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Asymmetric olefin aziridination using a newly designed Ru(CO)(salen) complex as the catalyst†

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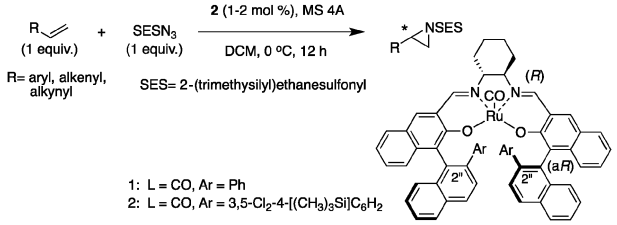
Highly enantioselective and good to high-yielding aziridination of conjugated and non-conjugated terminal olefins and cyclic olefins was achieved using a newly designed Ru(CO)(salen) complex as the catalyst in the presence of $SESN_3$ under mild conditions.

Aziridines, three-membered ring heterocycles with one amino group, have been recognized as versatile intermediates for organic synthesis.[1] Since Kwart and Khan's first report on metal-catalyzed nitrene-transfer reactions in 1967,[2] much effort has been directed toward developing enantioselective aziridination of alkenes with a nitrene source. Highly enantioselective reactions have been developed by using a chiral copper or manganese complex as a catalyst in the last two decades.[3] These aziridination reactions, however, use *N*-arylsulfonyliminophenyliodinanes (PhI=NTs) or their equivalents as a nitrene source, and the reactions are thus not very atom-efficient. Although Kwart and Khan used atom-efficient azide compounds as nitrene sources,[2] azide compounds had not been employed as nitrene sources in the subsequent studies mainly because of two reasons:[4] (i) harsh conditions (heating or UV irradiation) are needed for azide decomposition[5,6] and (ii) *N*-deprotection is difficult. Recently, azides having readily removable *N*-protecting groups such as *o*- or *p*-nitrobenzenesulfonyl (*o*- or *p*-Ns)[7] and 2-(trimethylsilyl)ethanesulfonyl (SES)[8] groups have been developed. In addition, Bach and Körber reported that iron(II) chloride decomposes azides and transfers nitrenes to sulfides under mild conditions, though not with enantioselectivity.[9]

In previous reports, we also found that chiral Ru(CO)(salen) complexes efficiently decompose azides at room temperature and catalyze asymmetric imidation of sulfides and aziridination.[10]

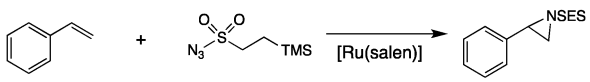
For example, complex **1** catalyzes alkyl aryl sulfide imidation with high enantioselectivity (93–99% ee).[10a] However, when the substrate was olefin, aziridination occurred competitively with intramolecular C–H amination at the C2″-phenyl ring of the complex.[11] Eventually, complex **2** having the 3,5-dichloro-4-trimethylsilylphenyl group at C2″ was synthesized to catalyze aziridination of conjugated terminal olefins using $SESN_3$ at low catalyst loading in a high enantioselectivity (92–>99% ee) (Scheme 1); however, the reactions of non-conjugated 1-alkenes such as 1-octene were slow even under reflux conditions and showed moderate enantioselectivity.[10d] The turnover number (TON) in the aziridination of styrene was 260 (Table 1, entry 1). Recently, Zhang *et al.* reported that a Co(II)–porphyrin complex catalyzed highly enantioselective aziridination of conjugated and non-conjugated terminal olefins with trichloroethoxysulfonyl azide ($TcesN_3$) in the presence of a co-catalyst, $Pd(OAc)_2$.[12]



Scheme 1 Asymmetric aziridination using a Ru(CO)(salen) complex as a catalyst.

However, there is still the need for identifying a catalyst that expands the substrate scope and reduces the catalyst loading and the additive amount of the substrate, effectively improving the asymmetric catalytic aziridination. In order to address these requirements, increasing the activity of a putative nitrenoid

Table 1 Comparison of the aziridination reaction conditions[a]



Entry	Catalyst	mol (%)	Temp (°C)	Time (h)	Yield[b] (%)	ee[c] (%)
1[d]	**2**	0.1	0	12	26	91
2	**3**	0.5	RT	20	99	90
3[e]	**3**	0.1	RT	20	57	90
4	**4**	1	RT	20	93	86

[a] Unless otherwise noted, reactions were carried out with styrene (0.12 mmol) and azide (0.1 mmol) in 0.25 mL of CH_2Cl_2. [b] Isolated yield after silica gel column chromatography. [c] Determined by chiral HPLC. [d] Taken from ref. 10d (styrene/$SESN_3$ = 1/1). [e] Run on a 0.3 mmol scale.

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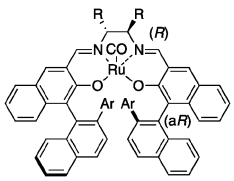
intermediate and enhancing catalyst durability are essential. Herein, we report the highly enantioselective aziridination of conjugated and non-conjugated olefins using a novel Ru(CO)(salen) complex as a catalyst in the presence of $SESN_3$ as a nitrene source.

It has been reported that a sulfonyl oxygen atom of *N*-sulfonyl nitrenoid interacts with the electrophilic nitrenoid *N*-atom or with the metal center and undergoes aziridination.[13] Based on these reports, we inferred that the reactivity of the nitrenoid intermediate would be enhanced if the sulfonyl oxygen atom on the metal-nitrenoid were to interact with a ligand having a vacant orbital in close proximity to the oxygen atom.[14] Moreover, if a C–F* antibonding orbital can interact with the π-orbital of the aryl group at the C2″ position,[15] the tolerance of the complex to an electrophile should also be enhanced. As such, we expected that a Ru(CO)(salen) complex bearing a C–F bond located at the appropriate position would show good catalytic activity for aziridination. Thus, we synthesized complexes **3** and **4** as having a 3,5-di(trifluoromethyl)phenyl group at the C2″ position. Complex **3** was stable under the conditions for the aziridination of styrene (Table 1) and its turnover number amounted to 570 without diminishing enantioselectivity (entry 3). Complex **4** also showed good tolerability, though enantioselectivity was slightly inferior to that of complex **3** (entry 4).



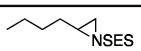
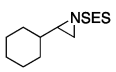
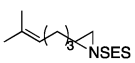
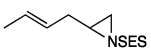
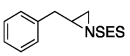
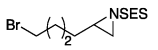
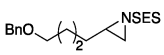
3: R = phenyl, L = CO, Ar = 3,5-$(CF_3)_2C_6H_3$
4: R,R = -$(CH_2)_4$-, L = CO, Ar = 3,5-$(CF_3)_2C_6H_3$

Based on these results, we examined the aziridination of non-conjugated terminal olefins using **3** as the catalyst (Table 2). To our delight, the aziridination of 1-hexene proceeded smoothly using 3 mol% of the catalyst **3** with a molar ratio of olefin/azide = 3/1 at room temperature in a good yield (74% yield) and excellent enantioselectivity (99% ee, entry 1). The reaction of vinylcyclohexane also showed excellent enatioselectivity (99% ee) under the same conditions (entry 2). To examine the regioselectivity for the aziridination of alkadienes, reactions of 7-methyl-1,6-octadiene and 1,4-hexadiene were carried out. Both reactions solely produced the terminal aziridine products over the internal aziridines in good yields (54% and 58%) and high enantioselectivity (89% ee at 0 °C and 91% ee) (entries 3 and 4). However, terminal allylic C–H amination was observed in the reaction of 1,4-hexadiene.

The reaction of 3-phenyl-1-propene was slower than that of other 1-alkenes, but the reaction proceeded at 40 °C under solvent-free conditions with high enantioselectivity (90% ee) and yield (91%) (entry 5). Moreover, 6-bromo-1-hexene was quite reactive and the reaction proceeded at 0 °C with high enantioselectivity (91% ee) (entry 6). The reaction of 6-benzyloxy-1-hexene also proceeded with a good yield and high enantioselectivity at 0 °C (65% and 87% ee) (entry 7).

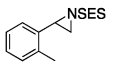
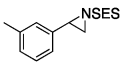
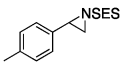
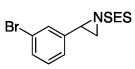
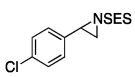
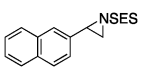
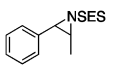
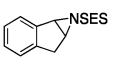
We also examined the aziridination of aromatic olefins (Table 3). Styrene derivatives, possessing an alkyl (entries 1–3) or a halogen (entries 4 and 5) group at different position, efficiently underwent aziridination in excellent yields and high enantioselectivity with low catalyst loading (0.5–1 mol%) under mild conditions. In particular, *o*-methylstyrene produced the highly enantioenriched aziridine (97% ee). Additionally, aziridination of 2-vinylnaphthalene proceeded in excellent yield and high enantioselectivity (entry 6). Moreover, the reactions of *cis*-disubstituted olefins, *cis*-β-methylstyrene and indene proceeded with excellent enantioselectivities (≥ 97% ee) and moderate

Table 2 Asymmetric aziridination of 1-alkenes using Ru(CO)(salen) **3** as the complex[a]

Entrty	Substrate	mol (%)	Temp (°C)	Time (h)	Yield[b] (%)	ee[c] (%)
1		3	25	24	74	99
2		3	25	24	45	99
3[d]		3	0	24	54	89
4[e]		3	25	24	58	91
5[f]		3	40	24	91	90
6		3	0	24	95	91
7		3	0	24	65	87

[a] Unless otherwise noted, reactions were carried out on a 0.3 mol scale in 0.4 mL of CH_2Cl_2. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] A trace amount of the C–H amination product was observed by TLC. [e] 6-(SESamino)hexa-1,4-diene was obtained in 35% yield. [f] Neat reaction.

Table 3 Asymmetric aziridination of aromatic olefins using Ru(CO)(salen) **3** as the complex[a]

Entry	Substrate	mol (%)	Temp (°C)	Time (h)	Yield[b] (%)	ee[c] (%)
1		0.5	25	6	95	97
2		0.5	25	6	98	90
3		0.5	25	6	95	89
4		1	25	6	95	90
5		1	25	6	96	90
6		0.5	25	6	99	91
7		1	25	12	72	99
8		1	25	12	66	97

[a] Unless otherwise noted, reactions were carried out on a 0.3 mol scale with styrene/azide (1.2/1.0) in 0.4 mL of CH_2Cl_2. [b] Isolated yield. [c] Determined by chiral HPLC analysis.

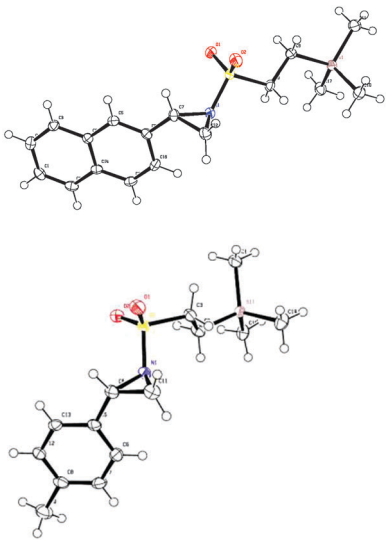


Fig. 1 X-ray crystal structures of 2-(naphthalene-2-yl)-1-[2-(trimethylsilylethane)sulfonyl]aziridine (a) and 2-(4-methylphenyl)-1-[2-(trimethylsilylethane)sulfonyl]aziridine (b).

yields (entries 7 and 8). The reaction of *trans*-β-methylstyrene gave only the allylic amination product in *ca.* 40%.[16]

The absolute configuration of the synthesized aziridines was unknown, except for that of *N*-SES-2-phenylaziridine which was determined by comparison of its optical rotation value with the reported one.[17] In this study, we obtained single crystals of 2-(naphthalen-2-yl)-1-[2-(trimethylsilylethane)sulfonyl]aziridine and 2-(4-methylphenyl)-1-[2-(trimethylsilylethane)sulfonyl]aziridine and determined their configuration to be *S* by X-ray crystallographic analysis (Fig. 1).[17] Absolute configuration of 2-methyl-3-phenyl-1-{[2-(trimethylsilyl)ethane]sulfonyl}aziridine was determined to be 2*R*,3*S* by comparison of chemical rotation, after the SES-group deprotection.[17]

In conclusion, we were able to develop a durable and catalytically active new Ru(CO)(salen) complex bearing 3,5-ditrifluoromethylphenyl group **3**, which efficiently facilitated the highly enantioselective aziridination of conjugated and non-conjugated olefins using low catalyst loading (0.5–1 mol%) for conjugated olefins and 3 mol% for non-conjugated olefins.

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16 Yield was determined by ^{1}H NMR analysis of the crude reaction mixture. No aziridination product was detected.

17 For details, see the ESI†.

