Electronic Supplementary Information

Acid promoted cyclodehydration of amino alcohols with amide acetal

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1. $^1$H NMR spectroscopy study

Figure S1. In situ $^1$H NMR spectra for the conversion of amino alcohol 1a to cyclized product 2a.

For a more sophisticated understanding of the reaction mechanism, we conducted an in situ $^1$H NMR spectroscopy analysis. DMADA (1.0 mmol) was added to a solution mixture of the amino alcohol 1a (0.50 mmol) and SnCl$_4$ (0.0050 mmol) in CD$_2$Cl$_2$ (10 mL) at room temperature. We could observe the reaction mixture transformed into the cyclized product 2a with a nearly stoichiometric amount of $N,N$-dimethylacetamide (DMA). No predominant intermediate was observed (Figure S1).
As mentioned in the manuscript, by quenching the reaction mixture with water during the course of the reaction, we could detect the formation of the $O$-acetyl derivative 3 and $N$-acetyl derivative 4 that may have originated from envisaged intermediate (scheme 2) and column chromatography allowed for the isolation of 3 and 4 (Figure S2). As a result, the identification of $O$-acetyl derivative 3 and detection of DMA firmly supported the hypothesis that the reaction proceeded via the putative intermediate I (scheme 2) and intramolecular nucleophilic attack of the amine.

**Figure S2.** $^1$H NMR spectrum of work-up residue of the reaction mixture quenched with water.
2. Stereochemical proofs for non-racemic compounds 1o and 2o

2.1 ¹H NMR analysis of \( N \)-Boc Mosher ester derivative of 1o

The enantiomeric excess for non-racemic 1o could not be determined because the enantiomers were not separable on a chiral HPLC column. The optical purity of 1o was determined by ¹H NMR spectroscopic analysis of its \( N \)-Boc Mosher ester derivative. The enantiomeric excess of non-racemic 1o was 91%.

Figure S3. ¹H NMR spectra of \( N \)-Boc Mosher ester derivative of 1o.
2.2 Chiral HPLC Analysis of Non-racemic 2o

To determine the enantiomeric excess, Agilent 1200 Series HPLC equipped with a DAD detector was used (Agilent Technologies, Palo Alto, CA, USA). The chiral column used was Chiralcel OJ (Daicel Chem. Ind., Ltd., 4.6 mm × 250 mm, 10 μm). The mobile phase used was hexane/isopropanol/dimethylamine (90/10/0.1) at a flow rate of 0.5 mL/min and the eluent was monitored using a DAD detector at 225 nm. Chiral HPLC results indicated the 2o was obtained in 92% ee.

Figure S4. Chiral HPLC data of 2o derived from racemic 1o and non-racemic 1o.
3. Copies of NMR spectra

($^1$H NMR & $^{13}$C NMR)
• $^1$H NMR spectrum of compound 1c

![1H NMR spectrum of compound 1c](image)

• $^{13}$C NMR spectrum of compound 1c

![$^{13}$C NMR spectrum of compound 1c](image)
• $^1$H NMR spectrum of compound 1e

![1H NMR spectrum](image)

$^{13}$C NMR spectrum of compound 1e

![13C NMR spectrum](image)
• $^1$H NMR spectrum of compound 1f

1f (CDCl$_3$, 400MHz)

• $^{13}$C NMR spectrum of compound 1f

1f (CDCl$_3$, 100MHz)
• $^1$H NMR spectrum of compound 1g

$^1$H NMR spectrum of compound 1g

1g (CDCl$_3$, 400MHz)

• $^{13}$C NMR spectrum of compound 1g

$^{13}$C NMR spectrum of compound 1g

1g (CDCl$_3$, 100Hz)
• $^1$H NMR spectrum of compound 1j

1j (CDCl$_3$, 400 MHz)

• $^{13}$C NMR spectrum of compound 1j

1j (CDCl$_3$, 100 MHz)
• $^1$H NMR spectrum of compound 1n

$^1$H NMR spectrum of compound 1n (CDCl$_3$, 400MHz)

$^1$H NMR spectrum of compound 1n

$^1$H NMR spectrum of compound 1n (CDCl$_3$, 400MHz)

• $^{13}$C NMR spectrum of compound 1n

$^{13}$C NMR spectrum of compound 1n (CDCl$_3$, 100MHz)
• $^1$H NMR spectrum of compound 2a

• $^1$H NMR spectrum of compound 2b
- **$^1$H NMR spectrum of compound 2c**

![NMR spectrum of 2c](image1)

- **$^{13}$C NMR spectrum of compound 2c**

![NMR spectrum of 2c](image2)
• $^1$H NMR spectrum of compound 2d

$^{1}$H NMR spectrum of compound 2d (CDCl$_3$, 400MHz)

• $^1$H NMR spectrum of compound 2e

$^1$H NMR spectrum of compound 2e (CDCl$_3$, 400MHz)
• **$^1$H NMR spectrum of compound 2f**

![H NMR spectrum of compound 2f](image)

• **$^1$H NMR spectrum of compound 2g**

![H NMR spectrum of compound 2g](image)
• $^1$H NMR spectrum of compound 2i

2i (CDCl$_3$, 400MHz)

• $^1$H NMR spectrum of compound 2j

2j (CDCl$_3$, 400MHz)
• $^1$H NMR spectrum of compound 2k

\[ \text{2k (CDCl$_3$, 400 MHz)} \]

• $^1$H NMR spectrum of compound 2m

\[ \text{2m (CDCl$_3$, 300 MHz)} \]
• $^1$H NMR spectrum of compound 2n

![NMR spectrum of compound 2n](image)

• $^1$H NMR spectrum of compound 2o

![NMR spectrum of compound 2o](image)
• $^1$H NMR spectrum of compound 3

![H NMR spectrum](image)

3 (CD$_2$Cl$_2$, 400MHz)

• $^{13}$C NMR spectrum of compound 3

![C NMR spectrum](image)

3 (CD$_2$Cl$_2$, 100MHz)
• $^1$H NMR spectrum of compound 4

• $^1$H NMR spectrum of compound 5
• $^{13}$C NMR spectrum of compound 5

![C NMR spectrum of compound 5](image)

5 (CDCl$_3$, 100MHz)

• $^1$H NMR spectrum of compound 7

![H NMR spectrum of compound 7](image)

7 (CDCl$_3$, 300MHz)