entry 9).

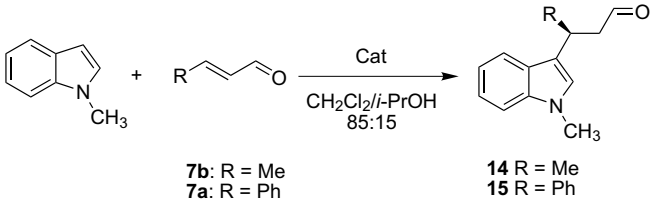
2.3. Enantioselective Friedel–Crafts alkylation to *N*-methyl-pyrrole and *N*-methyl-indole

The efficiency of the aziridine carbinol catalysts was then tested in the enantioselective catalytic Friedel–Crafts alkylation reaction of *N*-methyl-pyrrole and *N*-methyl-indole with (*E*)-crotonaldehyde **7b** and (*E*)-cinnamaldehyde **7a** in CH_2Cl_2/*i*-PrOH 85:15 (by volume) as the solvent (Schemes 3 and 4). Aziridine carbinols **1** were used as preformed TFA (trifluoroacetic acid) salts in 10 mol %. Only decomposition was observed when in situ prepared catalysts were used.

As shown in Table 2, the alkylation of *N*-methyl-pyrrole with (*E*)-crotonaldehyde **7b** in the presence of aziridine carbinol catalyst **1a** (entry 1) afforded the desired conjugate addition adduct **12** with moderate enantioselectivity after 18 h at 18 °C. The presence of a methyl group at the



Scheme 3. Organocatalyzed Friedel–Crafts alkylation of *N*-methyl pyrrole.



Scheme 4. Organocatalyzed Friedel–Crafts alkylation of *N*-methyl indole.

Table 2. Organocatalyzed Friedel–Crafts alkylation of *N*-methyl pyrrole with (*E*)-crotonaldehyde **7b**

Entry	Catalyst	*T* (°C)	Time (h)	Yield[a] (%)	ee[b] (%)	Abs. Config.[c]
1	**1a**-TFA	18	18	50	30	(*S*)
2	**1b**-TFA	18	18	60	69	(*S*)
3	**1a**-TFA	−20	60	42	26	(*S*)
4	**1a**-TFA	40	18	58	32	(*S*)
5	**1b**-TFA	40	18	51	75	(*S*)
6	**1b**-TFA	70[d]	1	60	60	(*S*)
7	**1b**-TFA	MW[e]	0.25	60	36	(*S*)

[a] The reactions were performed with an excess of *N*-methyl pyrrole in order to avoid the bis-alkylation of the heteroaromatic ring; yield calculated after chromatography.
[b] The ee was determined by chiral GLC (see Section 4).
[c] The absolute configuration was determined by chemical correlation.[14]
[d] 1,2-Dichloroethane as the solvent.
[e] Under microwave irradiation.

3-position of the aziridine ring **1b** gave a great increase in the ee (entry 2), whereas the presence of an electron withdrawing substituent at the *para*-position of the phenyl ring, as in **1c** and the replacement of the hydroxy group by a methoxy **4a** or **4b** had a detrimental effect on the asymmetric induction. With these preliminary results in hand we tried to optimize the reaction conditions by varying the amount of catalysts and the temperature. The use of 5 or 20 mol % of catalyst led to the desired product with a different rate but with no effect on the ee. Variation of the temperature only slightly affected the ee when catalyst **1a**-TFA was used (compare entries 1, 3, and 4). Conducting the reaction with **1b**-TFA at a higher temperature had a beneficial effect, with an ee of 75% for compound **12** (entry 5). A further increase of temperature to 70 °C using 1,2-dichloroethane instead of dichloromethane as the solvent (entry 6) as well as the application of microwave irradiation (entry 7) led to a lowering of the asymmetric induction.

The scope of the organocatalytic Friedel–Crafts alkylation was extended to the (*E*)-cinnamaldehyde **7a**. The conditions for the reaction with *N*-methyl-pyrrole are listed in Table 3. The ee values were in all cases higher compared to the corresponding reaction with the (*E*)-crotonaldehyde. Also in this case, catalyst **1b** with a methyl group on the aziridine ring gave the best ee value, viz. 75% (Table 3, entry 3). Variation of the temperature did not improve the performance of the catalyst.

Table 3. Organocatalyzed Friedel–Crafts alkylation of *N*-methyl pyrrole with (*E*)-cinnamaldehyde **7a**

Entry	Catalyst	Time (h)	*T* (°C)	Yield[a] (%)	ee[b] (%)	Abs. Config.[c]
1	**1a**-TFA	18	18	60	48	(*S*)
2	**1a**-TFA	18	40	62	50	(*S*)
3	**1b**-TFA	18	18	58	75	(*S*)
4	**1b**-TFA	18	40	55	74	(*S*)

[a] The reactions were performed with an excess of *N*-methyl pyrrole in order to avoid the bis-alkylation of the heteroaromatic ring; yield calculated after chromatography.
[b] The ee was determined by chiral GLC (see Section 4).
[c] The absolute configuration was determined by chemical correlation.[14]

Aziridine carbinol catalysts **1** were next employed in the Friedel–Crafts alkylation reaction of *N*-methyl-indole with α,β-unsaturated aldehydes. It has since long been established[21] that the pyrrole π-system is significantly more active toward electrophilic substitution than indole, despite the structural similarities.

The reactions were performed in CH_2Cl_2/*i*-PrOH 85:15 as the solvent and 10 mol % of catalyst as preformed TFA salt was used. As shown in Table 4, the reaction was successful with both aziridine carbinol catalysts **1a** and **1b** giving the desired conjugate addition products **14** and **15** with moderate enantioselectivity. In an attempt to improve the asymmetric induction, the temperature was varied: lowering of the temperature led to an improvement of the ee, with an increase from 20% to 58% at −10 °C (entries 3–5) when (*E*)-crotonaldehyde **7b** was employed and from 40% to 50% at −10 °C for (*E*)-cinnamaldehyde **7a** as the reactant (entries 7 and 8). The results show that asymmetric catalysis is less effective for indole than for pyrrole, as expected.

Table 4. Organocatalyzed Friedel–Crafts alkylation of *N*-methyl indole with (*E*)-crotonaldehyde **7b** or (*E*)-cinnamaldehyde **7a**

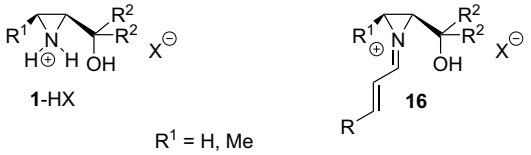
Entry	Product	*T* (°C)	Time (h)	Catalyst	Yield[a] (%)	ee[b] (%)	Abs. Config.[c]
1	**14**	40	18	**1a**-TFA	66	6	—
2	**14**	0	18	**1a**-TFA	70	0	—
3	**14**	18	18	**1b**-TFA	78	20	(*S*)
4	**14**	0	30	**1b**-TFA	85	40	(*S*)
5	**14**	−10	48	**1b**-TFA	30	58	(*S*)
6	**15**	18	48	**1a**-TFA	11	0	—
7	**15**	18	48	**1b**-TFA	42	40	(*S*)
8	**15**	−10	72	**1b**-TFA	40	50	(*S*)

[a] Calculated after chromatography.
[b] Determined by HPLC analysis (Chiracel AD-H) of the alcohol obtained by $NaBH_4$ reduction of the aldehyde.
[c] The absolute configuration was determined by chemical correlation or by comparison of the HPLC retention times with those reported in the literature.

3. Conclusion

A series of aziridine carbinol catalysts **1** was prepared with the aim of investigating their capacity to asymmetrically catalyze Diels–Alder reactions and Friedel–Crafts alkylations of *N*-methyl-pyrrole and *N*-methyl-indole using α,β-unsaturated aldehydes. The Diels–Alder reaction took place with moderate ee's ranging from 10% to 66% with catalyst **1a**-$HClO_4$ giving the best results. The asymmetric alkylation of *N*-methyl-pyrrole with (*E*)-crotonaldehyde **7b** as well as with (*E*)-cinnamaldehyde **7a**, occurred with ee values ranging from 26 to 75% with catalyst **1b**-TFA. The alkylation of *N*-methyl-indole with crotonaldehyde or cinnamaldehyde took place with moderate enantioselectivities (ee's ranging from 6% to 58%). A Friedel–Crafts alkylation performed with aziridinium TFA (**1b**-TFA) salts, derived from threonine, gave the best results. All

the prepared aziridinium salts **1**-HX are remarkably stable. The actual intermediates in all these reactions must be the iminium salt **16** derived from aziridine carbinol catalysts. It is surprising that these species are sufficiently stable to serve as reasonably effective chirality transferring intermediates in asymmetric carbon–carbon bond forming reactions.



4. Experimental

4.1. General methods

Unless stated otherwise, all reagents were obtained from commercial suppliers and used without further purification. Column chromatography was carried out with 70–230 mesh silica gel. Light petroleum ether refers to the fraction with a boiling range of 40–60 °C. Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, in $CDCl_3$ as solvent. Chemical shifts are reported on the δ scale and measured in parts per million relative to residual $CHCl_3$ ($\delta = 7.26$ ppm) for ^{1}H NMR and to the central line of $CDCl_3$ ($\delta = 77.0$ ppm) for ^{13}C NMR spectra. J values are given in Hertz. ^{13}C NMR spectra assignments were based on the results of DEPT experiments. The manufacturer's software was used for DEPT, gradient-enhanced COSY, as well as for the inversed-detected gradient selected heteronuclear correlations gHMBC and gHSQC data analysis. All the ESIMS spectra were performed using MeOH as the solvent. $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. Elemental analyses were performed using Flash EA1112 Automatic Elemental Analyzer CE instruments. The originality of all compounds was checked by a CAS on-line structure search.

Compounds **3a** and **3b**,[19] **5a** and **5b**[19] and **1a** and **1b**[19,20] were prepared following literature procedure.

4.2. (2*S*)-1-Tritylaziridin-2-yl bis[4-(trifluoromethyl)-phenyl]methanol 5c

To a stirred suspension of magnesium turnings (0.81 g, 33.3 mmol) in THF (5 mL) was gradually added 1-bromo-4-(trifluoromethyl)benzene (5.0 g, 22.2 mmol) in THF (20 mL). After heating the Grignard reagent for 1.5 h, compound **3a** (2.5 g, 7.3 mmol) in THF (25 mL) was added dropwise over a period of 20 min. The reaction was monitored with TLC and quenched after 1.5 h with saturated aqueous $(NH_4)_2SO_4$. The organic layer was extracted with diethyl ether (3×50 mL), dried over Na_2SO_4, and concentrated. The crude product was purified by chromatography (hexane/Et_2O 10:1) affording 3.78 g (6.3 mmol, 86% yield) of the title compound as a white solid. Mp 158–159 °C; $[\alpha]_D = -76.1$ (c 0.72, $CHCl_3$); MS (ESI) m/z: 626 $(M+Na)^+$; 604 $(M+1)^+$; Anal. Calcd for $C_{36}H_{27}F_6NO$: C, 71.63; H, 4.51; N, 2.32. Found; C, 71.69; H, 4.60, N, 2.29; IR (CCl_4): 1070, 1133, 1169, 1325 and 3376 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 1.31 (d, $J = 6.3$ Hz, 1H, H_a–CH_2), 2.05 (d, $J = 3.2$ Hz, 1H, H_b–CH_2), 2.44 (dd, $J = 6.3$, 3.2 Hz, 1H, CH), 4.57 (s, 1H), 7.14–7.20 (m, 9H, ArCH), 7.27–7.31 (m, 6H, ArCH), 7.41–7.57 (3 d, $J = 8.1$ Hz, 8H, $2C_6H_4$); ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 23.9 (CH_2), 40.4 (CH), 73.8, 74.0 (C), 123.99 (q, ^1J(CF) = 272 Hz, CF_3), 124.06 (q, ^1J(CF) = 272 Hz, CF_3), 125.0 (q, ^3J(CF) = 3.8 Hz), 125.2 (q, ^3J(CF) = 3.8 Hz), 126.1, 126.5 127.05, 127.5, 129.2 (ArCH), 129.3 (q, ^2J(CF) = 32.2 Hz, ArC), 129.4 (q, ^2J(CF) = 32.7 Hz, ArC), 143.2, 148.4, 150.4 (ArC); ^{19}F NMR (376 MHz, $CDCl_3$) δ: −63.03, −63.05 (CF_3). Proton and carbon assignments were made by gCOSY and gHSQC.

4.3. ((*S*)-Aziridin-2-yl)bis(4-[trifluoromethyl]phenyl)methanol 1c

To a solution of **5c** (3.7 g, 6.1 mmol) in a 1:1 mixture of THF and MeOH (10 mL) cooled at 0 °C, H_2SO_4 6 M (22 mL), was added dropwise. The resulting mixture was stirred at room temperature overnight. The white precipitate was removed by Et_2O extraction. NaOH 20% was slowly added to the aqueous layer (pH = 12) until precipitation of a white solid. The precipitate was then extracted with $CHCl_3$. The organic layer was dried over Na_2SO_4 and concentrated to dryness affording 1.55 g (4.3 mmol, 70% yield) of the title compound as a white solid. Mp 151–153 °C; $[\alpha]_D = -14.7$ (c 1.0, $CHCl_3$); MS (ESI) m/z: 384 $(M+Na)^+$; 362 $(M+1)^+$; Anal. Calcd for $C_{17}H_{13}F_6NO$: C, 56.52; H, 3.63; N, 3.88. Found; C, 56.58; H, 3.69, N, 3.82; IR (CCl_4): 1068, 1130, 1160, 1321, 3341, and 3414 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 0.81 (br s, 1H), 1.73 (d, $J = 3.5$ Hz, 1H, H_a–CH_2), 1.96 (d, $J = 6.0$ Hz, 1H, H_b–CH_2), 2.99 (m, 1H, CH), 3.99 (br s, 1H), 7.54–7.58 (d, $J = 8.2$ Hz, 4H, ArCH), 7.59–7.62 (d, $J = 8.2$ Hz, 4H, ArCH); ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 21.9 (CH_2), 36.3 (CH), 73.8 (C), 124.04 (q, ^1J(CF) = 272 Hz, CF_3), 124.06 (q, ^1J(CF) = 272 Hz, CF_3), 125.26 (q, ^3J(CF) = 3.9 Hz), 125.34 (q, ^3J(CF) = 3.9 Hz), 126.6, 126.8 (ArCH), 129.68 (q, ^2J(CF) = 32.4 Hz, ArC), 129.70 (q, ^2J(CF) = 32.2 Hz, ArC), 148.3, 150.6 (ArC); ^{19}F NMR (376 MHz, $CDCl_3$) δ: −63.0 (CF_3). Protons and carbons assignments were made by gCOSY and gHSQC.

4.4. Preparation of the HCl salts

The aziridine carbinol **1** (0.5 mmol) was dissolved in 4 mL of Et_2O and a solution of HCl 4 M in dioxane was added (pH = 2). The precipitated white solid was washed twice with diethyl ether, dried in vacuo, and used as catalyst without any further purification.

4.4.1. ((*S*)-Aziridin-2-yl)diphenylmethanol-HCl salt 1a-HCl. $[\alpha]_D = +44.9$ (c 1.00, MeOH); MS (ESI positive ions) m/z: 226 $(M)^+$; MS (ESI negative ions) m/z: 262 $(M^{37}Cl-1)^-$,

260 ($M^{35}Cl-1)^-$. IR (KBr): 1177, 1448, 1492, 1509, 2915, 2982, 3047, 3108, and 3272 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 2.68 (dd, $J = 1.5$, 7.0 Hz, 1H, H_a–CH_2), 2.83 (dd, $J = 1.5$, 5.9 Hz, 1H, H_b–CH_2), 3.95 (dd, $J_1 = J_2 = 6.5$ Hz, 1H, CH), 6.42 (br s, 1H, OH), 7.23–7.58 (m, 10H, ArCH), 8.40 (br s, 2H, NH_2). ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 24.5 (CH_2), 42.0 (CH), 74.1 (C), 127.1, 127.2, 128.4, 128.5, 129.1, 129.2 (ArCH), 145.3, 145.9 (ArC).

4.4.2. (2*S*,3*S*)-3-Methylaziridin-2-yl(diphenyl)methanol HCl salt 1b-HCl. $[\alpha]_D = +43.2$ (*c* 0.47, MeOH); MS (ESI positive ions) *m*/*z*: 240 $(M)^+$; MS (ESI negative ions) *m*/*z*: 262 $(M^{37}Cl-1)^-$, 260 $(M^{35}Cl-1)^-$. IR (KBr): 1178, 1408, 1449, 1536, 1611, 2890, 3040, 3260, 3387, and 3467 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 1.49 (d, $J = 6.4$ Hz, 3H, CH_3), 3.12–3.16 (m, 1H, CH), 3.79 (d, $J = 7.9$ Hz, 1H, CH), 6.82 (br s, 1H, OH), 7.35–7.52 (m, 10H, ArCH), 8.96 (br s, 2H, NH_2). ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 10.4 (CH_3), 37.2, 46.4 (CH), 75.1 (C), 127.17, 127.23, 128.56, 128.58, 129.18, 129.20 (ArCH), 144.6, 147.2 (ArC).

4.4.3. ((*S*)-Aziridin-2-yl)bis(4-(trifluoromethyl)phenyl)methanol-HCl salt 1c-HCl. $[\alpha]_D = +44.5$ (*c* 0.47, MeOH); MS (ESI positive ions) *m*/*z*: 362 $(M)^+$; MS (ESI negative ions) *m*/*z*: 398 $(M^{37}Cl-1)^-$, 396 $(M^{35}Cl-1)^-$. IR (KBr): 1071, 1118, 1170, 1331, 1619, 3200, and 3343 cm^{-1}; ^1H NMR (600 MHz, CD_3OD) δ (ppm): 3.05 (dd, $J = 2.4$, 7.4 Hz, 1H, H_a–CH_2), 3.10 (dd, $J = 2.4$, 6.3 Hz, 1H, H_b–CH_2), 4.16 (dd, $J_1 = J_2 = 7.0$ Hz, 1H, CH), 7.65 (br d, $J = 8.5$ Hz, 2H), 7.73 (m, 6H). ^{13}C NMR (150 MHz, CD_3OD) δ (ppm): 25.05 (CH_2), 41.9 (CH), 72.9 (C), 124.22 (q, $^1J(CF) = 272$ Hz, CF_3), 124.28 (q, $^1J(CF) = 271$ Hz, CF_3), 125.5 (q, $^3J(CF) = 3.7$ Hz, ArCH), 125.6 (q, $^3J(CF) = 4.0$ Hz, ArCH), 127.06, 127.70 (ArCH), 130.05 (q, $^2J(CF) = 37.7$ Hz, ArC), 130.07 (q, $^2J(CF) = 37.1$ Hz, ArC), 147.21, 148.06 (ArC); ^{19}F NMR (376 MHz, CD_3OD) δ: −64.7, −64.6 (CF_3).

4.5. Preparation of the TFA salts

The aziridine carbinol **1** (0.5 mmol) was dissolved in 4 mL of Et_2O and trifluoroacetic acid (0.6 mmol) was added. The precipitated white solid was washed twice with diethyl ether, dried in vacuo, and used as catalyst without any further purification.

4.5.1. ((*S*)-Aziridin-2-yl)diphenylmethanol-TFA salt 1a-TFA. $[\alpha]_D = +31.3$ (*c* 0.67, MeOH); MS (ESI positive ions) *m*/*z*: 226 $(M)^+$; MS (ESI negative ions) *m*/*z*: 113 $(CF_3CO_2)^-$. IR (KBr): 1206, 1393, 1447, 1493, 1587, 1651, 3065, 3136, 3217, and 3380 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 2.54 (dd, $J = 1.6$, 7.0 Hz, 1H, H_a–CH_2), 2.98 (dd, $J = 6.0$, 1.6 Hz, 1H, H_b–CH_2), 3.70 (dd, $J = 6.0$, 7.0 Hz, 1H, CH), 7.21–7.46 (m, 10H, ArCH). ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 24.3 (CH_2), 41.6 (CH), 77.45 (C), 126.0, 126.5, 128.2, 128.8, 129.05 (ArCH), 143.3, 145.7 (ArC).

4.5.2. (2*S*,3*S*)-3-Methylaziridin-2-yl(diphenyl)methanol TFA salt 1b-TFA. $[\alpha]_D = +35.2$ (*c* 0.885, MeOH); MS (ESI positive ions) *m*/*z*: 240 $(M)^+$; MS (ESI negative ions) *m*/*z*: 113 $(CF_3CO_2)^-$. IR (KBr): 1208, 1450, 1550, 1661, 1689, 3033, 3068, 3173, and 3291 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 1.48 (d, $J = 6.3$ Hz, 3H, CH_3), 3.21 (m, 1H, CH), 3.85 (d, $J = 7.8$ Hz, 1H, CH), 6.93 (br s, 1H, OH), 7.28–7.58 (m, 10H, ArCH), 8.67 (br s, 2H, NH_2). ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 10.5 (CH_3), 37.5, 46.6 (CH), 75.0 (C), 127.2, 127.3, 128.6, 129.2 (ArCH), 144.6, 147.2 (ArC).

4.6. Diels–Alder reaction

4.6.1. General procedure using the preformed salt 1-HCl. To a solution of **1**-HCl (0.05 mmol), in 1 mL of MeOH/H_2O (95:5 by volume) was added the α,β-unsaturated aldehydes (1 mmol). The solution was stirred for 10 min before the addition of cyclopentadiene (2 mmol). The reaction was stirred for the given time and at the temperature reported in Table 1 and then diluted with Et_2O and washed with water. The organic layer was dried over Na_2SO_4, filtered, and concentrated. *endo*/*exo* Ratios were determined by ^1H NMR on the crude reaction mixtures. Chromatography (hexane/Et_2O 10:1 as eluent) of the crude afforded a mixture of aldehydes and dimethylacetals. The mixture was completely acetalized with MeOH and catalytic amounts of *p*-toluensulfonic acid for the ee determination.

4.6.2. General procedure using the in situ formed salt 1-$HClO_4$. To a suspension of **1** (0.1 mmol) in H_2O (0.2 mL), was added the α,β-unsaturated aldehydes (1 mmol) and then 70% $HClO_4$ (0.1 mmol). The solution was stirred for 10 min before the addition of cyclopentadiene (2 mmol). The reaction was stirred for the given time and at the temperature reported in Table 1, and then diluted with Et_2O and washed with water. The organic layer was dried over Na_2SO_4, filtered, and concentrated. *endo*/*exo* Ratios were determined by ^1H NMR on the crude reaction mixtures. Chromatography (hexane/Et_2O 10:1 as eluent) of the crude afforded the aldehydes that were acetalized for the determination of ee.

4.6.3. *endo*-3-Phenylbicyclo[2.2.1]hept-5-ene-2-carboxaldehyde 8.[22] ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.59–1.65 (m, 1H), 1.79–1.84 (m, 1H), 2.98 (ddd, $J = 2.3$, 3.5, 4.9 Hz, 1H), 3.09 (dd, $J = 1.6$, 4.9 Hz, 1H), 3.14 (br s, 1H), 3.34 (br s, 1H), 6.17 (dd, $J = 2.8$, 5.8 Hz, 1H), 6.42 (dd, $J = 3.3$, 5.8 Hz, 1H), 7.13–7.34 (m, 5H), 9.60 (d, $J = 2.3$ Hz, 1H).

4.6.4. *exo*-3-Phenylbicyclo[2.2.1]hept-5-ene-2-carboxaldehyde 8. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.53–1.59 (m, 2H), 2,60 (ddd, $J = 2.3$, 3.5, 4.9 Hz, 1H), 3.22 (m, 2H), 3.72 (dd, $J = 3.4$, 4.9 Hz, 1H), 6.07 (dd, $J = 3.2$, 5.8 Hz, 1H), 6.34 (dd, $J = 3.5$, 5.8 Hz, 1H), 7.13–7.34 (m, 5H), 9.92 (d, $J = 2.1$ Hz, 1H). The *endo*/*exo* ratio was determined by ^1H NMR analysis (400 MHz): δ 9.60 (d, $J = 2.3$ Hz, 1H, CHO *endo*), 9.93 (d, $J = 2.3$ Hz, 1H, CHO *exo*).

4.6.5. *endo*-5-(Dimethoxymethyl)-6-phenylbicyclo[2.2.1]-hept-2-ene 10. MS (ESI) *m*/*z*: 267 $(M+Na)^+$. ^1H NMR

(400 MHz, $CDCl_3$) δ (ppm): 1.52–1.57 (2br dd, 1H, H_a–CH_2), 1.77 (d, $J = 8.7$ Hz, 1H, H_b–CH_2), 2.40 (dd, $J = 1.5$, 4.8 Hz, 1H, CH), 2.51–2.56 (m, 1H, CH), 2.87 (br s, 1H, CH), 2.96 (br s, 1H, CH), 3.13 (s, 3H, OCH_3), 3.33 (s, 3H, OCH_3), 3.94 (d, $J = 9.0$ Hz, 1H, $CH(OCH_3)_2$), 6.16 (dd, $J = 2.8$, 5.7 Hz, 1H, CH=), 6.36 (td, $J = 2.8$, 5.7 Hz, 1H, CH=), 7.12–7.37 (m, 5H, ArCH).

4.6.6. *exo*-5-(Dimethoxymethyl)-6-phenylbicyclo[2.2.1]hept-2-ene 10. MS (ESI) *m/z*: 267 $(M+Na)^+$. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.46–1.52 (m, 1H, H_a–CH_2), 1.68 (d, 1H, $J = 8.6$ Hz, H_b–CH_2), 2.03 (ddd, $J = 1.6$, 5.1, 8.2 Hz, 1H, CH), 2.90 (d, $J = 1.4$, 4.9 Hz, 1H, CH), 3.00 (br s, 1H, CH), 3.07 (s, 3H, OCH_3), 3.12 (dd, $J = 3.4$, 5.1 Hz, 1H), 3.38 (s, 3H, OCH_3), 4.37 (d, $J = 8.3$ Hz, 1H, $CH(OCH_3)_2$), 5.94 (dd, $J = 2.9$, 5.6 Hz, 1H, CH=), 6.36 (td, $J = 2.8$, 5.7 Hz, 1H, CH=), 7.12–7.37 (m, 5H, ArCH). Protons and carbon assignments were made by gCOSY and gHSQC.

The ee was determined in the presence of (*S*)-(+)-1-(9-anthryl)-2,2,2-trifluoroethanol as the chiral solvating agent in $CDCl_3$. The singlets of the methoxy group of the *exo* and *endo* acetals **10** were split into two: 3.30, 3.31 (s, 3H, OCH_3 *endo*-isomer); 3.34, 3.35 (s, 3H, OCH_3 *exo*-isomer).

4.6.7. *endo*-3-Methylbicyclo[2.2.1]hept-5-ene-2-carbaldehyde 9.[22] ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.17 (d, $J = 6.9$ Hz, 3H), 1.44–1.51 (m, 1H), 1.55–1.60 (m, 1H), 1.77–1.87 (m, 1H), 2.34 (dd, $J = 3.2$, 4.3 Hz, 1H), 2.56 (br s, 1H), 3.13 (br s, 1H), 6.05 (dd, $J = 2.8$, 5.6 Hz, 1H), 6.29 (dd, $J = 3.0$, 5.8 Hz, 1H), 9.37 (d, $J = 3.2$ Hz, 1H).

4.6.8. *exo*-3-Methylbicyclo[2.2.1]hept-5-ene-2-carbaldehyde 9.[11] ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.90 (d, $J = 6.9$ Hz, 3H), 1.44–1.48 (m, 2H), 1.70–1.73 (m, 1H), 2.37–2.45 (m, 1H), 2.79 (br s, 1H), 3.02 (br s, 1H), 6.16 (dd, $J = 5.7$, 3.0 Hz, 1H), 6.24 (dd, $J = 5.7$, 3.1 Hz, 1H) 9.78 (d, $J = 2.8$ Hz, 1H). The *endo*/*exo* ratio was determined by ^1H NMR analysis (400 MHz): δ 9.37 (d, $J = 3.2$ Hz, 1H, CHO *endo*), 9.78 (d, $J = 2.8$ Hz, 1H, CHO *exo*).

4.6.9. *endo*-5-(Dimethoxymethyl)-6-methylbicyclo[2.2.1]-hept-2-ene 11. MS (ESI) *m/z*: 159 $(M+Na)^+$. ^1H NMR (400 MHz, CD_2Cl_2) δ (ppm): 1.11 (d, $J = 6.3$ Hz, 3H, CH_3), 1.16 (m, 1H, CH), 1.34–136 (2br dd, 1H, H_a–CH_2), 1.47–1.50 (2br dd, 1H, H_a–CH_2), 1.76–1.82 (m, 1H, CH), 2.38 (br s, 1H, CH), 2.76 (br s, 1H, CH), 3.27 (s, 3H, OCH_3), 3.29 (s, 3H, OCH_3), 3.72 (d, $J = 9.2$ Hz, 1H, $CH(OCH_3)_2$), 5.98 (dd, $J = 2.9$, 5.8 Hz, 1H, CH=), 6.22 (dd, $J = 2.9$, 5.8 Hz, 1H, CH=). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 21.1 (CH_3), 36.8, 44.7 (CH), 45.9 (CH_2), 49.1, 50.5 (CH), 52.0, 53.6 (OCH_3), 108.6 (CH), 133.5, 138.3 (CH=). Protons and carbons assignments were made by gCOSY and gHSQC.

4.6.10. *exo*-5-(Dimethoxymethyl)-6-methylbicyclo[2.2.1]-hept-2-ene 11. MS (ESI) *m/z*: 159 $(M+Na)^+$. ^1H NMR (400 MHz, CD_2Cl_2) δ (ppm): 0.85 (d, $J = 6.7$ Hz, 3H, CH_3), 1.12 (m, 1H), 1.34–136 (2br dd, 1H, H_a–CH_2), 1.44–1.48 (2br dd, 1H, H_a–CH_2), 1.82–1.86 (m, 1H), 2.63 (br s, 1H, CH), 2.66 (br s, 1H, CH), 3.30 (s, 3H, OCH_3), 3.31 (s, 3H, OCH_3), 4.18 (d, $J = 8.6$ Hz, 1H, $CH(OCH_3)_2$), 6.06 (dd, $J = 2.9$, 5.7 Hz, 1H, CH=), 6.22 (dd, $J = 2.9$, 5.8 Hz, 1H, CH=). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 19.1 (CH_3), 37.4, 44.9 (CH), 47.1 (CH_2), 47.9, 49.6 (CH), 52.4, 53.8 (OCH_3), 108.6 (CH), 134.9, 137.5 (CH=). Protons and carbons assignments were made by gCOSY and gHSQC.

The ee was determined in the presence of (*S*)-(+)-1-(9-anthryl)-2,2,2-trifluoroethanol as the chiral solvating agent in CD_2Cl_2. The singlets of the methoxy group of the *endo* and *exo* acetals **11** were split into two: 3.27, 3.29 (s, 3H, OCH_3 *endo*-isomer); 3.30, 3.31 (s, 3H, OCH_3 *exo*-isomer).

4.7. Alkylation of *N*-methyl-pyrrole. General procedure

A 10 mL vial equipped with a magnetic stir bar was charged with the appropriate aziridine-salt (0.10 equiv), 2 mL of CH_2Cl_2/*i*-PrOH (85:15 by volume), then cooled at the desired temperature. The solution was stirred for 5 min before the *N*-methyl-pyrrole (5 equiv) was added. After stirring for 5 min, the α,β-unsaturated aldehyde (1 equiv) was added in one portion. The resulting suspension was stirred at constant temperature until complete consumption of the aldehyde as determined by TLC. The reaction mixture was then passed through a silica gel plug using Et_2O as eluent and then concentrated. The resulting residue was purified by silica gel chromatography (hexane/EtOAc 5:1) to afford the title compound. The ee was determined by GLC analysis of the aldehyde.

4.7.1. (*R*)-3-(1-Methyl-1*H*-pyrrol-2-yl)-butanal 12.[14] ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 1.15 (d, $J = 6.8$ Hz, 3H, CH_3), 2.56 (ddd, $J = 2.0$, 7.6, 17.2 Hz, 1H, CH_2), 2.72 (ddd, $J = 2.0$, 6.8, 17.2 Hz, 1H, CH_2), 3.32–3.42 (m, 1H, CH), 3.53 (s, 3H, N–CH_3), 5.75 (dd, $J = 1.6$, 3.2 Hz, 1H, ArCH), 5.85 (t, $J = 3.2$ Hz, 1H, ArCH), 6.56 (t, $J = 2.2$ Hz, 1H, ArCH), 9.61 (t, $J = 1.8$ Hz, 1H, CHO). The ee was determined by GLC analysis of the aldehyde (RT-BetaDEX-sm 50 °C, 5 °C/min; (*S*)-isomer rt = 26.8 min and (*R*)-isomer rt = 26.5 min). Absolute configuration was determined via reduction to the corresponding alcohols and comparison of specific rotation.

4.7.2. (*S*)-3-Phenyl-3-(1-methyl-1*H*-pyrrol-2-yl)-propanal 13.[14] ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 2.89 (ddd, $J = 1.6$, 6.8, 16.8 Hz, 1H, CH_2), 3.09 (ddd, $J = 2.0$, 8.4, 16.8 Hz, 1H, CH_2), 3.30 (s, 3H, N–CH_3), 4.63 (t, $J = 7.6$ Hz, 1H, CH), 5.92 (t, $J = 3.0$ Hz, 1H, ArCH), 5.99–5.98 (m, 1H, ArCH), 6.59 (t, $J = 2.0$ Hz, 1H, ArCH), 7.15–7.29 (m, 5H, ArCH), 9.61 (t, $J = 1.6$ Hz, 1H, CHO). The ee was determined by GLC analysis of the aldehyde (RT-BetaDEXsm isotherm 160 °C; (*S*)-isomer rt = 35.1 min and (*R*)-isomer rt = 34.1 min). Absolute configuration was determined via reduction to the corresponding alcohols and comparison of optical rotation power.

4.8. Alkylation of *N*-methyl-indole. General procedure

A 10 mL vial equipped with a magnetic stir bar was charged with the aziridine-salt (0.10 equiv), 2 mL of CH_2Cl_2/*i*PrOH (85:15), and then cooled to the desired temperature. The solution was stirred for 5 min before the α,β-unsaturated aldehyde (2.5 equiv) was added. After stirring for 5 min, the *N*-methyl indole (1 equiv) was added in one portion. The resulting suspension was stirred at constant temperature until complete consumption of the *N*-methyl-indole as determined by TLC. The reaction mixture was then passed through a silica gel plug using diethyl ether as eluent and then concentrated. The resulting residue was purified by silica gel chromatography (hexane/EtOAc 10:1) to afford the title compound. The ee was determined by HPLC analysis of the alcohol obtained by $NaBH_4$ reduction of the aldehyde.

4.8.1. 3-(1-Methyl-1*H*-indol-3-yl)-butanal 14.[15] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.44 (d, $J = 7.2$ Hz, 3H, CH_3), 2.71 (ddd, $J = 2.7$, 6.9, 16.2 Hz, 1H, CH_2), 2.88 (ddd, $J = 2.7$, 6.9, 16.2 Hz, 1H, CH_2), 3.68 (dt, $J = 6.9$, 13.8 Hz, 1H, CH), 3.75 (s, 3H, N–CH_3), 6.84 (s, 1H, ArCH), 7.12 (ddd, $J = 1.5$, 7.4, 8.1 Hz, 1H, ArCH), 7.21–7.32 (m, 2H, ArCH), 7.63 (d, $J = 7.8$ Hz, 1H, ArCH), 9.75 (dd, $J = 2.1$, 2.1 Hz, 1H, CHO).

4.8.2. 3-(1-Methyl-1*H*-indol-3-yl)-butanol. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.44 (d, $J = 6.9$ Hz, 3H, CH_3), 1.90–2.12 (m, 2H, CH_2), 3.20–3.30 (m, 1H, CH), 3.66–3.72 (m, 2H, CH_2), 3.76 (s, 3H, N–CH_3), 6.88 (s, 1H, ArCH), 7.16 (d, $J = 7.5$ Hz, 1H, ArCH), 7.25–7.35 (m, 2H, ArCH), 7.71 (d, $J = 7.8$ Hz, 1H, ArCH). The ee was determined by HPLC using a Chiralcel AD-H (95:5 hexane/*i*PrOH 0.75 mL/min), (*S*)-isomer rt = 19.68 min and (*R*)-isomer rt = 21.07 min.

4.8.3. 3-(1-Methyl-1*H*-indol-3-yl)-3-phenyl-propanal 15.[15] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.10 (4d, $J = 2.7$, 8.4, 16.5 Hz, 1H, H_a–CH_2), 3.22 (4d $J = 2.7$, 8.4, 16.5 Hz, 1H, H_b–CH_2), 3.76 (s, 3H, NCH_3), 4.88 (dd, $J_1 = J_2 = 7.5$ Hz, 1H, Ph–CH), 6.88 (s, 1H, NCH), 7.04 (ddd, $J = 1.2$, 6.9, 8.1 Hz, 1H, ArH), 7.19–7.26 (m, 2H, ArH), 7.28–7.36 (m, 5H, ArH), 7.43 (dt, $J = 0.9$, 8.0 Hz, 1H, ArH), 9.76 (dd, $J = 2.8$, 1.8 Hz, 1H, CHO).

4.8.4. 3-(1-Methyl-1*H*-indol-3-yl)-3-phenyl-propanol. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.28 (m, 1H, H_a–CH_2), 2.46 (m, 1H, H_b–CH_2), 3.68 (m, 2H, CH_2), 3.75 (s, 3H, NCH_3), 4.39 (dd, $J_1 = J_2 = 7.8$ Hz, 1H, Ph–CH), 6.90 (s, 1H, NCH), 7.01 (ddd, $J = 1.1$, 6.9, 8.0 Hz, 1H, ArH), 7.14–7.20 (m, 1H, ArH), 7.24–7.30 (m, 2H, ArH) 7.31–7.35 (m, 4H, ArH), 7.46 (dt, $J = 0.9$, 8.0 Hz, 1H, ArH).

The ee was determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiralcel AD-H (90:10 hexane/*i*PrOH 1.0 mL/min), (*S*)-isomer rt = 43.5 min and (*R*)-isomer rt = 35.6 min.

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