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Highly asymmetric cobalt-catalyzed aziridination of alkenes with trichloroethoxysulfonyl azide $(TcesN_3)^{\dagger \ddagger}$

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A Co(Π)-based catalytic system has been developed for asymmetric aziridination of alkenes with trichloroethoxysulfonyl azide (TcesN₃) under mild conditions, forming the corresponding *N*-Tces-aziridines in high yields and excellent enantioselectivities.

Aziridines, the smallest nitrogen heterocyclic compounds, exhibit numerous important applications, including serving as essential motifs of biologically interesting compounds and as valuable synthons for preparation of various amine derivatives.¹ Among several approaches, metal-catalyzed asymmetric aziridination of alkenes with proper nitrene sources represents one of the most general and direct methods for stereoselective construction of the three-membered ring structure.² As the common nitrene source, iminoiodane derivatives such as PhI=NTs and its variants have been successfully employed for asymmetric aziridination of certain types of alkenes in catalytic systems that are primarily based on chiral Cu complexes.³ While some of the most promising Cu-catalyzed systems can efficiently aziridinate internal alkenes having additional functionalities (such as cinnamate esters) with high enantioselectivity, they are significantly less effective for simple terminal olefins (such as styrenes), suggesting the requirement of secondary binding interactions.³ Despite the perceived ineffectiveness of azides for metal-catalyzed nitrene transfer reactions, recent results from several groups⁴⁻⁸ suggest the potential of azides as a class of general nitrene sources with several attractive features.⁹ Through the discovery of new chiral catalysts, asymmetric aziridination with azides may be further developed into a broad and useful catalytic process.

We recently disclosed the unique catalytic properties of Co(II) complexes of porphyrins for olefin aziridination and C–H amination with different azides, including diaryl-phosphoryl and arylsulfonyl azides.⁸ To improve catalytic efficacy and to control enantioselectivity, efforts have been made to identify more effective azides and to employ suitable chiral porphyrin ligands for the development of Co-catalyzed asymmetric aziridination with azides. Herein, we report a highly asymmetric aziridination process that consists of

trichloroethoxysulfonyl azide (TcesN₃) as a new nitrene source and Co(II) complexes of D_2 -symmetrical chiral porphyrins ([Co(Por*)]) (Fig. 1) as catalysts (Scheme 1).¹⁰ The [Co(Por*)]– TcesN₃-based system is operationally simple and capable of aziridinating both aromatic and aliphatic olefins under mild conditions, forming the corresponding *N*-Tces-aziridines in high yields and excellent enantioselectivities. Furthermore, the catalytic system could be conveniently recycled and reused multiple times through a simple precipitation/filtration protocol without significant loss of reactivity and selectivity. In addition, a noteworthy additive effect of Pd(OAc)₂ on the yield of the Co-catalyzed aziridination is also described.

Among the various azides that were evaluated, TcesN₃, a new azide that was readily synthesized from CCl₃CH₂OH in high yield and on a multigram scale, turned out to be one of the most promising nitrene sources for [Co(Por*)]-catalyzed asymmetric aziridination due to its high reactivity and convenient usage.^{11,12} As summarized in Table 1 and Table S1 (ESI[‡]) for the aziridination of styrene, although the Co(II) complexes of P1 and P2 derived from chiral cyclopropanecarboxamide could effectively catalyze the reaction at room temperature, the enantioselectivities were low (entries 1 and 2). Employment of P3 and P4, which contain chiral methoxypropionamide, improved both yield and enantioselectivity (entries 3 and 4). While no further improvement was observed with P5, high enantioselectivity was achieved by using [Co(P6)] where the Co(II) center is surrounded by methoxy and chiral tetrahydrofurancarboxamide units, albeit in lower



Fig. 1 Structures of D_2 -symmetric chiral cobalt(II) porphyrins.



Scheme 1 Asymmetric Co(II)-catalyzed aziridination with TcesN₃.

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[‡] Electronic supplementary information (ESI) available: Experimental procedures and analytical data for all compounds; crystallography data for 2-(4-chlorophenyl)-1-aziridine-sulfonic acid 2',2',2'-trichloroethyl ester. CCDC 724786. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b905727g

 Table 1
 Enantioselective aziridination of styrene with trichloroethoxysulfonyl azide by chiral cobalt(II) porphyrins^a

<u> </u>	N ₃ SO ₃ CH ₂ CCl ₃	[Co(Por*)] N ₂	
	TcesN ₃	C ₆ H ₅ Cl, 4 Å MS	Tces

Entry	$[Co(Por^*)]^b$	mol (%)	$Temp/^{\circ}C$	$\operatorname{Yield}^{c}(\%)$	$\operatorname{Ee}^{d}(\%)$
1	[Co(P1)]	2.0	RT	80	25
2	[Co(P2)]	2.0	RT	84	4
3	[Co(P3)]	2.0	RT	90	-39
4	[Co(P4)]	2.0	RT	95	-51
5	[Co(P5)]	2.0	RT	85	52
6	[Co(P6)]	2.0	RT	58	86
7	[Co(P6)]	5.0	RT	79	88
8	[Co(P6)]	5.0	RT	90	88
9	[Co(P6)]	5.0	0	69	94
10^e	[Co(P6)]	5.0	0	91	94
11	[Co(P6)]	5.0	-10	15	96
12^e	[Co(P6)]	5.0	-10	59	96

yields. ^d Measured by chiral HPLC. ^e Added 5 mol% Pd(OAc)₂

yield (entries 5 and 6). The yield of [Co(**P6**)]-catalyzed reaction could be greatly increased by raising catalyst loading without affecting the high ee value (entries 7 and 8). When conducted at lower temperatures, the enantioselectivity was further improved to 94–96% ee, but at a sacrifice of yields (entries 9 and 11). Interestingly, addition of a catalytic amount of Pd(OAc)₂ resulted in a dramatic increase in yields with no effect on the high enantioselectivity (entries 10 and 12), presumably due to the activation of styrene by the π -electrophilic Lewis acid, Pd(OAc)₂.¹³

With the optimization of catalytic conditions, the substrate scope of the [Co(P6)]-TcesN₃-based system was examined (Table 2). Like styrene (entry 1), its various derivatives were also excellent substrates, including those substituted with alkyl (entries 2-5) and halogen (entries 6-10) groups at different ring positions. The corresponding aziridines were produced in high yields and excellent enantioselectivities.⁴ In the case of 2-bromostyrene, the desired product was isolated in 92% yield and 99% ee (entry 10). Styrene derivatives containing strongly electron-withdrawing groups were suitable substrates as well albeit in lower ee (entries 11 and 12). Furthermore, the aziridination of 2-vinylnaphthalene and α-methylstyrenes was successfully performed (entries 13-15). When an enol derivative was used as the substrate, the corresponding α-amino ketone was obtained in high yield as a result of ringopening of the aziridine product (entry 16). In addition to aromatic olefins, aliphatic olefins could be aziridinated in high enantioselectivities, but low yields (entries 17-19).¹⁴ Finally, the catalytic system could also be applied for the aziridination of aliphatic dienes and cyclic olefins (entries 20 and 21).

The absolute configuration of the aziridination product of 4-chlorostyrene, 2-(4-chlorophenyl)-1-aziridine-sulfonic acid 2',2',2'-trichloroethyl ester (Table 2, entry 6), was established to be (*R*) by X-ray crystallographic analysis (Fig. 2). In view of the same sign of optical rotations, all the other aziridine derivatives from aromatic olefins and conjugate dienes (Table 2, entries 1–15 and 20) are expected to have the same

Table 2	[Co(P6)]-catalyzed enantioselective aziridination of different
alkenes	with trichloroethoxysulfonyl azide (TcesN ₃) ^a

Entry	Olefin	Aziridine	Temp/°C	Yield ^b (%)	Ee ^c (%)	$[\alpha]^d$
1	\bigcirc	NTces	0	91	94	(-)
2	Me	Me	0	89	90	(-)
3 ^f	Me	Me ANTCES	RT	85	82	(-)
4 ^{<i>f</i>}	Me	Me NTces	RT	86	84	(-)
5	t-Bu	<i>t</i> -Bu	0	89	85	(-)
6		CI	0	93	91	(-) $(R)^e$
7	Br	Br	0	92	91	(-)
8	F	F NTces	0	90	90	(-)
9	Br		0	91	88	(-)
10	Br		0	92	99	(-)
11	CF3	CF3	0	88	81	(-)
12	NO ₂	NTces	0	82	80	(-)
13	\bigcirc	NTces	0	85	90	(-)
14 ^f	Me	Me NTces	RT	48	80	(-)
15 ^f	CI	CI Me NTces	RT	43	80	(-)
16 ^f	OTMS		40	87	—	_
17 ^g	Et~~		40	42	91	(+)
18^g	Bu	Bu	40	30	90	(+)
19 ^f	Ph~~	Ph	0	26	94	(+)
20 ^{<i>h</i>}	Me Me		RT	53	87	(-)
21 ^{<i>f</i>}	A	A NITaga	40	85	_	_

^{*a*} Performed in C₆H₃Cl using 5 mol% [Co(**P6**)] for 48 h under N₂ with 4 Å MS in the presence of 5 mol% Pd(OAc)₂; alkene : TcesN₃ = 5 : 1; [alkene] = 0.25 M. ^{*b*} Isolated yields. ^{*c*} Measured by chiral HPLC. ^{*d*} Sign of optical rotation. ^{*e*} Determined by X-ray crystal structural analysis. ^{*f*} 24 h without Pd(OAc)₂. ^{*g*} Using [Co(**P5**)] in CH₂Cl₂ for 48 h. ^{*h*} In MeCO₂Et.

Fig. 2 X-ray crystal structure of 2-(4-chlorophenyl)-1-aziridinesulfonic acid 2', 2', 2'-trichloroethyl ester (Table 2, entry 6).

 Table 3 Reusability of [Co(P6)] for asymmetric aziridination^a

	+ N₃SO₃C⊢ βr TcesN₃	$\frac{[Co(P6)]}{C_6H_5Cl/4}$	A MS Br	1 N Tces
Entry	Cycle	Temp/°C	$\operatorname{Yield}^{b}(\%)$	ee ^c (%)
1	First	RT	95	96
2	Second	RT	89	94
3	Third	RT	81	94

^{*a*} Performed in C₆H₅Cl using 5 mol% [Co(**P6**)] for 48 h under N₂ with 4 Å MS in the presence of 5 mol% Pd(OAc)₂: alkene–TcesN₃ = 5 : 1; [alkene] = 0.25 M. ^{*b*} Isolated yields. ^{*c*} Measured by chiral HPLC.

(*R*) absolute configuration by analogy. It was interesting to note that the aziridine products from the reactions of aliphatic olefins exhibited the opposite sign of optical rotations (Table 2, entries 17-19).

To enhance the practicality of the [Co(P6)]-TcesN₃-based catalytic system, a simple precipitation/filtration protocol was established to allow for the recycling/reusing of the catalyst. After each catalytic cycle, [Co(P6)] could be completely precipitated without change (see ESI‡) by adding hexanes where it absorbed uniformly to the molecular sieves (MS) preexisting in the system. The MS-absorbed [Co(P6)] was then filtered, dried under vacuum with heating, and reused. As demonstrated with the reaction of 2-bromostyrene, the catalytic system could be recycled/reused three times without significant loss of either yield or enantioselectivity (Table 3).

In summary, we have developed a highly efficient aziridination system based on [Co(P6)] and $TcesN_3$. This represents the first highly effective and enantioselective catalytic system for asymmetric aziridination of a broad range of simple olefins, without the need of additional functionalities in the substrates for secondary binding interactions. In addition to the common attributes associated with the use of azides as the nitrene sources,⁹ a simple protocol has been established for the [Co(P6)]-TcesN₃-based system to allow for the recycling/reusing of the catalyst, further enhancing its potential for practical synthetic applications. This Co-catalyzed asymmetric aziridination with TcesN₃ complements the previous Cu/ArI==NTs-based systems,³ which are suitable for internal olefins having additional functionalities.

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