Catalytic Asymmetric Aziridination of Enol Derivatives in the Presence of Chiral Copper Complexes to give Optically Active α-Amino Ketones

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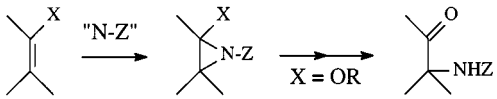
A series of acyclic and cyclic enol derivatives **1** has been transformed into the corresponding α-amino-functionalized ketones **2** by means of enantioselective catalytic aziridination with chiral Cu complexes, prepared in situ from $[Cu(MeCN)4]PF_6$ and the optically active ligands **3**, by using (*N*-tosylimino)iodobenzene (PhINTs) as a nitrogen source. The best enantioselectivities (*ee* values of up to 52%) have been achieved for the electronically deactivated enol acetate **1aδ**, but the incorporation of steric bulk and the substitution pattern at the enol double bond do not improve the *ee* values. The cyclic substrates react considerably less readily (only up to 45% conversion) compared to their acyclic counterparts (complete consumption). A transition structure is suggested for the asymmetric Cu-catalyzed aziridination of the enol acetate **1aδ** in the presence of the chiral ligand **3b** that could account for the sense of the (*R*)-configured product **2a**.

Introduction

The amino functionality is ubiquitous and is of immense importance in natural products, in drugs, as well as in building blocks in organic synthesis.[1] Since most of these compounds possess at least one chiral center, it is of general interest to develop synthetic methods for their preparation in enantiomerically enriched form.

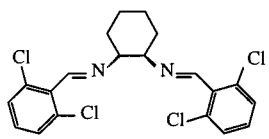
An attractive target molecule is Cathinone, or (–)-(2*S*)-2-amino-1-phenylpropanone, the main active component of fresh leaves of *Catha edulis*, which shows cardiovascular biological activity.[2] Moreover, its reduction to the corresponding β-amino alcohol furnishes a valuable chiral auxiliary for use in asymmetric catalysis.[3]

An elegant way of introducing a nitrogen atom into a molecule is by means of aziridination, in which a nitrene or a nitrenoid species is transferred onto the olefin (Scheme 1).[4] A convenient way of generating a nitrene is either by photolysis or thermolysis of an azide,[5] while oxaziridines[6] serve as efficient thermal sources for nitrenoid-type aza functionalization.

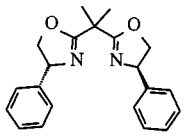


Scheme 1. Aziridination of olefins (X = R or Ar) and enol derivatives (X = OR)

In order to achieve metal-mediated nitrogen transfer, nitridomanganese(V) complexes may be activated by *p*-toluenesulfonic or trifluoroacetic anhydride,[7] or in situ generated copper and rhodium nitrene complexes ($M{=}N{-}SO_2Ar$) may be utilized.[8–10] Notable enantioselective examples involving the Cu-catalyzed asymmetric aziridination of styrene and cinnamate derivatives by employing the C_2-symmetric ligands **3a** and **3b** as chiral auxiliaries have been independently developed by Evans[8b] and by Jacobsen.[9a]



3a



3b

Following the aziridination of enol derivatives (X = OR, Scheme 1), ring-opening of the aziridine intermediate affords the corresponding α-amino ketone. For this purpose, a few stoichiometric methods are available, allowing the enantio- or diastereoselective α-amination of ketones.[5,7c,7d] For example, Komatsu and co-workers[7c] and Jørgensen et al.[7d] have recently used optically active nitridomanganese(V) complexes to good effect in the stoichiometric aziridination of enols (*ee* values of up to 79%). However, as far as we are aware, no catalytic asymmetric nitrene transfers to enol derivatives have hitherto been reported.

The aim of this study was to employ the Evans[8b] and the Jacobsen method[9a] for Cu-catalyzed asymmetric amination of enol derivatives of propiophenone bearing silyl, methyl, and acetyl groups (**1aα–δ**, *cf.* Table 1) in order to generate optically active Cathinone derivatives. It was of interest to vary the steric bulk and the electronic properties of the enol substrate so as to allow optimization of the enantioselectivity of this catalytic aza functionalization.

Results

The enol derivatives **1a–d** were prepared from the corresponding ketones according to literature methods.[11] The *Z*-configured acyclic enol derivatives **1aα–bβ** (for structures,

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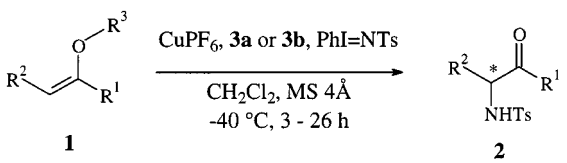
Table 1. Copper-catalyzed aziridination of the enol derivatives **1a–d**[a]

entry	enol	L*[b]	t [h]	convn. [%][c]	ee [%][d]
1	**1aα** 	**3a**	5	>95	18 (*S*)
2		**3b**	4	90	16 (*S*)
3	**1aβ** 	**3a**	3	>95	12 (*S*)
4		**3b**	16	92	13 (*S*)
5	**1aγ** 	**3a**	3	87	9 (*R*)
6		**3b**	3	76	10 (*S*)
7	**1aδ** 	**3a**	5	>95	28 (*R*)[e]
8		**3b**	26	61	52 (*R*)[e]
9	**1bα** 	**3a**	4	89	20 (*R*)
10		**3b**	4	92	19 (*S*)
11	**1bβ** 	**3a**	4	91	27 (*R*)
12		**3b**	4	>95	21 (*R*)
13	**1c** 	**3a**	5	45	19 (-)
14		**3b**	9	traces	20 (-)
15	**1d** 	**3a**	3	16	6 (-)
16		**3b**	3	10	7 (+)

[a] A 1.0:0.6:0.05 molar ratio of **1**:PhINTs:$CuPF_6$ was employed, rection temperature –40 °C. – [b] 5.5 mol-% of chiral ligand **3a** or 6.0 mol-% of **3b** was used. – [c] Referred to the amount of PhINTs consumed, determined by ^1H NMR analysis, error ca. ±5%. – [d] Enantiomeric excess of amino ketone **2**, determined by HPLC analysis on a chiral column, error ca. ±2%. – [e] After acid-catalysed hydrolysis of the aziridine **4** with HCl/MeOH to the amino ketone **2a**, the *ee* values of aziridine (+)-**4** are 28% and 53%, respectively.

see Table 1) were obtained almost exclusively ($Z/E > 95:5$) under optimized reaction conditions. Racemic samples of α-tosylamino ketones **2a–c** were prepared by copper-catalyzed aziridination of the corresponding enols **1a–c** according to a literature method,[8c] while derivative **2d** was obtained by tosylation of the corresponding amino ketone hydrochloride.[12]

The copper-catalyzed asymmetric aziridinations of the enols **1a–d** with *N*-tosyl-iminoiodobenzene (PhINTs) were carried out using the C_2-symmetric ligands diimine **3a** and bis(oxazoline) **3b** as sources of chirality (Scheme 2). The results are summarized in Table 1.



1 **2**

Scheme 2. Copper-catalyzed asymmetric amination of enol derivatives **1**

The reaction conditions were optimized with regard to degree of conversion and enantioselectivity by employing the trimethylsilyl enol ether **1aα** as a model substrate. The best results (conversion > 90%, *ee* value 16–18%) were obtained by using 5 mol-% of $[Cu(MeCN)_4]PF_6$ as the copper source and 5.5 or 6.0 mol-% of ligand **3a** or **3b** in CH_2Cl_2 at –40 °C (entries 1 and 2). At lower temperatures (–70 °C), no conversion of the enol derivative **1aα** was observed after 5 h using ligand **3a**, while with ligand **3b** the reaction was appreciably retarded (ca. 95% conversion only after 10 h) without any significant increase in enantioselectivity (data not shown) as compared with that of the reaction at –40 °C (entry 2). Both the conversion and the enantioselectivity in the aziridination of silyl enol ether **1aα** with PhINTs in the presence of ligand **3a** or **3b** were decreased when CuOTf · 1/2 C_6H_6 or $Cu(OTf)_2$ was used instead of $[Cu(MeCN)_4]PF_6$ as the copper source (data not shown). Therefore, all subsequent catalytic asymmetric aziridinations of the enol derivatives **1aβ–d** were carried out with $[Cu(MeCN)_4]PF_6$ under the optimized reaction conditions (CH_2Cl_2, –40 °C).

To assess the effect of the steric bulk of the silyloxy group on the enantioselectivity, the catalytic aziridination of the TBDMS-substituted enol ether **1aβ** was investigated. For this substrate, a decrease in the *ee* values to 12–13% was observed (entries 3 and 4), as compared with the 16–18% obtained for the enol ether **1aα**, which is functionalized with the sterically less demanding TMS group (entries 1 and 2).

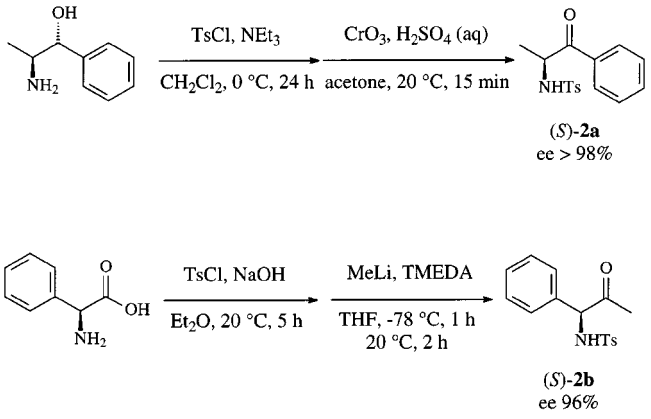
Once it had been established that the steric demand of the R^3 substituent has no significant effect on the enantioselectivity, its electronic influence was tested by carrying out asymmetric aziridinations of the methyl enol ether **1aγ** and the enol acetate **1aδ**. Remarkably higher *ee* values (28% and 52%) were achieved for the less electron-rich enol acetate **1aδ** (entries 7 and 8) compared to the more electron-rich methyl enol ether **1aγ** (ca. 10%, entries 5 and 6). Both substrates **1aγ** and **1aδ** preferentially afforded the (*R*)-configured α-amino ketone **2a** in the presence of the chiral ligand **3a** (*cf.* entries 5 and 7), while in the case of ligand **3b** the sense of the enantioselectivity with these substrates was reversed (*cf.* entries 6 and 8). Fortunately, the aziridine **4** of the enol acetate **1aδ** persisted under the reaction conditions, which permitted its isolation. Subsequent hydrolysis by treatment with methanolic HCl to give the α-amino ketone **2a** proceeded without loss of optical purity.

To evaluate whether the substitution pattern of the R^1 and R^2 groups of the enol derivative has an influence on the enantioselectivity, the silyl enol ethers **1bα** and **1bβ**, which, in contrast to the substrates **1aα** and **1aβ**, bear the methyl group in the α- and the phenyl group in the β position with respect to the silyloxy functionality, were reacted with PhINTs under the optimized catalytic conditions. Similar *ee* values (ca. 20%) were observed for the TMS-substituted derivatives **1aα** and **1bα** (entries 1, 2, 9, and 10). For the TBDMS-substituted silyl enol ether **1bβ**, slightly higher *ee* values (21% and 27%) were observed (entries 11 and 12), compared to 12% and 13% seen with **1aβ** (entries 3 and 4). Moreover, the sense of the enantioselectivity was reversed in the case of the TBDMS-substituted derivatives **1aβ** (entries 3 and 4) and **1bβ** (entries 11 and 12). Whereas the former preferentially produced the (*S*)-configured amino ke-

tone **2a**, the (*R*)-enantiomer of **2b** was preferentially formed from **1bβ**.

In contrast to the acyclic enol derivatives **1aα–bβ** (entries 1–12), for the cyclic substrates **1c**,**d** only poor conversion (up to 45%) to the corresponding α-amino ketones **2c**,**d** was observed (entries 13–16). With these cyclic derivatives, copper-catalyzed decomposition of PhINTs to tosyl amide prevailed over aziridination, which, surprisingly, has not been observed in the absence of chiral ligands.

The absolute configurations of amino ketones **2a**,**b** were determined by independent synthesis (*cf.* SchemeS)-**2a** was prepared by tosylation of (1*R*,2*S*)-norephedrine and subsequent Jones oxidation,[13] while the α-amino ketone (+)-(*S*)-**2b** was obtained in 96% *ee* from (*S*)-phenylglycine by tosylation and subsequent reaction with MeLi.[14]



Scheme 3. Synthesis of authentic samples of (*S*)-**2a** and (*S*)-**2b**

Discussion

As mentioned in the Results Section, Cu-catalyzed asymmetric aziridination of the enol derivatives **1a–d** with PhINTs yielded the corresponding α-amino ketones **2a–d** with poor to moderate enantiomeric excesses (*ee* values up to 52%, Table 1). In control experiments using the silyl enol ether **1aα** as a model substrate in the absence of the Cu catalyst, under otherwise identical reaction conditions, no PhINTs was consumed, from which it can be concluded that the non-catalytic reaction is not responsible for the low enantioselectivity. Furthermore, when a stoichiometric amount of the chiral Cu complex prepared from $CuPF_6$ and the chiral ligand **3a** was employed in the aziridination of the enol ether **1aα**, no significant increase in the *ee* value was observed (data not shown) as compared to that obtained under catalytic conditions. These results imply that the low enantioselectivity of this asymmetric aziridination is not due to a competing reaction catalyzed by the copper source $[Cu(MeCN)_4]PF_6$. Since no loss of optical purity was observed when the enantiomerically pure (*R*)-configured α-tosylamino ketone **2a** was exposed to the standard reaction conditions, product racemization may also be excluded as a possible reason for the low *ee* values of the α-amino ketones **2a–d**. Thus, the low enantiodifferentiation in the catalytic aziridination of the enol derivates **1a–d** seems to be intrinsic to the nitrogen-transfer process.

The *ee* values in Table 1 reveal that neither the substitution pattern of the substrate **1** (entries 1, 2, 9, and 10) nor the steric bulk of silyloxy groups (entries 1–4) has an appreciable effect on the enantioselectivity of Cu-catalyzed aziridination of these enol derivatives. However, the electronic property of the substituent on the oxygen atom of the enol substrate does influence the degree of enantioselectivity. For example, considerably higher *ee* values of up to 52% (entries 7 and 8) were obtained for the more electron-deficient enol acetate **1aδ** as compared to only ca. 10% for the methoxy derivative **1aγ** (entries 5 and 6). Let us now attempt to rationalize these electronic effects on the enantioselectivity.

For the Jacobsen–Katsuki epoxidation of chromene derivatives, it has been reported[15a] that methoxy-substituted salen ligands give rise to higher *ee* values than their nitro-substituted counterparts. This has been explained in terms of stabilization of the electrophilic, oxygen-transferring oxo-Mn(III) species by the electron-donating methoxy substituent, which decreases the reactivity of the oxo complex. According to the Hammond postulate, a less reactive reagent favors a late, more product-like transition state,[15b] which, for a reaction without substrate–reagent precoordination, implies a more ordered transition structure. Thus, stronger steric interactions are operative during the encounter of the substrate and reagent and a higher selectivity is to be expected. In analogy to the Jacobsen–Katsuki epoxidation, we propose that in the asymmetric aziridination of the less electron-rich, less reactive enol acetate **1aδ**, a more ordered, product-like transition state is involved. Hence, the enantioselectivity in the case of the more electron-deficient enol acetate **1aδ** is significantly higher than that seen with the methyl enol ether **1aγ**. Indeed, the electron-deficient cinnamates are aziridinated with *ee* values of up to 85%,[8b][9b] which substantiates the aforementioned rationale for the observed electronic effect on the enantioselectivity of the catalytic asymmetric aziridination.

It remains to suggest a likely transition structure for the Cu-catalyzed aziridination of the enol acetate **1aδ** (chosen as a model substrate in view of the highest *ee* value of 52%) in the presence of the chiral ligand **3b**, that would account for the sense of the (*R*)-configured α-amino ketone **2a** (entry 8). A monomeric, trigonal-planar nitrene–copper(III) complex was initially suggested by Jacobsen and co-workers[9b] for the asymmetric aziridination of styrene derivatives, and was later applied by Uemura and Taylor[16] to Cu-catalyzed sulfimide formation. Assuming that this active Cu complex holds true for our nitrogen transfer, we propose the trajectory shown in Figure 1, where the plane ***a*** of the substrate double bond attacks the plane ***b*** of the Cu–N bond in a perpendicular orientation.

To minimize steric interactions, the enol acetate orients itself in such a way that its phenyl group points away from the chiral ligand of the complex and is *anti* to the Ts group of the nitrene, as shown in the uppermost-left structure in Figure 1. A similar substrate approach has been proposed by Pfaltz et al.[17] for the Cu-catalyzed asymmetric cyclo-

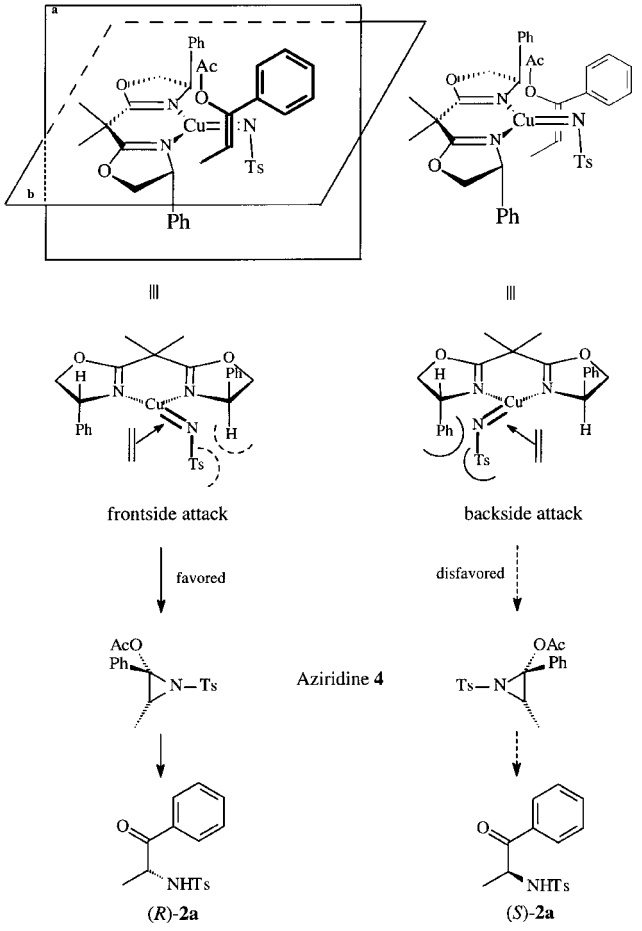


Figure 1. Proposed trajectories for the approach of enol acetate **1aδ** in asymmetric aziridination with the catalyst system $CuPF_6$/**3b**; plane ***a*** relates to the substrate and plane ***b*** to the bis(oxazoline) complex.

Table 2. HPLC conditions for the amino ketone

Compound	Column	Flow [mL/min] [a]	Retention time [min]
2a	Chirapak AS	0.5	29.5 (*S*), 33.1 (*R*)
2b	Chirapak AS	0.2	64.8 (*R*), 68.1 (*S*)
2c	Chiracel OB-H	0.5	28.2 (+), 33.7 (–)
2d	Chirapak AS	0.5	40.3 (+), 44.0 (–)
4	Chirapak AS	0.5	17.5 (2*S*,3*R*), 21.9 (2*R*,3*S*)[b]

[a] A mixture of *n*-hexane and ethanol (80:20) was used as eluent. [b] The configuration was assigned following acid-catalyzed hydrolysis to give the known optically active **2a**.

ropanation of styrene. For our proposed trajectory, two options are possible, namely frontside or backside attack of the substrate. Frontside attack should be favored over backside attack, since in the latter a repulsive steric interaction would be operative between the NTs moiety and a phenyl group of the ligand. Therefore, in the asymmetric Cu-catalyzed aziridination of the enol acetate **1aδ**, the (*R*)-configured α-amino ketone (*R*)-**2a** should be formed preferentially, as is indeed observed experimentally. This trajectory also correctly accounts for the stereoselectivity observed by Evans[8b] in the aziridination of cinnamate esters.

In conclusion, while Cu-catalyzed asymmetric aziridination of the electron-rich silyl enol ethers **1a–d** proceeds with low enantioselectivity, appreciable *ee* values (up to 52%) have been achieved with the less electron-rich enol acetate **1aδ**. A late transition state is proposed for the asymmetric aziridination of this less reactive substrate, where enhanced steric interactions with the chiral ligand **3b** and the tosyl amide group dictate preferential formation of the (*R*)-configured α-amino ketone **2a**.

Experimental Section

General Remarks: IR: Perkin–Elmer model 1605 FT-IR spectrophotometer. – ^{1}H NMR (250 MHz): Bruker AC 250 ($CHCl_3$ at δ = 7.26 as internal standard). – ^{13}C NMR (63 MHz): Bruker AC 250 ($CHCl_3$ at δ = 77.0 as internal standard). – Melting points: Büchi B-545 apparatus (uncorrected values). – Column chromatography was performed on silica gel (32–63 μm mesh, Merck). – HPLC: Kontron Instruments pump system 322, UV detection on a Kontron UVIKON 720 LC micro spectrophotometer; optical rotations detected with an IBZ Meßtechnik GmbH Chiralyser. – Optical rotations: Perkin–Elmer 241 MC polarimeter.

Asymmetric Aziridination of Enol Derivatives 1a–d: A solution of 18.6 mg (50.0 μmol) of $[Cu(MeCN)_4]PF_6$ and 23.6 mg (55.0 μmol) of ligand **3a** or 20.1 mg (60.0 μmol) of ligand **3b** in 4 mL CH_2Cl_2 was stirred for 15 min. at room temp. (ca. 20 °C) under an atmosphere of argon. To this mixture, a solution of 1.00 mmol of the appropriate enol ether **1a–d** in 0.5 mL of CH_2Cl_2 and about 0.5 g of molecular sieves 4 Å were added and the resulting mixture was stirred for 15 min. at room temp. After cooling to –40 °C, 250 mg (670 μmol) of PhI=NTs was added in small portions over a period of 5 min. The resulting suspension was stirred until a clear, green solution was obtained (typically after 3 to 5 h), which was then passed through a short column of neutral Al_2O_3 (ca. 15 g), eluting with 200 mL of EtOAc. Removal of the solvent (30 °C, 10 mbar) afforded a colorless oil, which was subjected to ^{1}H NMR analysis to assign its structure (comparison with authentic racemic samples) and to determine the degree of conversion (relative to the PhINTs consumed, using dimethyl 1,3-benzenedicarboxylate as an internal standard). The enantiomerically enriched amino ketones **2a–d** were analyzed by HPLC on chiral columns (Table 2).

Preparation of Racemic Samples of 2d and 4

3-{[(4-Methylphenyl)sulfonyl]amino}-4-chromanone (2d): A sample of 124 mg (621 μmol) of 3-amino-4-chromanone hydrochloride was dissolved in 3 mL of pyridine and the solution was cooled to 0 °C. After the addition of 133 mg (700 μmol) of tosyl chloride, the reaction mixture was stirred at room temp. (ca. 20 °C) for 21 h. After removal of the solvent (30 °C, 10 mbar), the residue was treated with 10 mL of a mixture of ice and 2 N HCl. The orange precipitate thus formed was collected, washed with cold ethanol, and dried over P_4O_{10} (156 mg, 79%). Double recrystallization from ethanol yielded 61.8 mg (31%) of **2d** as colorless needles; m.p. 129–130 °C. – IR (KBr): $\tilde{\nu}$ = 3264 cm^{-1} (NH), 3030 (CH), 2889 (CH), 1696 (C=O), 1647 (C=C), 1608, 1578, 1480, 1345, 1216, 1168, 961, 820. – ^{1}H NMR: δ = 2.40 (s, 3 H), 3.98–4.25 (m, 2 H), 4.89 (dd, *J* = 5.2 Hz, *J* = 15.4 Hz, 1 H), 5.76 (br. s, 1 H, NH), 6.96 (d, *J* =

8.4 Hz, 1 H), 7.03 (d, J = 7.2 Hz, 1 H), 7.32 (d, J = 7.9 Hz, 2 H), 7.50 (t, J = 7.3 Hz, 1 H), 7.79 (t, J = 6.2 Hz, 1 H), 7.81 (d, J = 8.2 Hz, 2 H). – ^{13}C NMR: δ = 21.5, 54.8, 70.4, 118.0, 118.8, 121.9, 127.3, 127.5, 130.0, 135.1, 137.0, 144.2, 161.8, 188.6. – $C_{16}H_{15}NO_4S$ (317.4): calcd. C 60.55, H 4.76, N 4.41, S 10.10; found C 60.46, H 4.70, N 4.35, S 9.95.

(*Z*)-3-Methyl-1-[(4-methylphenyl)sulfonyl]-2-phenyl-2-aziridinol Acetate (4): To a solution of 176 mg (1.00 mmol) of enol acetate **1aδ** and 336 mg (900 μmol) of (*N*-tosylimino)iodobenzene in 7 mL of MeCN at 0 °C was added a solution of 29.8 mg (80.0 mmol) of $[Cu(MeCN)_4]PF_6$ in 3 mL of acetonitrile and the mixture was stirred for ca. 2 h. It was then passed through a short column of neutral Al_2O_3 (ca. 15 g) and eluted with 200 mL of EtOAc. After removal of the solvent (30 °C, 10 mbar), purification of the crude product by flash chromatography (PE/EtOAc, 8:1, + 1% NEt_3) yielded 234 mg (75%) of **4** as a colorless powder; m.p. 103–104 °C. – IR (KBr): $\tilde{\nu}$ = 3056 cm^{-1} (CH), 2979 (CH), 1753 (C=O), 1679, 1595, 1451, 1334, 1209, 1160, 1089, 1001, 956, 816. – ^{1}H NMR: δ = 1.33 (d, J = 5.8 Hz, 3 H), 2.03 (s, 3 H), 2.42 (s, 3 H), 3.79 (q, J = 5.8 Hz, 1 H), 7.22–7.39 (m, 5 H), 7.53 (d, J = 7.8 Hz, 2 H), 7.60 (d, J = 8.3 Hz, 2 H). – ^{13}C NMR: δ = 12.6, 20.8, 21.5, 44.7, 79.1, 127.6, 127.9, 129.1, 129.4, 129.8, 131.5, 135.9, 144.3, 168.3. – $C_{18}H_{19}NO_4S$ (345.4): calcd. C 62.59, H 5.54, N 4.06, S 9.28; found C 62.64, H 5.61, N 3.78, S 9.35.

Synthesis of Optically Active Amino Ketones 2a,b

(*S*)-2-{[(4-Methylphenyl)sulfonyl]amino}propiophenone (2a): To a solution of 893 mg (2.92 mmol) of (1*R*,2*S*)-[*N*-(4-methylphenyl)sulfonyl]norephedrine in 60 mL of acetone at 0 °C was added 0.95 mL (2.09 mmol, 1.07 equiv.) of Jones' reagent (2.2 M) and the reaction mixture was stirred for 15 min. at room temp. After the addition of 5 mL of ethanol, the mixture was diluted with 90 mL of distilled water, extracted with ethyl ether (4 × 50 mL), and the combined extracts were dried over Na_2SO_4. After removal of the solvent (30 °C, 10 mbar), flash chromatography of the residue on silica gel (hexane/EtOAc, 5:1) yielded 480 mg (54%) of a colorless powder (*ee* > 98%). – ^{1}H NMR: δ = 1.37 (d, J = 7.3 Hz, 3 H), 2.28 (s, 3 H), 4.94 (quint., J = 7.4 Hz, 1 H), 5.92 (d, J = 7.9 Hz, 1 H, NH), 7.14 (d, J = 8.7 Hz, 2 H), 7.41 (t, J = 7.5 Hz, 2 H), 7.56 (t, J = 7.3 Hz, 1 H), 7.69 (d, J = 8.3 Hz, 2 H), 7.73 (d, J = 7.2 Hz, 2 H). – ^{13}C NMR: δ = 20.9, 21.3, 53.2, 126.9, 128.4, 128.7, 129.5, 133.2, 134.0, 137.0, 143.4, 198.0. – $[\alpha]_D^{20}$ = +62.6 ($CHCl_3$, c = 1.00).

(*S*)-1-{[(4-Methylphenyl)sulfonyl]amino}-1-phenylacetone (2b): To a solution of 763 mg (2.50 mmol) of (*S*)-α-{[(4-methylphenyl)sulfonyl]amino}benzeneacetic acid and 1.17 mL (7.75 mmol) of TMEDA in 12.5 mL of THF at –78 °C was added 6.20 mL (7.75 mmol) of MeLi in Et_2O (1.25 M). After stirring for 1 h at –78 °C, the reaction mixture was allowed to warm to room temp. and stirred for a further 2 h. It was then cooled by means of an ice-bath and poured into 75 mL of ice-cold 2 M H_3PO_4 solution. The resulting mixture was extracted with EtOAc (3 × 20 mL), the combined organic layers were washed with aq. $NaHCO_3$ solution (3 × 20 mL) and brine (2 × 20 mL), and dried over Na_2SO_4. Removal of the solvent (30 °C, 10 mbar) and subsequent flash chromatography of the residue on silica gel (hexane/EtOAc, 4:1) yielded 75.0 mg (10%) of **2b** as a colorless powder (*ee* 96%); m.p. 139–140 °C (ref.[18] 142 °C). – ^{1}H NMR: δ = 1.91 (s, 3 H), 2.26 (s, 3 H), 4.94 (d, J = 5.0 Hz, 1 H), 5.98 (d, J = 4.9 Hz, 1 H, NH), 6.99–7.41 (m, 9 H). – ^{13}C NMR: δ = 21.1, 26.2, 66.3, 127.2, 128.4, 129.0, 135.4, 137.6, 143.6, 202.6. – $[\alpha]_D^{20}$ = +258.4 ($CHCl_3$, c = 1.00).

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