Supporting Information

Kinetic Resolution and Chemoenzymatic Dynamic Kinetic Resolution of Functionalized γ -Hydroxy Amides.

Ann-Britt L. Fransson, Linnéa Borén, Oscar Pàmies, and Jan-E. Bäckvall*

Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University,
SE-10691 Stockholm, Sweden.

Supporting Information Table of Contents:

General procedures	S1
^1H - and ^{13}C -NMR Spectra of compounds 1a-h and 5a-h	S2-S33

General Procedures. All reactions were carried out under dry argon atmosphere in oven-dried glassware. Solvents were purified according to standard procedures. Commercially available reagents were used without further purification. *Pseudomonas fluorescens* (PF, 61u/g) was purchased from Fluka. *Pseudomonas species* lipase (PS-C “Amano” II, $\geq 600\text{u/g}$) was a donation from Amano Pharmaceutical Co. Ltd., Japan. *Candida antarctica* lipase B (Novozyme 435, N-435, 10000 PLU/g) was a donation from Novo Nordisk A/S, Denmark. The *p*-chlorophenyl acetateⁱ and 4,5-epoxy-1-penteneⁱⁱ were prepared according to a literature procedures. The ruthenium catalyst was synthesized according to a literature procedureⁱⁱⁱ and recrystallized from CH_2Cl_2 /pentane prior to use. The corresponding ketones **6a-d**, **6f-g** were obtained by oxidation of the alcohols **1a-d**, **1f-g** using Ru-catalyst **4** in acetone at 56 °C. Ketones **6e** and **6h** were obtained from the alcohols **1e** and **1h** via oxidation by Jones’ reagent. ^1H (400 or 300 MHz) and ^{13}C NMR (100 or 75 MHz) spectra were recorded with chemical shifts (δ) reported in ppm, using residual solvent as internal standard (CDCl_3 , ^1H δ 7.26, ^{13}C δ 77), and coupling constants (J) given in Hertz. Solvents for extraction and chromatography were of technical grade and distilled before use. Purification of synthesized material was performed by column chromatography with silica gel 60 (240-400 mesh). The enantiomeric excess of compounds **1**, **5** and **12** was determined by analytical GLC employing a CP-Chirasil-Dex CB column, or analytical HPLC employing an OJ column, using racemic compounds as references.

ⁱ Persson, B. A.; Larsson, A. L. E.; LeRay, M.; Bäckvall, J.-E. *J. Am. Chem. Soc.* **1999**, *121*, 1645-1650.

ⁱⁱ Schuda, A. D.; Mazzocchi, P. H.; Fritz, G.; Morgan, T. *Synthesis* **1986**, *4*, 309.

ⁱⁱⁱ Huerta, F. F.; Laxmi, Y. R. S.; Bäckvall, J.-E. *Org. Lett.* **2000**, *2*, 1037.

1N,1N-diisopropyl-4-hydroxypentanamide (1a)

Pulse Sequence: s2pul

Solvent: CDCl₃

Temp. 25.0 C / 298.1 K

File: AR268

INOVA-500 "nmr6"

Relax. delay 1.000 sec

Pulse 50.4 degrees

Acq. time 1.998 sec

Width 4500.5 Hz

100 repetitions

OBSERVE H1, 299.9464283 MHz

DATA PROCESSING

Line broadening 0.1 Hz

FT size 32768

Total time 5 min, 12 sec

1a

1N,1N-diisopropyl-4-hydroxypentanamide (1a)

Pulse Sequence: s2pul

Solvent: CDCl₃
Temp. 25.0 C / 298.1 K
Mercury-300BB "nmr3"

1a

Relax. delay 1.000 sec
Pulse 67.0 degrees
Acq. time 1.815 sec
Width 18761.7 Hz
1000 repetitions
OBSERVE C13, 75.4215714 MHz
DECOUPLE H1, 299.9479605 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 51 min, 52 sec

1N,1N-diisopropyl-4-hydroxyhexanamide (1b)

Pulse Sequence: s2pul

Solvent: CDCl3

Temp. 25.0 C / 298.1 K

File: AR300-h

INOVA-500 "nmr6"

Relax. delay 1.000 sec

Pulse 57.3 degrees

Acq. time 1.998 sec

Width 4500.5 Hz

50 repetitions

OBSERVE H1, 299.9464283 MHz

DATA PROCESSING

Line broadening 0.1 Hz

FT size 32768

Total time 2 min, 36 sec

1b

1N,1N-diisopropyl-4-hydroxyhexanamide (1b)

Pulse Sequence: s2pu1

Solvent: CDCl₃

Temp. 25.0 C / 298.1 K.

File: ar300-c

INOVA-500 "nmr6"

Relax. delay 1.000 sec

Pulse 50.0 degrees

Acq. time 1.199 sec

Width 25000.0 Hz

259 repetitions

OBSERVE C13, 100.5652122 MHz

DECOUPLE H1, 399.9426336 MHz

Power 42 dB

continuously on

WALTZ-16 modulated

DATA PROCESSING

Line broadening 1.0 Hz

FT size 65536

Total time 42 min, 5 sec

1b

1N,1N-diisopropyl-4-hydroxyheptanamide (1c)

Pulse Sequence: s2pu1

Solvent: CDC13

Temp. 25.0 C / 298.1 K

File: ar304-h

INOVA-500 "nmr6"

Relax. delay 1.000 sec

Pulse 44.3 degrees

Acq. time 2.731 sec

Width 5998.8 Hz

16 repetitions

OBSERVE H1, 399.9408614 MHz

DATA PROCESSING

Line broadening 0.1 Hz

FT size 65536

Total time 1 min, 2 sec

1c

1N,1N-diisopropyl-4-hydroxyheptanamide (1c)

Pulse Sequence: s2pul

Solvent: CDCl₃

Temp. 25.0 C / 298.1 K

File: ar304-c

INOVA-500 "nmr6"

Relax. delay 1.000 sec

Pulse 50.0 degrees

Acq. time 1.199 sec

Width 25000.0 Hz

325 repetitions

OBSERVE C13, 100.5651856 MHz

DECOUPLE H1, 399.9428336 MHz

Power 42 dB

continuously on

WALTZ-16 modulated

DATA PROCESSING

Line broadening 1.0 Hz

FT size 65536

Total time 42 min, 5 sec

1c

N,N-diisopropyl-4-hydroxyoctanamide (1d)

Pulse Sequence: s2pul

Solvent: CDCl₃
Temp. 25.0 C / 298.1 K
File: AR319-h-butylamide
INOVA-500 "nmr5"

Relax. delay 1.000 sec
Pulse 45.4 degrees
Acq. time 2.731 sec
Width 5998.8 Hz
39 repetitions
OBSERVE H1, 399.9408614 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 3 min, 47 sec

1N,1N-diisopropyl-4-hydroxyoctanamide (1d)

Pulse Sequence: s2pul

Solvent: CDCl₃
Temp. 25.0 C / 298.1 K
File: Ar319-butylamide
INOVA-500 "nmr5"

Relax. delay 1.000 sec
Pulse 50.0 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
466 repetitions
OBSERVE C13, 100.5652092 MHz
DECOUPLE H1, 399.9428336 MHz
Power 42 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 42 min, 5 sec

5-Cyano-1N,1N-diisopropyl-4-hydroxypentanamide (1e)

Pulse Sequence: s2pul

Solvent: CDCl₃

Temp. 25.0 C / 298.1 K

File: amid-cn

INOVA-500 "nmr5"

Relax. delay 1.000 sec

Pulse 57.8 degrees

Acq. time 2.731 sec

Width 5998.8 Hz

16 repetitions

OBSERVE H1, 399.9356500 MHz

DATA PROCESSING

Line broadening 0.1 Hz

FT size 65536

Total time 1 min, 2 sec

5-Cyano-1N,1N-diisopropyl-4-hydroxypentanamide (1e)

Pulse Sequence: s2pu1

Solvent: CDCl3

Temp. 25.0 C / 298.1 K

File: cn-amid-c

INOVA-500 "nmr5"

Relax. delay 1.000 sec

Pulse 57.0 degrees

Acq. time 1.199 sec

Width 25000.0 Hz

154 repetitions

OBSERVE C13, 100.5638752 MHz

DECOUPLE H1, 399.9376154 MHz

Power 41 dB

continuously on

WALTZ-16 modulated

DATA PROCESSING

Line broadening 1.0 Hz

FT size 65536

Total time 42 min, 5 sec

1N,1N-diisopropyl-4-hydroxyhept-6-enamide (1f)

Pulse Sequence: s2pu1

Solvent: CDCl3

Temp. 25.0 C / 298.1 K

File: ar318-h

INOVA-500 "nmr5"

Relax. delay 1.000 sec

Pulse 45.4 degrees

Acq. time 2.731 sec

Width 5998.8 Hz

30 repetitions

OBSERVE H1, 399.9408614 MHz

DATA PROCESSING

Line broadening 0.1 Hz

FT size 65536

Total time 1 min, 57 sec

1N,1N-diisopropyl-4-hydroxyhept-6-enamide (1f)

Pulse Sequence: s2pu1

Solvent: CDCl₃

Temp. 25.0 C / 298.1 K

File: AR318-c

INOVA-500 "nmr5"

1f

Relax. delay 1.000 sec
Pulse 50.0 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
720 repetitions
OBSERVE C13, 100.5652092 MHz
DECOUPLE H1, 399.9426336 MHz
Power 42 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 42 min, 5 sec

1N,1N-diisopropyl-4-hydroxy-5-methoxypentanamide (1g)

Pulse Sequence: s2pu1

Solvent: CDCl₃
Temp. 25.0 C / 298.1 K
File: ar306-flash
INOVA-500 "nmr6"

1g

Relax. delay 1.000 sec
Pulse 57.3 degrees
Acq. time 1.998 sec
Width 4500.5 Hz
100 repetitions
OBSERVE H1, 299.9464283 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 5 min, 12 sec

1N,1N-diisopropyl-4-hydroxy-5-methoxypentanamide (1g)

Pulse Sequence: s2pu1

Solvent: CDCl₃
Temp. 25.0 C / 298.1 K
File: ar306-flash-c
INOVA-500 "nmr5"

1g

Relax. delay 1.000 sec
Pulse 75.4 degrees
Acq. time 1.815 sec
Width 18761.7 Hz
563 repetitions
OBSERVE C13, 75.4215904 MHz
DECOUPLE H1, 299.9479604 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 53 min, 4 sec

5-chloro-1N,1N-diisopropyl-4-hydroxypentanamide (1h)

Pulse Sequence: s2pu1

Solvent: CDCl₃
Temp. 25.0 C / 298.1 K
File: AR305-h
INOVA-500 "nmr6"

1h

Relax. delay 1.000 sec
Pulse 57.3 degrees
Acq. time 1.998 sec
Width 4500.5 Hz
50 repetitions
OBSERVE H1, 299.9464283 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 2 min, 36 sec

5-chloro-1N,1N-diisopropyl-4-hydroxypentanamide (1h)

Pulse Sequence: s2pu1

Solvent: CDCl₃
Temp. 25.0 C / 298.1 K
File: ar305-c
INOVA-500 "nmr6"

1h

Relax. delay 1.000 sec
Pulse 75.4 degrees
Acq. time 1.815 sec
Width 18761.7 Hz
1024 repetitions
OBSERVE C13, 75.4215901 MHz
DECOUPLE H1, 299.9479604 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 53 min, 4 sec

4-Acetoxy-1N,1N-diisopropylpentanamide (5a)

Pulse Sequence: s2pu1

Solvent: CDCl₃

Temp: 25.0 C / 298.1 K-

File: AR280

INOVA-500 "nmr5"

Relax. delay 1.000 sec

Pulse 44.3 degrees

Acq. time 2.731 sec

Width 5998.8 Hz

185 repetitions

OBSERVE H1, 399.9408614 MHz

DATA PROCESSING

Line broadening 0.1 Hz

FT size 65536

Total time 0 min, 0 sec

4-acetoxy-1N,1N-diisopropylpentanamide (5a)

Pulse Sequence: s2pu1

Solvent: CDCl₃
Temp. 25.0 C / 298.1 K
File: armetylacetate-c
INOVA-500 "nmr5"

Relax. delay 1.000 sec
Pulse 67.0 degrees
Acq. time 1.815 sec
Width 18761.7 Hz
1024 repetitions
OBSERVE C13, 75.4215580 MHz
DECOUPLE H1, 299.9479605 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 0 min, 0 sec

4-Acetoxy-1N,1N-diisopropylhexanamide (5b)

Pulse Sequence: s2pu1

Solvent: CDCl3

Temp. 25.0 C / 298.1 K

File: AR307

INOVA-500 "nmr5"

Relax. delay 1.000 sec

Pulse 57.3 degrees

Acq. time 1.998 sec

Width 4500.5 Hz

50 repetitions

OBSERVE H1, 299.9464283 MHz

DATA PROCESSING

Line broadening 0.1 Hz

FT size 32768

Total time 2 min, 36 sec

4-Acetoxy-1N,1N-diisopropylhexanamide (5b)

Pulse Sequence: s2pu1

Solvent: CDCl₃
Temp. 25.0 C / 298.1 K
File: ar307-c
INOVA-500 "nmr5"

5b

Relax. delay 1.000 sec
Pulse 75.4 degrees
Acq. time 1.815 sec
Width 18761.7 Hz
565 repetitions
OBSERVE C13, 75.4215912 MHz
DECOUPLE H1, 299.9479604 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 53 min, 4 sec

4-Acetoxy-1N,1N-diisopropylheptanamide (5c)

Pulse Sequence: s2pu1

Solvent: CDCl₃

Temp. 25.0 C / 298.1 K

File: ar308-h

INOVA-500 "nmr5"

Relax. delay 1.000 sec

Pulse 57.3 degrees

Acq. time 1.998 sec

Width 4500.5 Hz

100 repetitions

OBSERVE H1, 299.9464283 MHz

DATA PROCESSING

Line broadening 0.1 Hz

FT size 32768

Total time 5 min, 12 sec

4-Acetoxy-1*N*,1*N*-diisopropylheptanamide (5c)

Pulse Sequence: s2pu1

Solvent: CDCl₃

Temp. 25.0 C / 298.1 K

File: ar308-c

INOVA-500 "nmr5"

Relax. delay 1.000 sec

Pulse 75.4 degrees

Acq. time 1.815 sec

Width 18761.7 Hz

738 repetitions

OBSERVE C13, 75.4215906 MHz

DECOUPLE H1, 299.9479604 MHz

Power 39 dB

continuously on

WALTZ-16 modulated

DATA PROCESSING

Line broadening 1.0 Hz

FT size 131072

Total time 53 min, 4 sec

4-acetoxy-1N,1N-diisopropyl-octanamide (5d)

Pulse Sequence: s2pu1

Solvent: CDCl₃
Temp. 25.0 C / 298.1 K
File: Ar322
INOVA-500 "nmr5"

Relax. delay 1.000 sec
Pulse 43.6 degrees
Acq. time 2.731 sec
Width 5998.8 Hz
30 repetitions
OBSERVE H1, 399.9408614 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 1 min, 57 sec

4-Acetoxy-1N,1N-diisopropyloctanamide (5d)

Pulse Sequence: s2pul

Solvent: CDCl₃
Temp. 25.0 C / 298.1 K
File: ar322-int-c-d45
INOVA-500 "nmr5"

Relax. delay 45.000 sec
Pulse 75.4 degrees
Acq. time 1.815 sec
Width 18761.7 Hz
880 repetitions
OBSERVE C13, 75.4215904 MHz
DECOUPLE H1, 299.9479605 MHz
Power 39 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 3.0 Hz
FT size 131072
Total time 26 hr, 10 min, 19 sec

4-acetoxy-5-cyano-1*N*,1*N*-diisopropylpentanamide (5e)

Pulse Sequence: s2pu1

Solvent: CDCl₃
Temp. 25.0 C / 298.1 K
File: ar401-cn-oac
INOVA-500 "nmr5"

Relax. delay 1.000 sec
Pulse 57.8 degrees
Acq. time 2.731 sec
Width 5998.8 Hz
48 repetitions
OBSERVE H1, 399.9356677 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 3 min, 7 sec

4-Acetoxy-5-cyano-1N,1N-diisopropylpentanamide (5e)

Pulse Sequence: s2pu1

Solvent: CDCl₃
Temp. 25.0 C / 298.1 K
File: ar401-cn-aoc-c
INOVA-500 "nmr5"

Relax. delay 1.000 sec
Pulse 57.0 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
581 repetitions
OBSERVE C13, 100.5639023 MHz
DECOUPLE H1, 399.9376154 MHz
Power 41 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 42 min, 5 sec

4-Acetoxy-1N,1N-diisopropylhept-6-enamide (5f)

Pulse Sequence: s2pul

Solvent: CDCl₃

Temp. 25.0 C / 298.1 K

File: ar321-h

INOVA-500 "nmr5"

Relax. delay 1.000 sec

Pulse 57.3 degrees

Acq. time 1.998 sec

Width 4500.5 Hz

16 repetitions

OBSERVE H1, 299.9464283 MHz

DATA PROCESSING

Line broadening 0.1 Hz

FT size 32768

Total time 0 min, 49 sec

4-acetoxy-1N,n-diisopropylhept-6-enamide (5f)

Pulse Sequence: s2pul

Solvent: CDCl₃

Temp. 25.0 C / 298.1 K

File: ar321-c

INOVA-500 "nmr6"

Relax. delay 1.000 sec

Pulse 75.4 degrees

Acq. time 1.815 sec

Width 18761.7 Hz

419 repetitions

OBSERVE C13, 75.4215907 MHz

DECOUPLE H1, 299.9479605 MHz

Power 39 dB

continuously on

WALTZ-16 modulated

DATA PROCESSING

Line broadening 1.0 Hz

FT size 131072

Total time 53 min, 4 sec

4-Acetoxy-1*N*,1*N*-diisopropyl-5-methoxypentanamide (5g)

Pulse Sequence: s2pu1

Solvent: CDCl₃

Temp. 25.0 C / 298.1 K

File: ar314-meo2-h

INOVA-500 "nmr6"

Relax. delay 1.000 sec

Pulse 57.3 degrees

Acq. time 1.998 sec

Width 4500.5 Hz

100 repetitions

OBSERVE H1, 299.9464263 MHz

DATA PROCESSING

Line broadening 0.1 Hz

FT size 32768

Total time 5 min, 12 sec

4-Acetoxy-1N,1N-diisopropyl-5-methoxypentanamide (5g)

Pulse Sequence: s2pu1

Solvent: CDCl₃
Temp. 25.0 C / 298.1 K
File: ar314-mtoch2-c
INOVA-500 "nmr6"

Relax. delay 1.000 sec
Pulse 75.4 degrees
Acq. time 1.815 sec
Width 18761.7 Hz
326 repetitions
OBSERVE C13, 75.4215714 MHz
DECOUPLE H1, 299.9479604 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 53 min, 4 sec

4-Acetoxy-5-chloro-1N,1N-diisopropylpentanamide (5h)

Pulse Sequence: s2pul

Solvent: CDCl₃
Temp. 25.0 C / 298.1 K
File: ar312-h
INOVA-500 "nmr6"

Relax. delay 1.000 sec
Pulse 57.3 degrees
Acq. time 1.998 sec
Width 4500.5 Hz
50 repetitions
OBSERVE H1, 299.9464283 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 2 min, 36 sec

4-Acetoxy-5-chloro-1N,1N-diisopropylpentanamide (5h)

Pulse Sequence: s2pu1

Solvent: CDCl₃

Temp. 25.0 C / 298.1 K

File: ar312-c

INOVA-500 "nmr5"

Relax. delay 1.000 sec

Pulse 67.0 degrees

Acq. time 1.815 sec

Width 18761.7 Hz

1024 repetitions

OBSERVE C13, 75.4215890 MHz

DECOUPLE H1, 299.9479605 MHz

Power 38 dB

continuously on

WALTZ-16 modulated

DATA PROCESSING

Line broadening 1.0 Hz

FT size 131072

Total time 53 min, 4 sec