Supporting Information

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

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**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, ≥600u/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 acetate and 4,5-epoxy-1-pentene were prepared according to a literature procedures. The ruthenium catalyst was synthesized according to a literature procedure and recrystallized from CH2Cl2/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 13C NMR (100 or 75 MHz) spectra were recorded with chemical shifts (δ) reported in ppm, using residual solvent as internal standard (CDCl3, 1H δ 7.26, 13C 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.


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

IN.1N-dilisopropy1-4-hydroxypentanamide (1a)

Pulse Sequence: s2pul
Solvent: CDC13
Temp. 25.8 C / 298.1 K
File: ARZ26
INOVA-500 "narc"

Relax. delay 1.000 sec
Pulse 55.6 degrees
Acq. time 1.888 sec
Width 4592.5 Hz
100 repetitions
OBSERVE H1 299.8644263 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 5 min, 12 sec

1a
INN-diisopropyl-4-hydroxypentanamide (1a)

Pulse Sequence: s2pul
Solvent: CDC13
Temp. 25.8 °C / 298.1 K
Mercury=30088 "ner3"

Relax. delay 1.000 sec
Pulse 67.0 degrees
Acq. time 1.015 sec
Width 18761.7 Hz
1000 repetitions
OBSERVE C13, 75.4215714 MHz
DECOUPLE H1, 299.847605 MHz
Power 38 dB
continuously on
VALT2=16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 51 min, 52 sec
1H,1H-difluoropropyl-4-hydroxyhexanamide (1b)

Pulse Sequence: z2pul
Solvent: CDCl3
Temp. 25.0 °C / 295.1 K
Pff= 40000 Hz
INOVA-500 MHz

Relax. delay 1.000 sec
Pulse 57.3 degrees
Acq. time 1.386 sec
Width 450.5 Hz
50 repetitions

OBSERVE H1, 299.9464283 MHz
DATA PROCESSING
Line broadening 9.1 Hz
FT size 32768
Total time 2 min, 36 sec

1b
IN.1N-dl-isopropyl-4-hydroxyhexanamide (1b)

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.8 C / 298.1 K
File: ar500-c
INOVA-500 "merd"

Relax. delay 1.000 sec
Pulse 90.8 degrees
Acq. time 1.189 sec
Width 25088.8 Hz
250 repetitions
OBSERVE C13, 100.5653122 MHz
DEOUPLE H1, 399.8428336 MHz
Power 42 dB continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 85536
Total time 42 min, 5 sec
IN IN-dl isopropyl-4-hydroxyheptanamide (1c)

Pulse Sequence: z2pul
Solvent: CDCl3
Temp. 25.9 C / 298.1 K
F1 gr: er304-h
INDEVA-500 "nare"

Relax. delay 1.000 sec
Pulse 44.3 degrees
Acq. time 2.731 sec
Width 5956.8 Hz
16 repetitions
OBSERVE HL 299.241561 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 1 min, 2 sec
IN.1N-difospropyl-4-hydroxyheptanamide (1c)

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 °C / 288.1 K
File: ar39c-c
INOVA-500 "nere"

Relax. delay 1.000 sec
Pulse 50.0 degrees
Acq. time 1.180 sec
Width 2000.0 Hz
325 repetitions
OBSERVE C13, 100.5651856 MHz
DECOPUPLE H1, 399.9428336 MHz
Power 42 dB continuously on
WALTZ-15 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 42 min, 5 sec
**N,N-difisopropyl-4-hydroxyoctanamide (1d)**

**Pulse Sequence:** s2pul

**Solvent:** CDCl3

**Temp:** 25.1 °C / 298.1 K

**Pfie:** AR215-N-butylamide

**INDIA-500 nmr5**

- Relax. delay 1,000 sec
- Pulse 45.4 degrees
- Acq. time 2.751 sec
- Width 598.0 Hz
- 38 repetitions

**OBSERVE** H1, 399.9408614 MHz

**DATA PROCESSING**
- Line broadening 0.1 Hz
- FT size 65536
- Total time 3 min, 47 sec
IN. IN-diol propyl-4-hydroxyoctanamide (1d)

Pulse Sequence: s2pu1
Solvent: CDCl3
Temp.: 25.0 °C / 298.1 K
Fluor: AR319-dutylamide
INOVA-500 "nmrs"

Relax. delay 1.000 sec
Pulse 50.0 degrees
Acq. time 1.199 sec
Width 20000.0 Hz
466 repetitions
OBSERVE C13, 100.5652592 MHz
DECOUPLE H1, 399.3428336 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

1d

180 160 140 120 100 80 60 40 20 ppm
5-Cyano-1H,1H-disopropyl-4-hydroxypentanamide (1e)

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
File: am1d-cn
INova-500 "nars"

Relax. delay 1.000 sec
Pulse 57.0 degrees
Acq. time 2.731 sec
Width 3598.8 Hz
18 repetitions

Observe H1, 395.8356500 MHz
Data Processing
Line broadening 0.1 Hz
FT Size 65536
Total time 1 min, 2 sec.
S-Cyano-1H,1H-difluoropropyl-4-hydroxypentanamide (1e)

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 °C / 298.1 K
F1A: C=amid-C
INOVA-500 "nmr5"

Relax. delay 1.000 sec
Pulse 57.0 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
156 repetitions

OBSERVE C13, 106.6838752 MHz
DECOUPLE H2, 299.3376154 MHz
Power 41 dB
continuously on
VOLT2-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 42 min, 5 sec
Pulse Sequence: z3pu7
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Files: ar318-h
INova-500 "nnmr"

Relax. delay 1.000 sec
Pulse 45.4 degrees
Acq. time 2.731 sec
Width 5986.8 Hz
30 repetitions

OBSERVE HL 339.948614 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 1 min, 37 sec
IN.IN-dimethyl-4-hydroxyhept-6-enamide (1f)

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0°C / 298.1 K
File: AR318-c
INOVA-500 "nars"

Relax, delay 1.000 sec
Pulse 90.0 degrees
Acq. time 1.198 sec
Width 25260.0 Hz
729 repetitions

OBSERVE C13, 100.6552882 MHz
DECOUPLE H1, 399.9428336 MHz
Power 42 dB
continuously on

VALTZ-15 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 42 min, 5 sec
IN-1N-diflpropyl-4-hydroxy-5-metboxypentanamide (1g)

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
F1 filter: sw388-Flash
INOVA-500 "nars"

Relax. delay 1.000 sec
Pulse 57.3 degrees
Acq. time 1.998 sec
Width 4500.5 Hz
195 repetitions
OBSERVE Hz 298.8464283 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 5 min, 12 sec
IN-N-didesopropyl-4-hydroxy-5-methoxypentanamide (10)

Pulse Sequence: 1'H
Solvent: CDC13
Temp: 25.4 C / 298.1 K
File: ar398-Flash-C
INova-500 "narrow"

Relax. delay 1.000 sec
Pulse 75.4 degrees
Acq. time 1.015 sec
Width 18781.7 Hz
603 repetitions
OBSERVE 13. 75.4215684 MHz
DECOUPLE 1H, 298.9478584 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 23 min, 4 sec
$\text{S-chloro-1H,1H-dilisopropyl-4-hydroxypentanamide (1h)}$

**Pulse Sequence:** s2pul

**Solvent:** CDCl3

**Temp.** 25.0°C / 298.1 K

**Slice:** AB399-h

**INOVA-500** "hr6"

- Relax. delay: 1.000 sec
- Pulse: 57.3 degrees
- Acq. time: 1.308 sec
- Width: 4500.3 Hz
- 50 repetitions

**Observe:** H 1.298.94644288 MHz

**Data Processing:**
- Line broadening: 0.1 Hz
- FT size: 32768
- Total time: 2 min, 36 sec

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![Chemical Structure](attachment:structure.png)
5-chloro-1H,1H-difluoroprop-1-ene (1h)

Pulse Sequence: szpul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Films are50-80°C
INOVA-500 MHz

Relax. delay 1.000 sec
Pulse 75.4 degrees
Acq. time 1.015 sec
Width 10781.7 Hz
1284 repetitions

OBSERVE C13, 75.4215801 MHz
DECouple H1, 299.9478804 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-dimethylpentanamide (5a)

Pulse Sequence: s2pul
Solvent: CDC13
Temp: 25.0°C / 298.1 K
Field: AR200
INOVA-500 "nars"

Relax. delay 1.000 sec
Pulse 44.3 degrees
Acc. time 0.001 sec
Width 5998.6 Hz
185 repetitions
OBSERVE NL 398.84066154 MHz
DATA PROCESSING
Line broadening 0.1 Hz
PT size 55536
Total time 5 min, 0 sec

ppm
4-acetoxy-1,1-dimethylpentanamide (5a)

Pulse Sequence: s2pu
Solvent: CDCl3
Temp. 25.0 °C / 298.1 K
Field: aromatic acetate = 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, 75.4215586 MHz
DECOUPLE H1, 299.4678825 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-1H,1H-diisopropylethanolide [5b]

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 °C / 298.1 K
File: AR307
INOVA-500 "m65"

Relax. delay 1,000 sec
Pulse 57.3 degrees
Acq. time 1,950 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-dimethylhexanamide (5b)

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 °C / 298.1 K
file: ar357-0
INNOVA-500 "nars"

Relax. delay 1.000 sec
Pulse 75.4 degrees
Acc. time 1.015 sec
Width 176761.7 Hz
665 repetitions
OBSERVE C13, 75.4215912 MHz
DECUPLE NH, 895.8479564 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-1,1-dimethylheptanamide (5c)

Pulse Sequence: szpul
Solvent: CDCl3
Temp. 25.8 C / 298.1 K
File: ar388-h
INOVA-500 "nsr5"

Relax. delay 1.000 sec
Pulse 57.3 degrees
Acq. time 1.928 sec
Width 4500.5 Hz
180 repetitions
Observe H1, 299.446283 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 5 min, 12 sec
4-Acetoxyl-N,N-diisopropylheptanamide (5c)

Pulse Sequence: s2pu1
Solvent: CDCl3
Temp. 25.0 °C / 298.1 K
File: ar388-c
INOVA-500 "nmrs"

Relax. delay 1000 sec
Pulse 75.4 degrees
Acc. time 1.815 sec
Width 18761.7 Hz
738 repetitions

OBSERVE C13, 75.4215906 MHz
DECOUPLE H1, 298.3479604 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
d-acetoxy-IN-IN-dilisopropyl-octanamide (5d)

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
File: Aq321
INOVA-500 "nrs" "nrs"

Relax. delay 1.000 sec
Pulse 43.6 degrees
Acq. time 2.731 sec
Width 5998.8 Hz
35 repetitions
ORESSERVE H1, 399.9488614 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 51236
Total time 1 min, 57 sec
4-Acetoxy-1N,1N-difisopropyloctanamide (5d)

Pulse Sequence: szpul
Solvent: CDC13
File: ap322-int-c-d45

5d

Relax. delay 45.000 sec
Pulse 75.4 degrees
Acq. time 1.815 sec
Width 18761.7 Hz
800 repetitions

OBSERVE: Cl3, 75.4215804 MHz
DECouple: H1, 299.8479605 MHz
Power: 38 dB

on during acquisition
off during delay
WALTZ-16 modulated

DATA PROCESSING
Line broadening 3.0 Hz
FT size 131072
Total time 26 hr, 19 min, 19 sec
4-acetoxy-5-cyano-1H,1H-difluoropropylpentanamide (5e)

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 °C / 298.1 K
Files: ar461-cnm-pac
INOVA-500 "nms5"

Relax. delay 1.000 sec
Pulse 57.0 degrees
Acq. time 2.781 sec
Width 5998.6 Hz
48 repetitions
OBSERVE Hz, 398.9356877 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 3 min, 7 sec
4-Acetoxy-5-cyano-1IN,1IN-dipropylpentanamide (5e)

Pulse Sequence: 62pu1
Solvent: CDCl3
Temp. 29.8 C / 298.1 K
Field: ar401-K-arc-C
INova-500 "nmr"

Relax. delay 1.000 sec
Pulse 57.2 Degrees
Avg. time 1.125 sec
Wait 20000.0 Hz
501 repetitions
OBSERVE 13C, 100.63 MHz
DECOUPLE H2, 399.27 MHz
Power 41 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
PT size 25526
Total time 42 min, 5 sec
4-Acetoxy-1.1N-difluoropropylhept-6-ynamide (5f)

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Fid: a321-n
INOMA-566 "nms5"

Relax. delay 1.200 sec
Pulse 57.3 degrees
Acq. time 1.996 sec
Width 4508.5 Hz
16 repetitions
OBSERVE H2, 299.9444286 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 0 min, 49 sec
4-acetoxy-1,1-dimethylbutane-2-thiol (5f)

Pulse Sequence: sz-pul
Solvent: CDCl3
Temp. 25.0 °C / 298.1 K
File: ar321-c
INova-500 "mar6"

Relax. delay 1.000 sec
Pulse 75.4 degrees
Acq. time 1.618 sec
Width 18761.7 Hz
419 repetitions
Observe C13, 75.4215907 MHz
Decouple H1, 293.9478685 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
4-Acetoxy-1N,N-diisopropyl-5-methoxypentanamide (5g)

Pulse Sequence: szpul
Solvent: CDCl3
Temp. 25.8 C / 298.1 K
File: ar314-nedoch2-h
INova-500 "nara"

Relax. delay 1.888 sec
Pulse 37.5 degree
Acq. time 1.386 sec
Width 400.0 Hz
100 repetitions
OBSERVE M1, 259.2464283 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 5 min, 12 sec

ppm
e-Acetoxy-1N,1N-difisoxypropyl-5-methoxypentanamide (5g)

Pulse Sequence: z2p1
Solvent: CDCl3
Temp. 298.1 K
Field: 296-400 MHz
INNOVA-500 "mac6"

Relax. delay 1.00 sec
Pulse 75.4 degrees
Acq. time 6.016 sec
Width 1.87617 Hz
329 repetitions
Observe CH₃, 75.421574 MHz
Decouple H₂, 298.3478694 MHz
Power 35 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-1H,1H-difluoropropylpentanamide (5h)

Pulse Sequence: apdpu
Solvent: CDCl3
Temp: 25.0 °C / 298.1 K
File: ar312b
INDVA-500 "nme6"

Relax. delay 1.000 sec
Pulse 57.3 degrees
Acq. time 1.836 sec
Width 4506.5 Hz
50 repetitions
Observe Hz, 299.9444639 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 2 min, 36 sec
4-Acetoxy-5-chloro-1H,1H-dioisopropylpentanamide (5h)

Pulse Sequence: z2pu7
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
File: ar312-c
INOVA-500 "nmr3"

Relax. delay 1.000 sec
Pulse 97.4 degrees
Acq. time 1.815 sec
Width 18761.7 Hz
1024 repetitions
OBSERVE CI3, 75.4215868 MHz
DECouple H2, 299.4467565 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