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Mn(salen)-catalyzed enantioselective C–H amination

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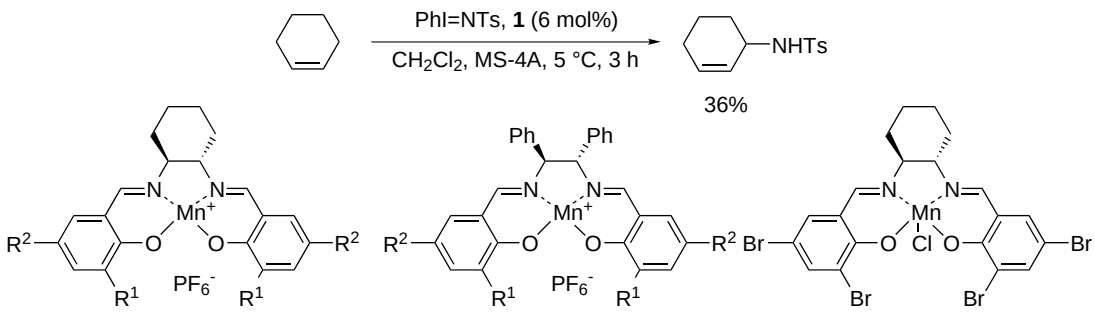
Abstract—A chiral 3,3′,5,5′-tetrabromosubstituted (salen)manganese(III) complex was found to be an efficient catalyst for asymmetric C–H amination (up to 89% ee). In the reaction of cycloalkenes, allylic amination occurred in preference to aziridination. © 2001 Elsevier Science Ltd. All rights reserved.

(Salen)manganese(III) complexes [hereafter referred to as Mn(salen)] serve as catalysts for aziridination.[1] We have disclosed that some optically active Mn(salen)s, especially second-generation Mn-salen possessing axial chirality as a chiral element, catalyze highly enantioselective aziridination of styrene derivatives.[1b,1c] On the other hand, a nitrido (salen)manganese(V) complex was recently found to undergo nitrene transfer reactions in the presence of triflic anhydride or trifluoroacetic anhydride.[2] Subsequent to this, an optically active nitrido (salen)manganese(V) complex was reported to undergo stoichiometric but highly enantioselective aziridination.[3] These aziridination reactions have been considered to proceed via nitrenoid intermediates which are an electrophilic species. In order to expand the scope of Mn(salen)-catalyzed aziridination, we synthesized cationic Mn(salen)s **1**–**10** bearing electron-withdrawing substituents, expecting that such Mn(salen)s would show higher catalytic activity. We first examined aziridination of cyclohexene using **1**[4] as the catalyst in the presence of [*N*-(*p*-toluenesulfonyl)imino]phenyliodinane. Contrary to our expectation, no aziridination occurred and allylic C–H amination proceeded exclusively (Scheme 1).

Thus far, many methodologies for C–H amination have been reported. The first C–H amination was reported with manganese–porphyrin complexes as catalysts.[5] Although C–H amination via a nitrenoid species often competes with aziridination,[6] electron-deficient manganese-,[7] ruthenium-,[7b] and rhodium porphyrin complexes[7c] were recently reported to catalyze C–H



Scheme 1.

Keywords: (salen)manganese(III) complex; asymmetric C–H amination; benzylic amination; allylic amination.
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amination exclusively. Besides metalloporphyrin complexes, ruthenium cyclic amine and bipyridine complexes[8] have been disclosed to be efficient catalysts for C–H amination, and copper salts have also been reported to promote C–H amination selectively under modified Kharash–Sosnovsky conditions using peroxycarbamate as an oxidant.[9,10] Efforts have been directed toward asymmetrization of some of these methodologies; however, success has been limited.[6d,9,11] On the other hand, our new result seemed to be compatible with the results observed with electron-deficient metalloporphyrin complexes. Therefore, we examined asymmetric C–H amination with chiral Mn(salen) complexes bearing electron-withdrawing groups as the catalysts.

We first examined benzylic amination of indan with various Mn(salen)s as catalysts (Table 1). Non-substituted Mn(salen) ent-**7** showed poor catalytic activity (entry 8). Mn(salen) **1** bearing electron-withdrawing fluoro groups exhibited higher catalytic activity as expected, especially when chloro and bromo groups were the electron-withdrawing group (entries 1–5). Complex **3** and its enantiomer ent-**3** showed the same level but opposite sense of enantioselectivity, suggesting that C–H amination occurred in the coordination sphere of Mn(salen) (entries 3 and 4). Based on the reactivity–selectivity principle,[12] we expected that enantioselectivity would be improved in the order of the reactions with **1**, **2**, **3**, and **4**. Differing from the expectation, complex **3** showed the best enantioselectivity (entry 3). We also synthesized Mn(salen)s, **5** and **6**, bearing a diphenylethylenediamine moiety and examined C–H amination. However, they showed lower enantioselectivity than the corresponding Mn(salen)s, **1** and **3**, bearing a cyclohexanediamine moiety (entries 6 and 7). Mn(salen)s, **8** and **9**, bearing nitro groups at the 5- and 5′-positions also showed catalytic activity but enantioselectivities were only modest (entries 9 and 10). Introduction of a bulky *tert*-butyl group at the 3- and 3′-positions had adverse effect on enantioselectivity (entry 10).

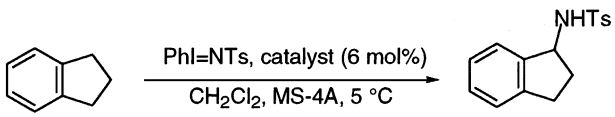
It should be noted that a neutral Mn(salen) such as **10** was inferior to cationic Mn(salen) **3** as the catalyst for the present reaction in terms of enantioselectivity and chemical yield (entry 11).[13]

We next examined the effect of the solvent and reaction temperature on enantioselectivity by using **3** as the catalyst (Table 2). The reactions in acetonitrile, ethyl acetate, acetone, and toluene were slow (entries 2–5). In general, the reaction proceeded smoothly in halocarbons (entries 1 and 6–9) and the best result, in terms of enantioselectivity and chemical yield, was obtained when 1,1,2,2-tetrachloroethane was used as the solvent (entry 9). As reaction temperature was lowered, enantioselectivity was improved without depressing chemical yield (entries 9–11) and the highest enantioselectivity of 66% ee was achieved at −40°C (entry 11).

Under the optimized conditions, we also examined the reaction of cyclohexene, cycloheptene, tetralin, 1,1-dimethyltetralin,[14] and 1,1-dimethylindan[14] (Table 3). The reaction of cyclohexene gave 1-[*N*-(*p*-toluenesulfonyl)amino]cyclohex-2-ene of 67% ee selectively and no aziridination product was detected, while the reaction of cycloheptene gave 1-[*N*-(*p*-toluenesulfonyl)-amino]cyclohept-2-ene of 41% ee together with a small amount of the aziridination product (amination product: aziridination product = 4.8:1).[15] The benzylic amination of tetralin and 1,1-dimethyltetralin proceeded with good enantioselectivity of 77% ee and 82% ee, respectively. High enantioselectivity of 89% ee was obtained in the reaction of 1,1-dimethylindan.

Typical experimental procedure was exemplified by the benzylic amination of indan with **3** as the catalyst at

Table 1. Asymmetric amination of indan with various Mn(salen)s as catalysts



Entry	Complex	Time (h)	Yield (%)[a]	ee (%)[b]	Config.[c]
1	**1**	3	37	5	*S*
2	**2**	3	59	41	*S*
3	**3**	3	63	44	*S*
4	ent-**3**	3	70	43	*R*
5	**4**	3	44	26	*S*
6	**5**	3	54	5	*S*
7	**6**	3	58	3	*S*
8	ent-**7**	3	18	6	*R*
9	**8**	3	32	16	*S*
10	**9**	3	25	4	*S*
11	**10**	3	12	23	*S*

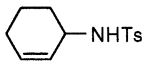
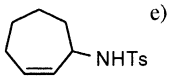
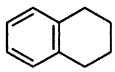
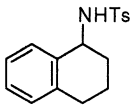
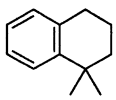
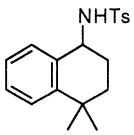
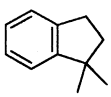
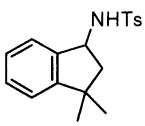
[a] Isolated yield. Yield was calculated based on the amount of [*N*-(*p*-toluenesulfonyl)imino]phenyliodinane used.
[b] Determined by HPLC analysis (DAICEL CHIRALPAK AD, hexane/2-propanol = 9:1).
[c] Determined by comparing the elution order of the present product and the *p*-toluenesulfonylated commercial (*R*)-(−)-1-aminoindan (Aldrich Chemical Co., Inc.) in HPLC analysis (see footnote b).

Table 2. Asymmetric amination of indan with **3** as the catalyst in various solvents

Entry	Solvent	Temp. (°C)	Time (h)	Yield (%)[a]	ee (%)[b]	Config.[c]
1	CH_2Cl_2	5	3	63	44	*S*
2	CH_3CN	5	3	0	–	–
3	$CH_3CO_2C_2H_5$	5	3	19	32	*S*
4	CH_3COCH_3	5	3	17	36	*S*
5	$C_6H_5CH_3$	5	3	9	42	*S*
6	C_6H_5Cl	5	3	62	47	*S*
7	$CHCl_3$	5	3	62	47	*S*
8	$(CH_2Cl)_2$	5	3	57	44	*S*
9	$(CHCl_2)_2$	5	3	74	54	*S*
10	$(CHCl_2)_2$	−20	12	72	61	*S*
11	$(CHCl_2)_2$	−40	24	63	66	*S*

[a] Isolated yield. Yield was calculated based on the amount of [*N*-(*p*-toluenesulfonyl)imino]phenyliodinane used.
[b] Determined by HPLC analysis (DAICEL CHIRALPAK AD, hexane/2-propanol = 9:1).
[c] Determined by comparing the elution order of the present product and the *p*-toluenesulfonylated commercial (*R*)-(−)-1-aminoindan (Aldrich Chemical Co., Inc.) in HPLC analysis (see footnote b).

Table 3. Asymmetric C–H amination of various substrates with **3** as the catalyst[a)]

Entry	Substrate	Product	Yield (%)[b)]	ee (%)	Confign.
1			44	67[c)]	*S*[d)]
2			42	41[c)]	*S*[f)]
3			67	77[g)]	*S*[h)]
4			44	82[i)]	–[j)]
5			71	89[k)]	–[j)]

[a)] Reaction was carried out in 1,1,2,2-tetrachloroethane at −40°C for 24 h.
[b)] Isolated yield. Yield was calculated based on the amount of [*N*-(*p*-toluenesulfonyl)imino]phenyliodinane used.
[c)] Determined by HPLC analysis (DAICEL CHIRALPAK AD, hexane/ethanol = 9:1).
[d)] Determined by comparison of the specific rotation of *tert*-butyl cyclohex-2-ene-1-carbamate derived from the product $\{[\alpha]_D^{25}$ −69.6° (*c* 0.48, $CHCl_3)\}$ with the reported value {(*R*)-isomer; $[\alpha]_D^{23}$ +101° (*c* 2.80, $CHCl_3$, 95% ee)} (Ref. 16).
[e)] Formation of a small amount of aziridine derivative was detected by ^1H NMR analysis (see text).
[f)] Determined by comparison of the specific rotation of cyclohept-2-en-1-ylamine hydrochloride derived from the product $\{[\alpha]_D^{23}$ −6.0° (*c* 0.095, $CH_3OH)\}$ with the reported value {(*S*)-isomer; $[\alpha]_D$ −14.5° (*c* 1.04, CH_3OH, 96% ee)} (Ref. 17).
[g)] Determined by HPLC analysis (DAICEL CHIRALPAK AD, hexane/2-propanol = 9:1).
[h)] Determined by comparison of the specific rotation of 1-amino-1,2,3,4-tetrahydronaphthalene derived from the product $\{[\alpha]_D^{25}$ +33.1° (*c* 1.48, $C_6H_6)\}$ with the reported value {(*R*)-isomer; $[\alpha]_D^{22}$ −46° (*c* 5, $C_6H_6)$} (Ref. 18).
[i)] Determined by HPLC analysis (DAICEL CHIRALPAK AD, hexane/ethanol = 19:1).
[j)] Configuration was not determined.
[k)] Determined by HPLC analysis (DAICEL CHIRALPAK AD, hexane/2-propanol = 40:1).

−40°C: To a mixture of molecular sieves 4 Å (50 mg), **3** (8.4 mg, 10 μmol), and 1,1,2,2-tetrachloroethane (4.0 mL) was added indan (49 μL, 0.4 mmol) under nitrogen and the whole mixture was stirred for 10 min at −40°C. To the mixture was added [*N*-(*p*-toluenesulfonyl)imino]phenyliodinane (61.8 mg, 0.17 mmol) and the reaction mixture was stirred at −40°C for a further 24 h. The mixture was directly subjected to a pad of silica gel (hexane/AcOEt = 7:3) and the filtrate was concentrated in vacuo. The residue was further purified by column chromatography on silica gel (hexane/AcOEt = 9:1 to 7:3) to give (*S*)-1-[*N*-(*p*-toluenesulfonyl)-

amino]-indan as a colorless solid (29.8 mg, 63%, 66% ee).

In conclusion, we were able to achieve good to high enantioselectivity in C–H amination for the first time by using the (salen)manganese complex appropriately modified with an electron-withdrawing group as the catalyst.

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