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Design of a robust Ru(salen) complex: aziridination with improved turnover number using *N*-arylsulfonyl azides as precursors†

Kazufumi Omura, Tatsuya Uchida, Ryo Irie and Tsutomu Katsuki*

Department of Chemistry, Faculty of Science, Graduate School, Kyushu University 33, Hakozaki, Higashi-ku, Fukuoka 812–8581, Japan and CREST, Japan Science and Technology Agency (JST). E-mail: katsuscc@mbox.nc.kyushu-u.ac.jp; Fax: +81 92 642 2607

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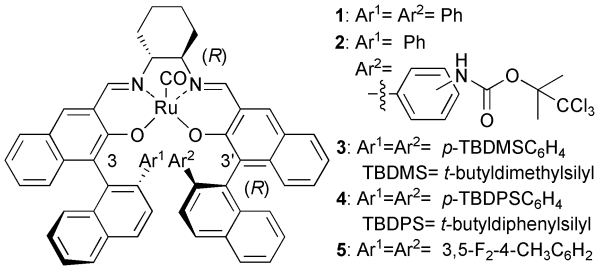
A new robust fluorinated (OC)Ru(salen) complex was designed on the basis of an X-ray structure of its parent complex to show improved turnover numbers (up to 878) and enantioselectivities (up to 99%) in aziridination reactions using *p*-toluenesulfonyl (Ts) or *p*-nitrobenzenesulfonyl (Ns) azide as the nitrene precursor; the latter is synthetically advantageous since the Ns group is *N*-protecting and can be removed under mild conditions.

Catalytic asymmetric nitrene transfer reactions such as aziridination, C–H amination and sulfimidation are current topics in organic synthesis and much effort has been directed toward these chemistries.[1–4] Although high enantioselectivity has been achieved in some reactions, most of them need *N*-arylsulfonyliminophenyliodinanes as the nitrene precursors. Use of such precursors incurs two problems in the reactions: (i) generation of iodobenzene as waste material and (ii) difficulty in removal of the arylsulfonyl group from the nitrene transfer products. In order to solve the first issue, use of arylsulfonyl azides has commanded much attention.[5–7] Although several reactions utilizing arylsulfonyl azide have been reported, most of them are non-stereoselective[5a,6,7] and the asymmetric version is only moderately enantioselective.[5b] Besides, some of them need severe reaction conditions like UV-irradiation or heating to promote the nitrene transfer.[5b,7] We have recently found that (OC)Ru(salen) complex **1** is an efficient catalyst for asymmetric sulfimidation[8] and aziridination of conjugated terminal olefins using arylsulfonyl azides as the nitrene precursor.[9] These reactions proceeded under mild conditions, but use of arylsulfonyl azides such as *p*-toluenesulfonyl azide has left the second issue unresolved. On the other hand, Fukuyama *et al.* have reported that a *p*-nitro- or *o, p*-dinitrobenzenesulfonyl group can be removed under mild conditions.[10] Unfortunately, *p*-nitrobenzenesulfonyl (Ns) azide was a less efficient nitrene precursor for the aziridination with **1** as the catalyst (*vide infra*). Furthermore, these reactions need another improvement: complex **1** was not very robust and the turnover number (TON), *e.g.*, in the aziridination, was moderate.[9]



In order to settle the second issue, we examined the use of alkoxycarbonyl azide as the precursor and found that 2,2,2-trichloro-1,1-dimethylethoxycarbonyl azide served as an efficient precursor for asymmetric sulfimidation using complex **1**.[11] During the course of this study, however, the active intermediate in the sulfimidation, the complex **1**–azide adduct,[12] was found to easily undergo intramolecular C–H amination, giving a catalytically inactive complex **2**. Since it was impossible to determine the exact location of the aminated carbon due to the complexity of the ^{1}H NMR spectrum of **2**,[12] we performed an X-ray analysis of complex **1** to pinpoint the amination site. A single crystal of **1** was obtained by recrystallization from acetonitrile–water. The X-ray structure given in Fig. 1‡ disclosed that one of the *meta*-carbons of the phenyl substituent on the 3- or 3′-naphthyl group is very close (3.59 Å) to the *N*-atom of the ruthenium-bound acetonitrile. The acetonitrile should be replaced with an azide compound upon nitrene transfer reaction,[12] and it was considered that the *meta*-carbon should be preferentially aminated by the ruthenium-bound azide. Thus, we expected that the Ru(salen) complex would become robust, if the hydrogen atoms at the *meta*-carbons are protected somehow from the C–H amination. Along this line, we synthesized complexes **3**, **4** and **5**. The bulky *p*-silyl groups introduced in **3** and **4** were expected to protect the vicinal *meta*-hydrogen atoms sterically against the intramolecular C–H amination. In the case of **5**, the *meta*-hydrogen atoms were replaced with fluorine atoms. The *para*-methyl group was introduced for the convenience of its synthesis. With these new complexes as catalysts, we first examined aziridination of styrene (Table 1). Aziridination using 2 mol% of **3** as the catalyst gave the desired product in a quantitative yield without diminishing enantioselectivity (entry 1). The reaction using 0.1 mol% of **3** gave the product in 41% yield, indicating that TON was remarkably improved to 410 (entry 2). It is noteworthy that, despite the presence of the bulky TBDMS group, **3** showed higher catalytic activity than **1** (entry 3): turnover frequency (TOF) of **3** in the initial minute was 27, though TOF of **1** was 8. The reason for this enhanced catalytic activity of **3** is unclear at present. Aziridination with **4** also showed the same enantioselectivity, but **4** was a little inferior to **3** in terms of TON (entry 4). However, TON was further improved up to 867 albeit with slightly diminished enantioselectivity (85% ee), when **5** was used as the catalyst (entry 5). TOF of **5** in the reaction amounted to 28. Aziridination of *p*-bromostyrene was also examined with complexes **3** and **5**: both reactions showed the same enantioselectivity of 90% ee, and the higher TON of 878 was again attained by using complex **5** as catalyst (entries 6 and 7).

Based on these results, we next examined aziridination of various conjugated terminal olefins using **5** as a catalyst. All the reactions

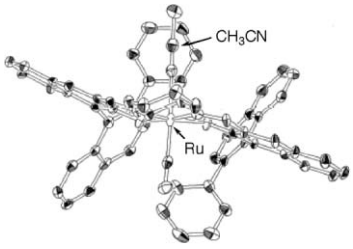


Fig. 1 An ORTEP diagram for the X-ray structure of **1**. The hydrogen atoms and solvent molecules are omitted for clarity.

† Electronic supplementary information (ESI) available: typical experimental procedures, determination of enantiomeric excess and elementary analysis for complexes **3** and **5**. See http://www.rsc.org/suppdata/cc/b4/b407693a/

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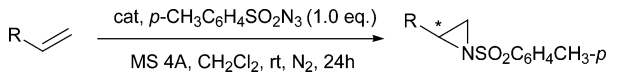
Table 1 Catalytic asymmetric aziridination of various olefins [a]



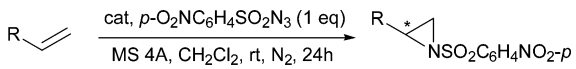
Entry	Catalyst	R or substrate	Yield (%)	ee (%)	TON
1[b]	**3** (2)	Ph	100	87	—
2[b]	**3** (0.1)	Ph	41	87	410
3[b]	**1** (2)	Ph	71	87	36
4[b]	**4** (0.1)	Ph	23	87	230
5[b]	**5** (0.09)	Ph	78	85	867
6	**3** (0.1)	*p*-BrC_6H_4	33	90	330
7	**5** (0.09)	*p*-BrC_6H_4	79	90	878
8	**5** (0.09)	*p*-$O_2NC_6H_4$	34	87	378
9	**5** (0.09)	2-$C_{10}H_7$	65	87	722
10	**5** (0.09)	PhC≡C	61	96	678
11	**5** (2)	*n*-C_6H_{13}	20	86	10
12	**3** (2)	*n*-C_6H_{13}	30	86	15
13[c]	**5** (2)	Indene	36	>99	18

[a] See ESI for the typical experimental procedures and the determination of ee. [b] Absolute configuration of the product is *S*. [c] Absolute configuration of the product is 1*S*,2*R*.

showed high enantioselectivity of 87% ee and above together with much improved TONs greater than 377 (entries 8–10). Furthermore, aziridination of 1-octene, a non-conjugated olefin, was also found to proceed with high enantioselectivity (86% ee), albeit with moderate yield (entry 11). Notably, this reaction did not occur when complex **1** was used as a catalyst.[13] It should be also mentioned that, in this reaction only, complex **3** showed somewhat better TON than complex **5**, though the reason is unclear (entry 12). Aziridination of indene with **5** showed excellent enantioselectivity of >99% ee, though the TON was again moderate (entry 13).[14]

As described above, Ns azide was a poor nitrene precursor for aziridination using **1** as catalyst (Scheme 1). The high catalytic activity of **5**, however, prompted us to examine the nitrene transfer reaction using Ns azide as the precursor. The reaction of styrene proceeded with high enantioselectivity (84% ee), albeit with moderate yield, to give the corresponding aziridine. The reaction was completed when catalyst-loading was increased to 4 mol%.† Aziridination of *p*-bromostyrene and 1-phenyl-3-buten-1-yne also proceeded with high enantioselectivity and good chemical yield. However, 1-octene did not undergo aziridination under the present conditions.

In conclusion, we were able to reasonably design new robust (OC)Ru(salen) complex **5**. This new complex shows much higher endurance and catalytic activity than **1**, remarkably expanding the scope of aziridination and possibly of other nitrene-transfer reactions using azide compounds as nitrene precursors. In particular, introduction of the complex allows the use of *p*-nitrobenzenesulfonyl azide as a useful precursor. Finally, the present study demonstrated that iminoiodinane compounds now generally used as nitrene precursors should be replaced by easily available and atom-efficient azide compounds.



R= Ph: **1** (4 mol%): 82% ee, 22%, (*S*), TON= 5
R= Ph: **5** (1 mol%): 84% ee, 34%, (*S*), TON= 34
R= Ph: **5** (4 mol%): 84% ee, 100%, (*S*)
R= PhC≡C: **5** (4 mol%): 90% ee, 100%
R= *p*-BrC_6H_4: **5** (4 mol%): 81% ee, 66%

Scheme 1 Catalytic asymmetric aziridination with NsN_3.

Notes and references

‡ Crystallographic data: **1**, $C_{61}H_{44}N_2O_3Ru{\cdot}5CH_3CN$, M = 1159.36, T = 123 K, orthorhombic, space group $P2_12_12_1$, a = 13.5262(3), b = 19.7791(5), c = 21.9184(6) Å, V = 5863.9(3) Å^3, Z = 4, R = 0.059 ($I > 2\sigma(I)$), wR = 0.160 (all data), GOF = 0.97. CCDC 236739. See http://www.rsc.org/suppdata/cc/b4/b407693a/ for crystallographic data in .cif format.

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