Applied Organometallic Chemistry (1987) 1 435–439

0268-2605/87/01506435/$03.50

Asymmetric hydrosilylation of prochiral ketones in the presence of *N*-benzyl-*N*-methylephedrinium halometallates

K I Rubina, Yu Sh Goldberg, M V Shymanska and E Lukevics*
Institute of Organic Synthesis, Latvian SSR Academy of Sciences, Riga, USSR

Received 16 April 1987   Accepted 8 June 1987

N-benzyl-N-methylephedrinium hexachloroplatinate(IV), bromotrichlororhodate(III), and dibromodichlorozincate(II) have been synthesized by reacting (−)-N-benzyl-N-methylephedrinium bromide with K_2PtCl_6, $RhCl_3 \cdot 4H_2O$ and $ZnCl_2$, respectively. The above halometallates have been found to catalyse the asymmetric hydrosilylation of acetophenone and 3-acetylpyridine with diphenylsilane. The hydrosilylation of 3-acetylpyridine in the presence of (−)-N-benzyl-N-methylephedrinium zincate followed by silyl ether hydrolysis gives 1-(3-pyridyl)ethanol in *ca* 50% optical yield.

Keywords: Asymmetric hydrosilylation, bis(N-benzyl-N-methylephedrinium) hexachloroplatinate(IV), N-benzyl-N-methylephedrinium bromotrichlororhodate(III), (−)-bis(N-benzyl-N-methylephedrinium) dibromodichlorozincate(II), chiral synthesis, enantioselectivity

INTRODUCTION

Enantioselective hydrosilylation of prochiral carbonyl compounds in the presence of chiral catalysts has been extensively studied over the last few years as a convenient asymmetric reaction model and as a route to optically active alcohols (for reviews see, for example, Refs 1–4). A large number of catalysts, mostly transition-metal (predominantly Pt and Rh) complexes with chiral ligands such as phosphines,[2,5,6] aminophosphines,[7,8] Schiff bases,[9–11] thiazolidines[12,13] or nitrogen-containing tropolone derivatives[14] have been proposed. These catalysts have been previously synthesized or prepared *in situ* by introducing chiral ligands into reaction mixtures containing an achiral metal complex. In some cases the application of chiral ligand complexes has resulted in a high degree of asymmetric induction.[1–4] The main disadvantage of the known catalytic systems lies in the necessity of preliminary synthesis (generally, a laborious and time-consuming procedure) of chiral ligands and/or complexes, most of which are susceptible to air and moisture. Therefore the search for simple and easily available catalysts for asymmetric hydrosilylation remains of high priority.

Recently, it has been shown that quaternary ammonium halometallates of the type $[Et_3NCH_2Ph]_m^+[MCl_n]^{m-}$ ($M = Fe^{III}, Ir^{III}, Pt^{IV}$), which can be easily prepared from the well-known phase-transfer agent, $Et_3^+NCH_2C_6H_5^-Cl$, act as bifunctional metal-complex and phase-transfer catalysts and, for example, catalyse effectively the homogeneous hydrosilylation of phenylacetylene with triethylsilane.[15] Moreover, commercially available quaternary ammonium salts containing an *N,N*-disubstituted ephedrinium cation have been found useful as asymmetric phase-transfer catalysts in various reactions occurring in a two-phase system.[16] Hence it is legitimate to assume that the conversion of quaternary ephedrinium halides into the corresponding halometallates using appropriate metals would give a potential metal-complex catalyst for asymmetric hydrosilylation. The objective of this work was to prepare such complexes and to study their catalytic properties in reactions of asymmetric hydrosilylation of prochiral ketones.

---

*Author to whom correspondence should be addressed.

EXPERIMENTAL

^{1}H NMR spectra were obtained on a Bruker WH-90/DS spectrometer (90 MHz). Mass spectra were recorded on a Kratos MS-25 (70 eV) GC MS apparatus. GC analysis was carried out using a Chrom-5 instrument equipped with a flame-ionization detector (FID) and a glass column (2.4 m × 3 mm) packed with 5% OV-17/Chromosorb W-HP (80–100 mesh). Helium ($50\,\mathrm{cm^3\,min^{-1}}$) was used as carrier gas; the column temperature was 220°C. Optical rotation was measured with Autopol® II (Rudolf Research) and Polamat A (Carl Zeiss) polarimeters. Melting points determined on a Boetius apparatus are given without correction. (−)-*N*-Benzyl-*N*-methylephedrinium bromide (**1**) ($[\alpha]^{24}_{546}$ −5.6°) ($c = 4.5$, MeOH) was a Fluka product. $RhCl_3 \cdot 4H_2O$, $ZnCl_2$ and K_2PtCl_6 were of reagent grade. Acetophenone and 3-acetylpyridine (Fluka) were dried over molecular sieves 4A and distilled *in vacuo* before use. Diphenylsilane[17] and camphanic acid chloride[18] were prepared as described elsewhere.

Bis(*N*-benzyl-*N*-methylephedrinium) hexachloroplatinate(IV) (2)

To a solution of (−)-*N*-benzyl-*N*-methylephedrinium bromide $[C_6H_5CH(OH)CH(CH_3)N(CH_3)_2CH_2C_6H_5^+Br^-]$ (0.35 g, 1 mmol) in dichloromethane (100 cm^3) a solution of K_2PtCl_6 (0.243 g, 0.5 mmol) in water (100 cm^3) was added. The two-phase mixture was stirred at room temperature until complete decolouration of the aqueous layer occurred (*ca* 2 h). The solid precipitate was filtered off, washed with dichloromethane and dried *in vacuo* to give 0.36 g of **2** (yield 76%) as a yellowish orange solid, m.p. 205–207°C. (Calc. for $C_{36}H_{48}N_2Cl_6O_2Pt$: C, 45.54; H, 5.06; N, 2.96. Found: C, 45.69; H, 5.07; N, 2.79%.) ^{1}H NMR spectrum (DMSO-d$_6$/TMS—aliphatic region), δ (ppm): 1.27 (d. 3H, $J = 7$ Hz, $\mathrm{CH{-}C\underline{H}_3}$), 3.08 (s, 6H, $N(CH_3)_2$), 3.78 (q, 1H, $J = 7$ Hz, $\mathrm{C\underline{H}{-}CH_3}$), 4.70 (s, 2H, $\mathrm{C\underline{H}_2Ph}$), 5.64 (d, 1H, $J = 4.5$ Hz, $\mathrm{C\underline{H}{-}OH}$, becomes singlet after D_2O addition), 6.16 (d, 1H, $J = 4.5$ Hz, OH, exchangeable with D_2O).

N-benzyl-*N*-methylephedrinium bromotrichlororhodate(III) (3)

A solution of $RhCl_3 \cdot 4H_2O$ (0.562 g, 2 mmol) in ethanol (20 cm^3) was added to a solution of (−)-*N*-benzyl-*N*-methylephedrinium bromide (0.70 g, 2 mmol) in ethanol (20 cm^3). The solid precipitate was filtered off, washed with absolute ethanol and dried in a vacuum dessicator over P_2O_5. Rhodate **3** (0.65 g; yield 58%) was obtained as a pinkish beige powder, m.p. 192–205°C. (Calc. for $C_{18}H_{24}NBrCl_3ORh$: C, 38.64; H, 4.32; N, 2.50. Found: C, 38.65; H, 4.45; N, 2.39%.) The ^{1}H NMR spectrum was the same as that for hexachloroplatinate **2**.

(−)-bis(*N*-benzyl-*N*-methylephedrinium) dibromodichlorozincate(II) (4)

To a solution of fused $ZnCl_2$ (0.237 g, 2 mmol) in 20 cm^3 of absolute ethanol was added a solution of (−)-*N*-benzyl-*N*-methylephedrinium bromide in ethanol (35 cm^3). The mixture was heated under reflux for 0.5 h and cooled to 0°C. The white precipitate formed was filtered off and recrystallized from ethanol to give 1.26 g (yield 75%) of **4** as white crystals, m.p. 192°C. (Calc. for $C_{36}H_{48}N_2Br_2Cl_2O_2Zn$: C, 51.60; H, 5.50; N, 3.35. Found: C, 52.29; H, 5.89; N, 3.33%.) The ^{1}H NMR spectrum was the same as that for hexachloroplatinate **2**; $[\alpha]^{20}_{D}$ −4.0° ($c = 1.5$, MeOH), $[\alpha]^{20}_{546}$ −4.5° ($c = 1.5$, MeOH).

Hydrosilylation of acetophenone (5) and 3-acetylpyridine (6) (general procedure)

A mixture of ketone **5** or **6** (22 mmol), diphenylsilane (22 mmol) and catalyst (0.02 mmol) was stirred at room temperature under GC and GC MS observation to achieve the maximum content of silyl ether **7** or **8** (Table 1). The unreacted starting compounds and products **7** or **8** were isolated by distillation under vacuum. Silyl ether **7**: b.p. 179–182°C/1 mm (lit.[6] b.p. 139/0.03 mm); the ^{1}H NMR spectrum of **7** was the same as that given in Ref. 6; m/z 304 (M^+) corresponding to $C_6H_5C(CH_3)(H)OSi(C_6H_5)_2H$. Silyl ether **8**: b.p. 230–240°C (bath temperature)/0.6 mm; ^{1}H NMR spectrum ($CDCl_3$/TMS), δ (ppm): 1.53 (d. 3H, $J = 7$ Hz, CH_3), 5.08 (q, 1H, $J = 7$ Hz, OCH), 5.42 (s, 1H, SiH), 7.1–8.6 (m, 14H, aromatic protons); m/z 305 (M^+) corresponding to $C_5H_4NC(CH_3)(H)OSi(C_6H_5)_2H$.

1-Phenylethanol (**9**) and 1-(-3-pyridyl)ethanol (**10**) were obtained following treatment of ethers **7** and **8**, respectively, after Brunner's procedure using aqueous HCl.[9] The secondary alcohols **9** and **10** were assigned by comparison with authentic samples. The results of hydrosilylation of ketones **5** and **6** are listed in Table 1.

Reaction of 1-(3-pyridyl)ethanol with camphanic acid chloride

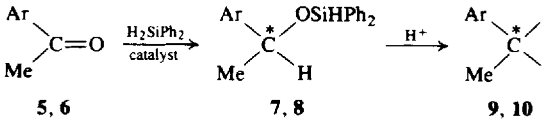
To a solution of **10** [26 mg, 0.2 mmol, $[\alpha]_D^{20} -21.5°$ ($c = 0.65$, MeOH) prepared by the hydrosilylation of ketone **6** with Ph_2SiH_2 in the presence of zincate **4**, followed by acid hydrolysis] in benzene (1 cm^3), were added $NaHCO_3$ (40 mg, 0.5 mmol) and camphanic acid chloride ($C_{10}H_{13}O_3Cl$) (66 mg, 0.3 mmol). The reaction was complete after a few minutes (observed by GC). The formation of ester was confirmed by GC MS analysis: *m/z* 303 (M^+). The reaction mixture was filtered to remove solid particles and the filtrate was evaporated *in vacuo* to give a viscous oil residue undergoing crystallization upon storage. The ^1H NMR spectrum of this product demonstrated two methyne proton quartets at 4.96 and 6.02 ppm in a 73:27 integral ratio corresponding to 46% diastereomeric excess.

RESULTS AND DISCUSSION

(−)-*N*-benzyl-*N*-methylephedrinium bromide (**1**) was used as the starting ephedrinium salt. To prepare ephedrinium halometallates platinum, rhodium and zinc salts were chosen because compounds containing these metals have been frequently used as hydrosilylation catalysts in reactions with carbonyl compounds.[19] *N*-benzyl-*N*-methylephedrinium halometallates were prepared by two routes. An exchange of the bromide anion in salt **1** for the $[PtCl_6]^{2-}$ anion in the two-phase CH_2Cl_2/H_2O system afforded bis(*N*-benzyl-*N*-methylephedrinium) hexachloroplatinate(IV) (**2**) in 76% yield. *N*-benzyl-*N*-methylephedrinium bromotrichlororhodate(III) (**3**) was synthesized by reacting salt **1** with rhodium trichloride in ethanol at room temperature (yield 56%). Similarly, the reaction between salt **1** and zinc chloride gave bis(*N*-benzyl-*N*-methylephedrinium) dibromodichlorozincate(II) (**4**) in 75% yield (see Scheme 1).

^1H NMR spectra of halometallates **2**–**4** resemble each other closely and differ little from that of the starting salt **1**. Elemental analysis data confirm the given composition. Optical rotation was measured only for zincate **4**, since the solutions of platinate **2** and rhodate **3** are intensely coloured even in low concentrations.

The catalytic properties of halometallates **2**–**4** were studied in the reaction of hydrosilylation of acetophenone (**5**) and 3-acetylpyridine (**6**) with diphenylsilane (Reaction 1). All experiments were carried out at room temperature.



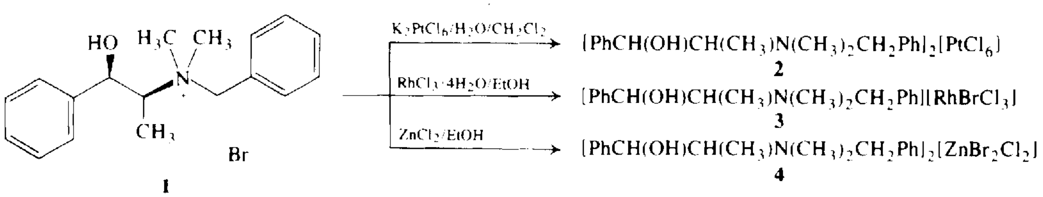
[1]

5, 7, 9: Ar = C_6H_5; 6, 8, 10: Ar = 3-pyridyl

Catalyst concentration was 10^{-3} mol/mol ketone; the latter compound and diphenylsilane were applied in equivalent amounts. The reactions were monitored by GC and GC MS. The products of ketone (**5** and **6**) hydrosilylation, the silyl ethers **7** and **8** were isolated by distillation under vacuum. When the yield of **7** and **8** was low, their content in the reaction mixture was determined by GC. The silyl ethers **7** and **8** were quantitatively converted into the corresponding secondary alcohols (**9** and **10**) by treatment with aqueous HCl in acetone according to Brunner's procedure.[9]

In some cases such treatment was carried out without prior isolation of the silyl ether. Optical purity and absolute configuration of the secondary alcohols obtained were determined on the basis of the signs and specific rotation values known for the pure enantiomers. The results are presented in Table 1.

In general, the catalysts under study are characterized by low activity, but with selectivity



1

Table 1 Asymmetric hydrosilylation of acetophenone (**5**) and 3-acetylpyridine (**6**) with diphenylsilane catalysed by *N*-benzyl-*N*-methylephedrinium halometallates (20°C; molar ratio ketone:Ph_2SiH_2:catalyst = 1:1:0.001)

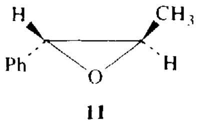
				Secondary alcohol[b]		
Ketone	Catalyst	Reaction time (h)	Silyl ether [GC yield (%)]	$[\alpha]_D^{20}$ (deg.)	Optical yield (%)	Configuration
5	**2**	500	**7** [62/50[a]]	+3.2 (neat)	7.0	(*R*)
5	**3**	24	**7** [78/64[a]]	+4.5 (neat)	9.8	(*R*)
5	**4**	720	**7** [9]	—	—	—
5	**1** + $RhCl_3.4H_2O$ (1:1)	24	**7** [72/60[a]]	+4.25 (neat)	9.3	(*R*)
5	$RhCl_3.4H_2O$	5	**7** [95]	—	—	—
6	**2**	200	**8** [6]	—	—	—
6	**3**	200	**8** [7]	—	—	—
6	**4**	200	**8** [18/15[a,c]]	−21.5 (*c* = 0.65, MeOH)	53.5 (46.0)[d]	(*S*)
6	**1** + $ZnCl_2$ (2:1)	200	**8** (15[e]]	−21.0 (*c* = 0.5, MeOH)	52.2	(*S*)
6	$ZnCl_2$	200	**8** [33]	—	—	—

[a] Isolated yield. [b] Maximum specific rotation of pure enantiomers: (*R*)-1-phenylethanol, $[\alpha]_D^{20}$ +45.7° (neat);[20] (*S*)-1-(3-pyridyl)ethanol, $[\alpha]_D^{20}$ −40.2° (MeOH).[21] [c] Silyl ether **8** had $[\alpha]_D^{20}$ −14.0° (*c* = 1, EtOH). [d] According to the ^1H NMR spectrum for diastereomeric camphanic acid esters. [e] The silyl ether **8** was converted into the corresponding secondary alcohol **10** without isolation.

toward the silyl ethers **7** and **8** in most cases being close to 100%. The rhodium-containing catalyst **3** was more active in the hydrosilylation of aromatic ketone **5**, whereas zincate **4** was a more suitable catalyst for heterocyclic ketone **6** hydrosilylation. A comparison of catalytic activity of the metallates **3** and **4** with that of the corresponding metallic chlorides has shown that the latter compounds were much more active than the corresponding complexes with aromatic compounds **3** and **4**. Thus, the conversion of neutral inorganic metal chlorides to the corresponding halometallates decreases the rate of ketone hydrosilylation in the presence of these catalysts. As asymmetric reactions are known to be kinetically controlled, the probability of optical induction during ketone hydrosilylation using catalysts of the **2**–**4** type is however increased.

When ketone **5** was allowed to react with Ph_2SiH_2 in the presence of platinate **2** or rhodate **3** the silyl ether **7** was isolated in 50 or 64% yield, respectively. The optical yield of alcohol **9** resulting from the hydrolysis of silyl ether **7** did not exceed 10% (Table 1). We also explored the possibility of obtaining a catalyst for asymmetric hydrosilylation from quaternary ephedrinium salt **1** and rhodium trichloride *in situ*. The catalytic activity of a mixture of **1** with $RhCl_3.4H_2O$ (1:1) in the reaction of ketone **5** with Ph_2SiH_2 was found to be close to that of the individual rhodate **3** (Table 1); the optical yield of the corresponding secondary alcohol **9** was also essentially the same as that reached with catalyst **3**. The zinc-containing catalyst **4** shows a very low activity in the hydrosilylation of acetophenone. This catalyst, however, appears to be extremely convenient for the hydrosilylation of 3-acetylpyridine (**6**). In general, this heterocyclic ketone is much less reactive than its aromatic analogue (Table 1). The maximum conversion of **6** to the corresponding silyl ether **8** did not exceed 20% (at almost 100% selectivity). Nearly the same result was achieved when a mixture of ephedrinium salt **1** and $ZnCl_2$ (2:1) was used as catalyst. Platinate **2** and rhodate **3** in the reaction of ketone **6** with diphenylsilane demonstrated very low activity. However the two zinc-containing catalytic systems permit (3-pyridyl)-methylcarbinol (**10**) to be obtained in a relatively high optical yield of *ca* 50% (Table 1).

It is a known fact that some results pertaining to asymmetric synthesis in the presence of *N*,*N*-disubstituted ephedrinium salts as catalysts might be distorted or even erroneous because these catalysts undergo conversion to epoxide **11**.[22]



11

The presence of traces of this epoxide, which is characterized by a high value for specific rotation, is capable of conferring spurious optical activity to the reaction products. According to our procedure, alcohols **9** and **10** were prepared in two stages including distillations *in vacuo*, which makes it very unlikely that there might be present traces of **11**. Moreover, the amount of the catalyst (0.1 mol% of reactant) is at least one order of magnitude smaller than that usually required with ephedrinium salts used as phase-transfer catalysts. Nevertheless we examined the validity of data indicating an enantiomeric excess of the (*S*)-isomer in carbinol **10** by an independent method. Following hydrolysis of the silyl ether **8** prepared by the hydrosilylation of ketone **6** with Ph_2SiH_2 in the presence of zincate **4** the product (**10**) was converted to the diastereomeric mixture of the corresponding camphanic acid esters by the reaction with camphanic acid chloride.[18] In the ^1H NMR spectrum of this mixture two methyne protone quartets of the two diastereomers were observed at 4.96 and 6.02 ppm respectively. The ratio of integral intensities of these signals (73:27) corresponds to a 46% enantiomeric excess of (*S*)-1-(3-pyridyl)-ethanol in the secondary alcohol **10**. This value approaches closely the value accounted for on the basis of optical rotation measurements for product **10** (Table 1).

CONCLUSIONS

N-benzyl-*N*-methylephedrinium halometallates [hexachloroplatinate(IV), bromotrichlororhodate(III), dibromodichlorozincate(II)] were found to catalyse the asymmetric hydrosilylation of prochiral ketones (acetophenone and 3-acetylpyridine) with diphenylsilane. In the case of the hydrosilylation of 3-acetylpyridine in the presence of (−)-bis(*N*-benzyl-*N*-methylephedrinium) dibromodichlorozincate, *ca* 50% optical yield of 1-(3-pyridyl)ethanol was achieved.

REFERENCES

1. Pino, P and Consiglio, G *Pure Appl. Chem.*, 1983, 55: 1781
2. Brunner, H *Angew. Chem. Int. Ed. Engl.*, 1983, 22: 897
3. Ojima, I *Pure Appl. Chem.*, 1984, 56: 99
4. Brunner, H *J. Organomet. Chem.*, 1986, 300: 39
5. Hayashi, J, Yamamoto, K and Kumada, M *Tetrahedron Lett.*, 1974, 4405
6. Hayashi, J, Yamamoto, K, Kasuga, K and Omizu, H *J. Organomet. Chem.*, 1976, 113: 127
7. Brunner, H and Weber, H *Chem. Ber.*, 1985, 118: 3380
8. Karim, A, Motreux, A and Petit, F *Tetrahedron Lett.*, 1986, 345
9. Brunner, H. and Riepl, G *Angew. Chem. Int. Ed. Engl.*, 1982, 21: 377; *Angew. Chem. Suppl.*, 1982, 769
10. Brunner, H, Reiter, B and Riepl, G *Chem. Ber.*, 1984, 117: 1330
11. Kintiny, A *Z. Chem.*, 1986, 26: 180
12. Brunner, H, Becker, R and Riepl, G *Organometallics*, 1984, 3: 1354
13. Brunner, H, Riepl, G and Weitzer, H *Angew. Chem. Int. Ed. Engl.*, 1983, 22: 331; *Angew. Chem. Suppl.*, 1983, 445
14. Brunner, H and Knott, A *J. Organomet. Chem.*, 1985, 295: 211
15. Iovel, I G, Goldberg, Yu Sh, Shymanska, M V and Lukevics, E *J. Chem. Soc. Chem. Commun.*, 1987, 31
16. Dehmlow, E V and Dehmlow, S S *Phase Transfer Catalysis*, Verlag Chemie, Weinheim, 1980
17. Benkeser, R A, Landesman, H and Foster, D J *J. Am. Chem. Soc.*, 1952, 74: 648
18. Gerlach, H *Helv. Chim. Acta*, 1968, 51: 1587
19. Lukevics, E, Belyakova, Z V, Pomerantseva, M G and Voronkov, M G *J. Organomet. Chem. Library*, 1977, 5: 1
20. Okamoto, K, Tomomi, K, Takemura, Y and Yoneda, H *J. Chem. Soc., Perkin Trans. 2*, 1975, 1426
21. Gottarelli, G and Samori, B *Tetrahedron Lett.*, 1970, 2055
22. Dehmlow, E V, Singh, P and Heider, J *J. Chem. Res. (S)*, 1981, 292