Supporting Information for

Asymmetric hydrogenation of ketone catalyzed by ruthenium(II)–indan-ambox complex

Wei Li,[ab] Guohua Hou,[a] Chunjiang Wang,[b] Yutong Jiang,[b] Xumu Zhang*[a]

[a] *Department of Chemistry and Chemical Biology & Department of Pharmaceutical Chemistry, Rutgers, The State University of New Jersey, Piscataway, NJ 08854, USA.*
[b] *Department of Chemistry, The Pennsylvania State University, University Park, PA 16802, USA.*

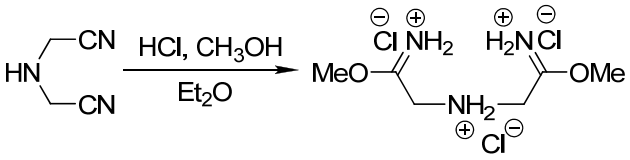
E-mail: xumu@rci.rutgers.edu; Fax: +1 732 445 6312; Tel: +1 732 445 1454.

CONTENTS

I. General Remarks

All reactions and manipulations were performed in a nitrogen-filled glovebox or under nitrogen using standard Schlenk techniques unless otherwise noted. Column chromatography was performed using Sorbent silica gel 60 Å (230×450 mesh). ^{1}H ^{13}C NMR spectral data were recorded on Bruker 360 MHz, Bruker 400 MHz spectrometers. Chemical shifts were reported in ppm. Enantiomeric excess values were determined by chiral GC on Agilent 7890 GC equipment and chiral HPLC on Agilent 1200 Series equipment.

II. Procedure for Preparation of indan-ambox ligand

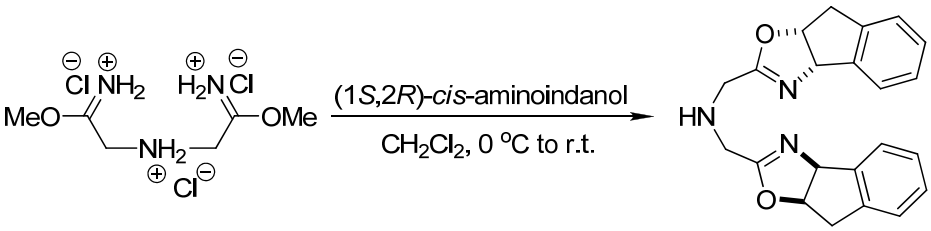


1

Preparation of Bis(acetimido methyl ether hydrochloride) amino hydrochloride **1**:

To a 125 mL filter flash was added iminodiacetonitrile (9.5 g, 0.1 mol, the Aldrich chemical was recrystallized from EtOAc before use), anhydrous methanol (6.4 g, 0.2 mol) and diethyl ether (60 mL). The suspension was cooled to 0˚C. Anhydrous HCl gas was bubbled into the above suspension while stirring. After about 2h, the bubbling was stopped and the reaction mixture was kept under HCl atmosphere at 0˚C overnight. The resulting white solid was filtered under nitrogen, whased with ether (3 × 20 mL), and dried under vacuum. The final product was a white hydroscopic power (20.4 g, 76%) and used for following step

without further purification.

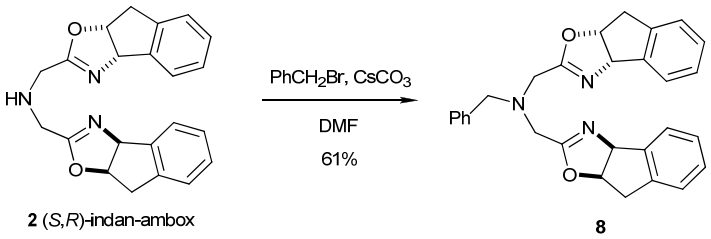


1 **2** (*S*,*R*)-indan-ambox

Preparation of indan-ambox 2 (bis[8,8a-dihydro-3aH-1-oxa-3aza-cyclopenta<α>inden-2-yl]methyl]amine) :

To a 50 mL Schlenk flask was added **1** (7.7 g, 28.7 mmol) and CH_2Cl_2 (100 mL). The white suspension was first cooled to 0˚C, then (*S*,*R*)-*cis*-1-amino-indan-2-ol (12.9 g, 86.6 mmol). The white suspension turned yellowish shortly after addition of aminoindanol. The reaction was slowly warmed up to r.t. and stirred overnight. The yellowish color gradually turned to white. After stirring at r.t. for 40h, the reaction was poured onto ice, and the aqueous layer was extracted with CH_2Cl_2 (4 × 50 mL). The combined organic layers were first greenish but then slowly changed to brownish. It was dried over Na_2SO_4 and concentrated under reduced pressure until solid was about to precipitate out. It was cooled on ice bath for 1h, and the subsequent filtration gave an off-white solid (2.6 g), which was unreacted aminoindanol. The rest of the crude product was then recrystallized from CH_2Cl_2/hexanes, washed with H_2O and drying over P_2O_5 under high vacuum to give the pure product **2** as an off-white powder: 4.39 g, 43% yield. ^{1}H NMR (400 MHz, CD_2Cl_2): δ 1.95 (br s, 1H), 3.19–3.24 (m, 2H), 3.37–3.42 (m, 6H), 5.28–5.32 (m, 2H), 5.51 (d, J = 8.0 Hz, 2H), 7.24–7.26 (m, 6H), 7.44–7.46 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 39.7, 45.8, 76.4, 83.3, 125.3, 125.5, 127.5, 128.5, 139.6, 141.8, 165.8. HRMS

$[MH]^+$ Calcd: 360.1712, Found: 360.1697.



Preparation of 8 (N-benzyl-1-((3aS,8aR)-8,8a-dihydro-3aH-indeno[1,2-d]oxazol-2-yl)-N-(((3aS,8aR)-8,8a-dihydro-3aH-indeno[1,2-d]oxazol-2-yl)methyl)methanamine) :

To a 50 mL Schlenk flask was added **2** (144 mg, 0.4 mmol), $CsCO_3$ (261 mg, 0.8 mmol) and DMF (15 mL). $PhCH_2Br$ (69 mg, 0.4 mmol) was added slowly to the suspension. The suspension was stirred overnight at r.t.. After the reaction is finished, the solvent was removed and dissolved in CH_2Cl_2 (20 mL). The solution was washed with H_2O, the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers was dried over Na_2SO_4 and concentrated under reduced pressure. Column chromatography on silica gel gave the product **8** as light yellow oil: 110 mg, 61% yield. ^1H NMR (400 MHz, acetone-d_6): δ 3.00 (d, J = 20.0 Hz, 2H), 3.16–3.29 (m, 6H), 3.51 (s, 1H), 3.87–4.07 (m, 1H), 5.10–5.18 (m, 2H), 5.28–5.33 (m, 2H), 6.99–7.13 (m, 6H), 7.23–7.25 (m, 2H). MS $[MH]^+$ Calcd: 450.5, Found: 450.3.

III. Procedure for preparation of $[RuCl_2(indan\text{-}ambox)(PPh_3)]$ complex 5

To a flame-dried 50 mL Schlenk flask was charged $Ru(PPh_3)_3Cl_2$ (38.4 mg, 0.04 mmol) and (*S*,*R*)-indan-ambox **2** (15.0 mg, 0.044 mmol). Under nitrogen protection anhydrous 2-propanol (15 mL) was added and the reaction mixture was heated to reflux for 3–4 h. The reaction mixture turned to dark greenish color. The solvent was removed under vacuum

and the greenish solid complex was washed with cold anhydours Et_2O (5mL × 3) to remove free PPh_3. ^{31}P NMR (162 MHz, acetone-d_6) of the Ru(II)–indan-ambox complex after wash: δ = 32.40 (s).

IV. General Procedure for Asymmetric Hydrogenation

The above precatalyst was dissolved in degassed 2-propanol (10 mL). The solution was equally divided into 10 vials. A solution of t-BuOK (1 mol/L, 0.020 mL, 0.02 mmol), ketone substrate (0.4 mmol, S/C = 100) and 1 mL of 2-propanol were added via syringe. The resulting mixture was transferred into an autoclave, and the autoclave was purged with H_2 (5 atm, for three times) and charged with H_2 (5 atm). After stirring at room temperature for 15 hours, the H_2 was carefully released. The reaction solution was purified by a silica gel column to give the corresponding hydrogenation product, which was then directly analyzed by chiral GC to determine the enantiomeric excess.

V. Hydrogenation Conditions of Substrates and Enantioselectivity Analysis Data of Products

(*R*)-1-phenylethanol:[1] $RuCl_2$(indan-ambox)(PPh_3) (0.004 mmol), acetophenone (0.4 mmol, S/C = 100), 2-propanol (2.0 mL), *t*-BuOK in 2-propanol (20 μmol), 5 atm, r.t., 15

h. GC (BETA DEX 120, 30 m × 0.25 mm × 0.25 μm; carrier gas, He (flow rate 1 mL/min); column temperature, 120 ˚C). t_R of (*R*)-1-phenylethanol, 11.46 min; t_R of (*S*)-1-phenylethanol, 12.17 min. >99% conversion, 95% ee.

(*R*)-1-(2′-Methylphenyl)ethanol:[1] $RuCl_2$(indan-ambox)(PPh_3) (0.004 mmol), 2′-methylacetophenone (0.4 mmol, S/C = 100), 2-propanol (2.0 mL), *t*-BuOK in 2-propanol (20 μmol), 5 atm, r.t., 12 h. GC (Supelco BETA DEX 120 , 30 m × 0.25 mm × 0.25 μm); carrier gas, He (flow rate 1 mL/min); column temperature, 140 ˚C; t_R of (*R*)-isomer, 9.35 min; t_R of (*S*)-isomer, 10.15 min. >99% conversion, 97% ee.

(*R*)-1-(2′-chlorophenyl)ethanol:[2] $RuCl_2$(indan-ambox)(PPh_3) (0.004 mmol), 2′-methylacetophenone (0.4 mmol, S/C = 100), 2-propanol (2.0 mL), *t*-BuOK in 2-propanol (20 μmol), 5 atm, r.t., 12 h. GC (Supelco BETA DEX 120 , 30 m × 0.25 mm × 0.25 μm); carrier gas, He (flow rate 1 mL/min); column temperature, 140 ˚C; t_R of (*R*)-isomer, 9.35 min; t_R of (*S*)-isomer, 10.15 min. >99% conversion, 92% ee.

(*R*)-1-(2′-Methoxyphenyl)ethanol:[2] $RuCl_2$(indan-ambox)(PPh_3) (0.004 mmol), 2′-methylacetophenone (0.4 mmol, S/C = 100), 2-propanol (2.0 mL), *t*-BuOK in 2-propanol (20 μmol), 5 atm, r.t., 12 h. GC (Supelco BETA DEX 120 , 30 m × 0.25 mm × 0.25 μm); carrier gas, He (flow rate 1 mL/min); column temperature, 140 ˚C; t_R of (*R*)-isomer, 9.35 min; t_R of (*S*)-isomer, 10.15 min. 82% conversion, 93% ee.

(*R*)-1-(3′-Methylphenyl)ethanol:[1] $RuCl_2$(indan-ambox)(PPh_3) (0.004 mmol), 3′-methylacetophenone (0.4 mmol, S/C = 100), 2-propanol (2.0 mL), *t*-BuOK in 2-propanol (20 μmol), 5 atm, r.t., 15 h. GC (Supelco BETA DEX 120 , 30 m × 0.25 mm × 0.25 μm); carrier gas, He (flow rate 1 mL/min); column temperature, 120 ˚C; t_R of (*R*)-isomer, 17.45 min; t_R of (*S*)-isomer, 18.66 min. >99% conversion, 95% ee.

(*R*)-1-(3′-Chlorophenyl)ethanol:[1] $RuCl_2$(indan-ambox)(PPh_3) (0.004 mmol), 3′-chlorolacetophenone (0.4 mmol, S/C = 100), 2-propanol (2.0 mL), *t*-BuOK in 2-propanol (20 μmol), 5 atm, r.t., 15 h. GC (Supelco BETA DEX 120 , 30 m × 0.25 mm × 0.25 μm); carrier gas, He (flow rate 1 mL/min); column temperature, 140 ˚C; t_R of (*R*)-isomer, 15,24 min; t_R of (*S*)-isomer, 15.97 min. >99% conversion, 81% ee.

(*R*)-1-(3′-Methoxyphenyl)ethanol:[1] $RuCl_2$(indan-ambox)(PPh_3) (0.004 mmol), 3′-methoxyacetophenone (0.4 mmol, S/C = 100), 2-propanol (2.0 mL), *t*-BuOK in 2-propanol (20 μmol), 10 atm, r.t., 4 h. GC (Supelco BETA DEX 120 , 30 m × 0.25 mm × 0.25 μm); carrier gas, He (flow rate 1 mL/min); column temperature, 130 ˚C; t_R of (*R*)-isomer, 28.40 min; t_R of (*S*)-isomer, 30.06 min. >99% conversion, 90% ee.

(*R*)-1-(4′-Methylphenyl)ethanol:[1] $RuCl_2$(indan-ambox)(PPh_3) (0.004 mmol), 4′-methylacetophenone (0.4 mmol, S/C = 100), 2-propanol (2.0 mL), *t*-BuOK in 2-propanol

(2.0 μmol), 5 atm, r.t., 15 h. GC (Supelco BETA DEX 120 , 30 m × 0.25 mm × 0.25 μm); carrier gas, He (flow rate 1 mL/min); column temperature, 120 ˚C; t_R of (*R*)-isomer, 16.85 min; t_R of (*S*)-isomer, 18.20 min. >99.9% conversion, 93% ee.

(*R*)-1-(4′-Chlorophenyl)ethanol:[1] $RuCl_2$(indan-ambox)(PPh_3) (0.004 mmol), 4′-chloroacetophenone (0.4 mmol, S/C = 100), 2-propanol (2.0 mL), *t*-BuOK in 2-propanol (20 μmol), 5 atm, r.t., 15 h. GC (Supelco BETA DEX 120 , 30 m × 0.25 mm × 0.25 μm); carrier gas, He (flow rate 1 mL/min); column temperature, 140 ˚C; t_R of (*R*)-isomer, 15.52 min; t_R of (*S*)-isomer, 16.59 min. >99% conversion, 80% ee.

(*R*)-1-(4′-Fluorophenyl)ethanol:[1] $RuCl_2$(indan-ambox)(PPh_3) (0.004 mmol), 4′-fluoroacetophenone (0.4 mmol, S/C = 100), 2-propanol (2.0 mL), *t*-BuOK in 2-propanol (20 μmol), 5 atm, r.t., 15 h. GC (Supelco BETA DEX 120 , 30 m × 0.25 mm × 0.25 μm); carrier gas, He (flow rate 1 mL/min); column temperature, 120 ˚C; t_R of (*R*)-isomer, 12.52 min; t_R of (*S*)-isomer, 13.67 min. >99% conversion, 83% ee.

(*R*)-1-(4′-Methoxyphenyl)ethanol:[1] $RuCl_2$(indan-ambox)(PPh_3) (0.004 mmol), 4′-methoxyacetophenone (0.4 mmol, S/C = 100), 2-propanol (2.0 mL), *t*-BuOK in 2-propanol (20 μmol), 5 atm, r.t., 15 h. GC (Supelco BETA DEX 120 , 30 m × 0.25 mm × 0.25 μm); carrier gas, He (flow rate 1 mL/min); column temperature, 130 ˚C; t_R of (*R*)-isomer, 28.89 min; t_R of (*S*)-isomer, 30.21 min. >99% conversion, 92% ee.

(*R*)-1-(1′-Naphthyl)ethanol:[1] $RuCl_2$(indan-ambox)(PPh_3) (0.004 mmol), 1′-acetonaphthone (0.4 mmol, S/C = 100), 2-propanol (2.0 mL), *t*-BuOK in 2-propanol (20 μmol), 5 atm, r.t., 15 h. GC (Supelco BETA DEX 120 , 30 m × 0.25 mm × 0.25 μm); carrier gas, He (flow rate 1 mL/min); column temperature, 145 ˚C; t_R of (*S*)-isomer, 73.59 min; t_R of (*R*)-isomer, 75.94 min. >99% conversion, 94% ee.

(*R*)-1-(2′-Naphthyl)ethanol:[1] $RuCl_2$(indan-ambox)(PPh_3) (0.004 mmol), 2′-acetonaphthone (0.4 mmol, S/C = 100), 2-propanol (2.0 mL), *t*-BuOK in 2-propanol (20 μmol), 5 atm, r.t., 15 h. GC (Supelco BETA DEX 120 , 30 m × 0.25 mm × 0.25 μm); carrier gas, He (flow rate 1 mL/min); column temperature, 145 ˚C; t_R of (*R*)-isomer, 68.84 min; t_R of (*S*)-isomer, 71.72 min. >99% conversion, 87% ee.

(*R*)-Phenylpropanol:[1] $RuCl_2$(indan-ambox)(PPh_3) (0.004 mmol), phenylpropanone (0.4 mmol, S/C = 100), 2-propanol (2.0 mL), *t*-BuOK in 2-propanol (20 μmol), 5 atm, r.t., 15 h. GC (Supelco BETA DEX 120 , 30 m × 0.25 mm × 0.25 μm); carrier gas, He (flow rate 1 mL/min); column temperature, 100 ˚C; t_R of (*R*)-isomer, 47.95 min; t_R of (*S*)-isomer, 52.62 min. >99% conversion, 93% ee.

(*R*)-2-Methyl-1-phenylpropanol:[2,3] $RuCl_2$(indan-ambox)(PPh_3) (0.004 mmol), isobutyrophenone (0.4 mmol, S/C = 100), 2-propanol (2.0 mL), *t*-BuOK in 2-propanol (20 μmol), 5 atm, r.t., 15 h. GC (Supelco BETA DEX 120 , 30 m × 0.25 mm × 0.25 μm); carrier gas, He (flow rate 1 mL/min); column temperature, 100 ˚C; t_R of (*R*)-isomer, 47.95 min; t_R of (*S*)-isomer, 52.62 min. 95% conversion, 91% ee.

(*R*)-Cyclopropyl(phenyl)methanol:[1] $RuCl_2$(indan-ambox)(PPh_3) (0.004 mmol), cyclopropyl phenyl ketone (0.4 mmol, S/C = 100), 2-propanol (2.0 mL), *t*-BuOK in 2-propanol (20 μmol), 5 atm, r.t., 15 h. GC (Supelco BETA DEX 120 , 30 m × 0.25 mm × 0.25 μm); carrier gas, He (flow rate 1 mL/min); column temperature, 90 ˚C; t_R of (*R*)-isomer, 76.33 min; t_R of (*S*)-isomer, 79.46 min. 80% conversion, 92% ee.

(*R*)-1-Cyclohexylethanol:[4] $RuCl_2$(indan-ambox)(PPh_3) (0.004 mmol), cyclohexyl methyl ketone (0.4 mmol, S/C = 100), 2-propanol (2.0 mL), *t*-BuOK in 2-propanol (20 μmol), 5 atm, r.t., 15 h. GC (Supelco ALPHA DEX 120 , 30 m × 0.25 mm × 0.25 μm); carrier gas, He (flow rate 2 mL/min); column temperature, 60 ˚C; t_R of (*R*)-isomer, 47.39 min; t_R of (*S*)-isomer, 7.62 min. >99% conversion, 95% ee.

(*R*)-3,3-dimethylbutan-2-ol: $RuCl_2$(indan-ambox)(PPh_3) (0.004 mmol), pinacolone (0.4 mmol, S/C = 100), 2-propanol (2.0 mL), *t*-BuOK in 2-propanol (20 μmol), 5 atm, r.t., 15 h. GC (Supelco BETA DEX 120 , 30 m × 0.25 mm × 0.25 μm); carrier gas, He (flow rate

2 mL/min); column temperature, 65 ˚C; t_R of (*R*)-isomer, 15.28 min; t_R of (*S*)-isomer, 15.48 min. 45% conversion, 42% ee.

(*R*)-3-methylbutan-2-ol: $RuCl_2$(indan-ambox)(PPh_3) (0.004 mmol), 3-methylbutan-2-one (0.4 mmol, S/C = 100), 2-propanol (2.0 mL), *t*-BuOK in 2-propanol (20 μmol), 5 atm, r.t., 15 h. GC (Supelco BETA DEX 120 , 30 m × 0.25 mm × 0.25 μm); carrier gas, He (flow rate 2 mL/min); column temperature, 50 ˚C; t_R of (*R*)-isomer, 18.47 min; t_R of (*S*)-isomer, 19.14 min. >99% conversion, 65% ee.

VI. **References**

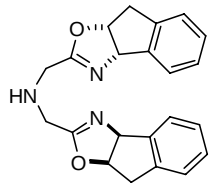
[1] W. Li, X. Sun, L. Zhou, G. Hou, S. Yu, X. Zhang, *J. Org. Chem.* **2009**, *74*, 1397.

[2] M. J. Burk, W. Hems, D. Herzberg, C. Malan, A. Zanotti-Gerosa, *Org. Lett.* **2000**, *2*, 4173.

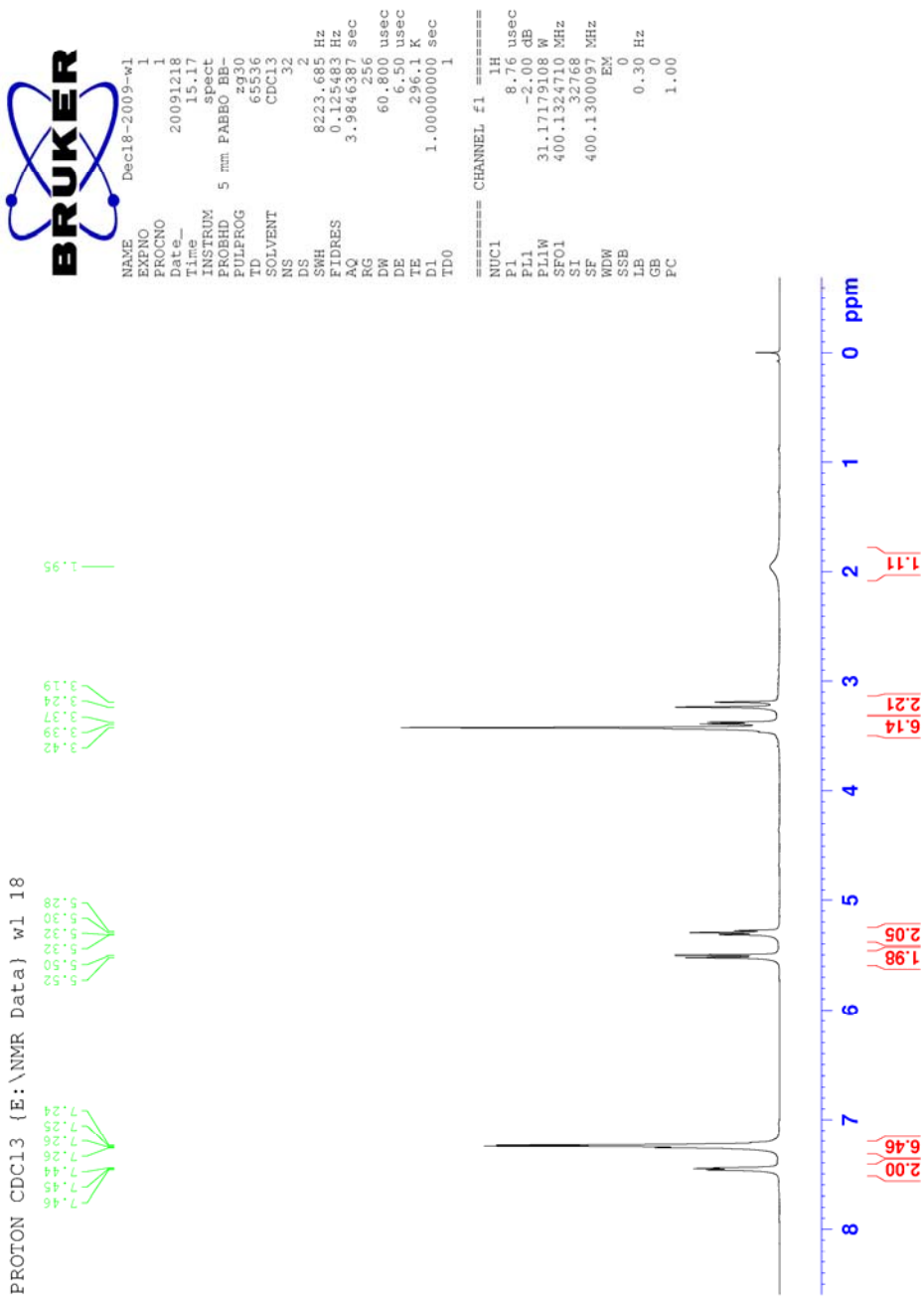
[3] D. Zhu, L. Hua, *J. Org. Chem.* **2006**, *71*, 9484.

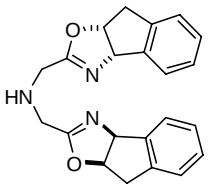
[4] H. Ooka, N. Arai, K. Azuma, N. Kurono, T. Ohkuma, *J. Org. Chem.* **2008**, *73*, 9084.

VII. ^{1}H NMR and ^{13}C NMR Spectra

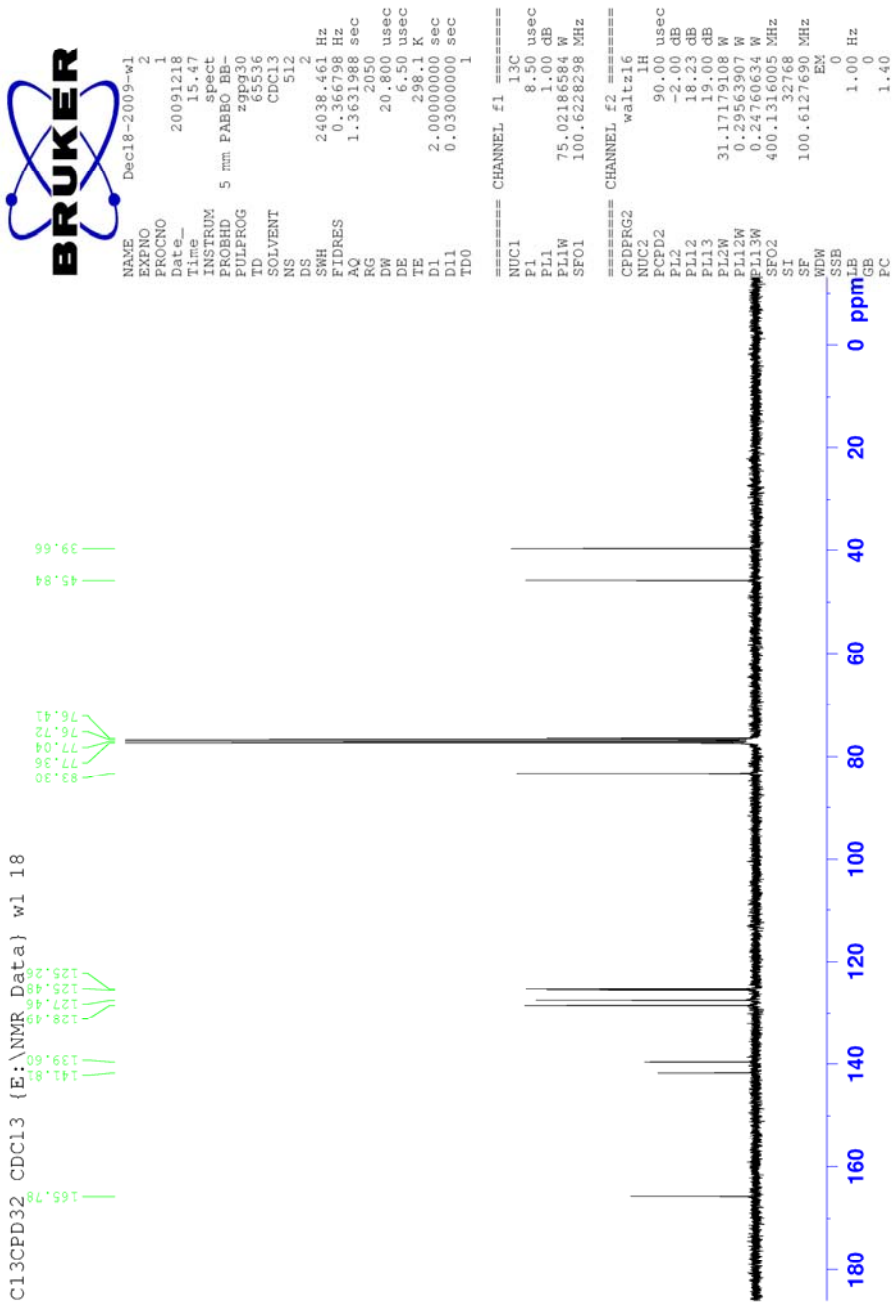


2 (*S*,*R*)-indan-ambox





2 (*S*,*R*)-indan-ambox


BRUKER
NAME Dec18-2009-w1
EXPNO 2
PROCNO 1
Date_ 20091218
Time_ 15.47
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 512
DS 2
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631988 sec
RG 2050
DW 20.800 usec
DE 6.50 usec
TE 298.1 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.50 usec
PL1 1.00 dB
PL1W 75.02186584 W
SFO1 100.6228298 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -2.00 dB
PL12 18.23 dB
PL13 19.00 dB
PL2W 31.17179108 W
PL12W 0.29563907 W
PL13W 0.24760634 W
SFO2 400.1316005 MHz
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
C13CPD32 CDCl3 (E:\NMR Data) w1 18
39.66
45.84
76.41
76.72
77.04
77.36
83.30
125.26
125.48
127.46
128.49
139.60
141.81
165.78
0 ppm
20
40
60
80
100
120
140
160
180