Effect of Ligand Structure on the Asymmetric Cyclization of Achiral Olefinic Organolithiums

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General Experimental Methods. Purification of reagents and precautions regarding the manipulation of organolithiums have been previously described.¹⁰ The concentration of commercial solutions of *t*-BuLi in heptane (FMC) was determined immediately prior to use by the method of Watson and Eastham.²⁷ Reaction products were analyzed by gas chromatography using a 25-m $\times$ 0.2-mm $\times$ 0.33- μ m cross-linked phenyl methyl (5 %) silicone capillary column connected to a flame ionization detector or mass spectrometer. Where appropriate, the deuterium content of products was determined by GC-MS using the method of Ashby.²⁸ CSP-GC analyses of enantiomeric purity were carried out on a 30-m $\times$ 0.25-mm $\times$ 0.125- μ m G-TA cyclodextrin column operating at a tank pressure of 50 psi, a head pressure of 20 psi, and a sample split ratio of 100 : 1. Literature procedures, incorporating some minor modifications, were followed for the preparation of **2**,^{6a} **10**,²⁹ **13**,¹⁵ **14**,³⁰ **16**,³¹ **21**,³² **28**,³³ **29**,³⁴ **30**,³⁵ **31**,³⁶ **32**,³⁷ **33**³⁸ and 2-bromo-3-methylaniline²⁵ in greater than 95 % purity as determined by capillary GC. An authentic sample of *N,N*-diallyl-3-methylaniline (**39**)²⁶ was prepared from *m*-toluidine by the general method described by Tidwell and Buchwald.²⁴ Compounds **3**, **7-9**, **27**, **34** and **35** are available from commercial suppliers.

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Current Data Parameters
NAME 185017
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20020520
Time 15.40
INSTRUM spect
PROBHD 5 mm Multinu
PULPROG zgpg
TD 15384
SOLVENT CDCl3
NS 15
DS 2
SWH 5502.241 Hz
FIDRES 0.341934 Hz
AQ 1.4623220 sec
RG 28.5
DW 89.250 usec
DE 127.50 usec
TE 300.0 K
D1 1.00000000 sec

===== CHANNEL f1 =====
NUC1 1H
P1 6.20 usec
PL1 -4.00 dB
SFO1 400.1324006 MHz

F2 - Processing parameters
SI 15384
SF 400.1300178 MHz
WDW EM
SSB 0
LB 0.20 Hz
GB 0
PC 1.00

1a NMR plot parameters
CX 20.00 cm
FIP 7.742 ppm
F1 3997.87 Hz
F2P -0.782 ppm
F2 -312.70 Hz
PPMCH 0.42618 ppm/cm
HZCH 170.52644 Hz/cm

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(1S, 2S)-N-ethyl-0-ethylpseudoephedrine

Current Data Parameters
NAME LB50170
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20020220
Time 18.48
INSTRUM spect
PROBHD 5 mm Multis
PULPROG zgpg30
TD 32768
SOLVENT CDCl3
VS 159
DS 4
SWH 22076.065 Hz
FIDRES 0.673577 Hz
AQ 0.7422458 sec
RG 2048
CW 22.690 usec
DE 4.50 usec
TE 300.0 K
SI 1.50000000 sec
C11 0.03000000 sec
C12 0.00000000 sec

----- CHANNEL f1 -----
NUC1 13C
P1 12.00 usec
PL1 -3.00 dB
SF01 100.6259993 MHz

----- CHANNEL f2 -----
CROSSP2 well136
NUC2 1H
PCPD2 112.00 usec
PL2 0.00 dB
PL12 25.00 dB
PL13 25.00 dB
SF02 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6127505 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

1D NMR plot parameters
GX 20.00 cm
FAP 150.458 cm
F1 15137.95 Hz
F2 -4.228 ppm
F2 -425.42 Hz
FREQN 7.73430 MHz/cm
ZCZ 778.16882 1

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Current Data Parameters
NAME LRS023
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20020531
Time 11.58
INSTRUM spect
PROBHD 5 mm M111nu
PULPROG zg30
TD 16384
SOLVENT CDCl3
NS 16
DS 2
SWH 5602.241 Hz
FIDRES 0.341934 Hz
AQ 1.4623220 sec
RG 71.8
DB 89.250 usec
DE 127.50 usec
TE 300.0 K
D1 1.00000000 sec

CHANNEL f1
NUC1 1H
P1 6.20 usec
PL1 -4.00 dB
SFO1 400.1304008 MHz

F2 - Processing parameters
SI 16384
SF 400.1300178 MHz
WDW EM
SSB 0
LB 0.20 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
F1P 9.064 ppm
F1 3226.79 Hz
F2P -0.366 ppm
F2 -154.46 Hz
PPMCH 0.422592 ppm/cm
HZCH 169.06343 Hz/cm

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Current Data Parameters
NAME LBS023C
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20020531
Time 12.08
INSTRUM spect
PROBHD 5 mm Multinu
PULPROG zgpg30
TD 32768
SOLVENT CDCl3
VS 4
SWH 22075.095 Hz
FIDRES 0.673577 Hz
AQ 0.7422452 sec
RG 8192
DM 22.850 usec
DE 4.50 usec
TE 300.0 K
D1 1.50000000 sec
D11 0.00000000 sec
D12 0.00000000 sec

===== CHANNEL f1 =====
NUC1 13C
P1 12.00 usec
PL1 -3.00 dB
SFO1 100.6262933 MHz

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
P2 112.00 usec
PL2 0.00 dB
PL12 25.00 dB
PL13 25.00 dB
SFO2 400.1318005 MHz

F2 - Processing parameters
SI 32768
SF 100.6127485 MHz
WDW EN
SSB 0
_B 1.00 Hz
GB 0
_C 1.40

3D NMR plot parameters
CX 20.00 cm
=JP 160.117 ppm
=I 16109.96 Hz
=2P -3.239 ppm
=E -331.04 Hz
=FNUC1 8.17033 /cm
-IZDM 822.04181 n

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References

- (27) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.
- (28) Ashby, E. C.; Welder, C. O. *J. Org. Chem.* **1997**, *62*, 3542.
- (29) (a) Winternitz, F.; Mousseron, M.; Dennilauler, R. *Bull. Chim. Soc. Fr.* **1956**, 382. (b) Cheng, W.-C.; Yu, W.-Y.; Zhu, J.; Cheung, K.-K.; Peng, S.; Poon, C.-K.; Che, C.-M. *Inorg. Chim. Acta* **1996**, *242*, 105.
- (30) (a) Elsevier, C. J.; Mooiweer, H. H. *J. Org. Chem.* **1987**, *52*, 1536. (b) Coote, S. J.; Davies, S. G.; Goodfellow, C. L.; Sutton, K. H.; Middlemiss, D.; Naylor, A. *Tetrahedron: Asymmetry* **1990**, *1*, 817.
- (31) Khruscheva, N. S.; Loim, N. M.; Sokolov, V. I.; Makhaev, V. D. *J. Chem. Soc., Perkin Trans. I* **1997**, 2425.
- (32) For a description of the enantiomer, refer to ref. 20b.
- (33) (a) Procedure: Wang, H.; Sun, L.; Glazebnik, S.; Zhao, K. *Tetrahedron Lett.* **1995**, *36*, 2953. (b) Substance: Wiggins, L. F. *J. Chem. Soc.* **1945**, 4.
- (34) Norman, R. O. C.; Parr, W. J. E.; Thomas, C. B. *J. Chem. Soc., Perkin Trans. I* **1976**, 811.
- (35) Waagen, V.; Partali, V.; Hollingsaeter, I.; Huang, M. S. S.; Anthonsen, T. *Acta. Chem. Scand.* **1994**, *48*, 506. Our optical rotation was: $[\alpha]_{\text{D}}^{25} = +28.2$ (*c* 5.69, hexane), while Waagen and co-workers report $[\alpha]_{\text{D}}^{20} = +2.7$ (*c* 1.30, hexane).
- (36) Brown, H. C.; Murali, D.; Singaram, B. *J. Organomet. Chem.* **1999**, *581*, 116.
- (37) Muskat, I. E. *J. Am. Chem. Soc.* **1934**, *56*, 693.

(38) Goldstein, I. J.; Hamilton, J. K.; Smith, F. *J. Am. Chem. Soc.* **1957**, 79, 1190.