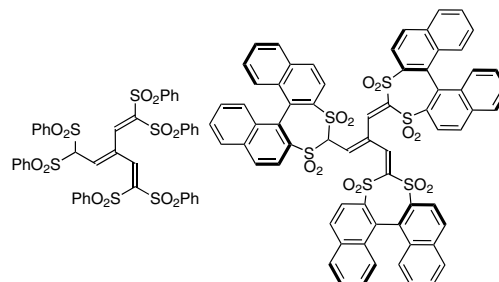


# A Chiral, Dendralenic C–H Acid

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Published as part of the Editorial Board Cluster



Received: 17.09.2021

Accepted after revision: 05.11.2021

Published online: 05.11.2021

DOI: 10.1055/a-1705-9786; Art ID: st-2021-u0338-c

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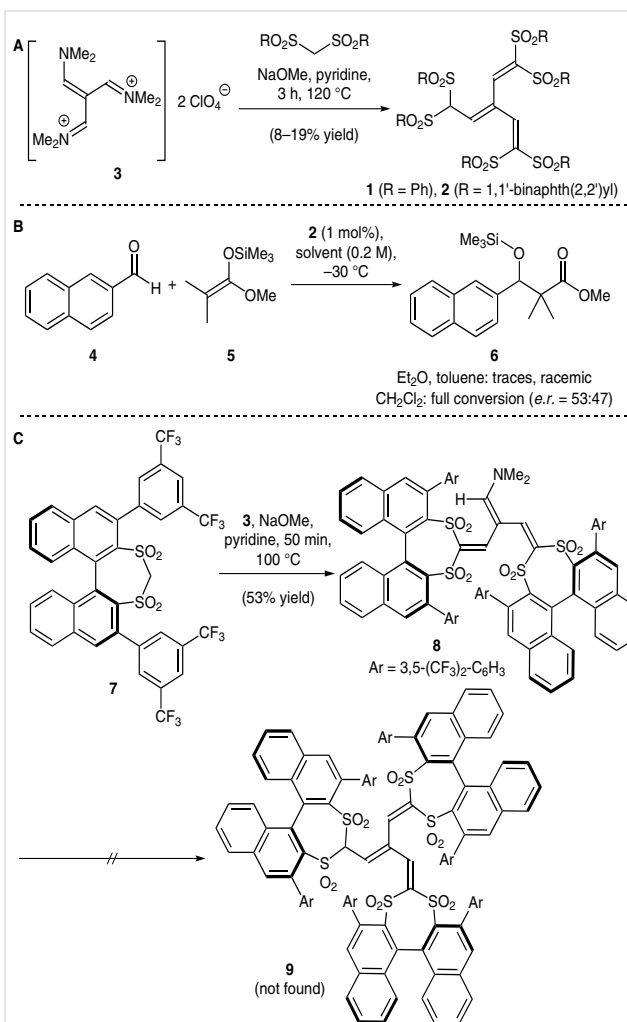
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**Abstract** We report the synthesis of a chiral dendralenic C–H acid, which contains three unsubstituted binaphthyl moieties. This motif and an achiral variant can be made from their corresponding bis(sulfone) precursors in one step. Despite the presence of the enantiopure binaphthyl backbone, the newly designed chiral C–H acid showed only poor enantioselectivity in a Mukaiyama aldol reaction. First attempts toward the synthesis of 3,3'-hexasubstituted binaphthyl-based dendralenic acids are also reported.

**Key words** dendralenic C–H acids,  $C_3$  symmetry, Brønsted and Lewis acid catalysis, binaphthyl backbone, conjugated anion

Confined, dimeric binaphthyl-based acids have shown great success in asymmetric Lewis and Brønsted acid catalysis.<sup>1</sup> In particular, scaffolds with two 3,3'-disubstituted binaphthyl backbones enable high levels of asymmetric induction in reactions with aromatic and with unbiased, aliphatic substrates.<sup>1</sup> Based on our previous studies on very strong dendralene-based C–H acids,<sup>2</sup> and our interest in ever more acidic and selective catalysts, we envisioned chiral dendralenic acids. We hypothesized that such acids with three binaphthyl moieties, delivering highly conjugated and  $C_3$ -symmetric anions, may possess unique and high reactivity and selectivity. This notion led to the design of chiral C–H acid **2**. After some experimental efforts, we found that this acid as well as its achiral version **1** can indeed be made in one step from perchlorate salt **3**<sup>3</sup> (Scheme 1).

Accordingly, when iminium salt **3** was treated with 3.5 equivalents of the corresponding bis(sulfone) and NaOMe, acids **1**<sup>4</sup> and **2**<sup>5</sup> were obtained in moderate yields. C–H acid



**Scheme 1** (A) Synthesis of dendralene-based C–H acids **1** and **2**. (B) Application of acid **2** in a Mukaiyama aldol reaction. (C) Attempted synthesis of hexasubstituted dendralenic C–H acid **9**.

**2** was evaluated in the Mukaiyama aldol reaction of 2-naphthaldehyde (**4**) with silyl ketene acetal **5**.<sup>6</sup> Unfortunately, the reactivity of acid **2** was lower than our previously developed disulfonimide catalysts,<sup>6</sup> and, depending on the solvent, no or poor enantioselectivity was obtained. Given the importance of 3,3'-substituents in other binaphthyl-based acid catalysts,<sup>7</sup> we envisioned substituted variants of acid **2**. However, when we employed 3,3'-disubstituted bis(sulfone) **7** in the base-mediated condensation reaction with salt **3**, we did not obtain the desired dendralenic acid **9**. Instead, we only obtained enamine **8** in 53% yield. A further conversion of enamine **8** into acid **9** has yet to be accomplished.

## Conflict of Interest

The authors declare no conflict of interest.

## Funding Information

Generous support from European Research Council (Advanced Grant 'C-H Acids for Organic Synthesis, CHAOS'), the Horizon 2020 Framework Programme, and the Deutsche Forschungsgemeinschaft (Leibniz Award to B.L. and Cluster of Excellence RESOLV, EXC 1069) is gratefully acknowledged.

## Acknowledgment

We also thank the members of our analytics groups for their excellent service.

## Supporting Information

Supporting information for this article is available online at <https://doi.org/10.1055/a-1705-9786>.

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- (4) **General Procedure for Achiral Acid 1**  
A Schlenk flask was charged with commercially available bis(phenylsulfonyl)methane (0.77 g, 2.5 mmol, 3.0 equiv) and perchlorate salt **3** (0.32 g, 0.83 mmol, 1.0 equiv). The solid mixture was partially dissolved in pyridine (5.4 mL) and a solution of NaOMe (0.42 g, 2.9 mmol, 3.5 equiv) in MeOH (0.53 mL, 5.4 M) was added. A clear, orange solution was obtained, and the reaction mixture was heated to 120 °C for 3 h which provided a dark red solution. All volatiles were removed under reduced pressure. Purification via flash column chromatography (silica, 0.5–10% gradient of MeOH in CH<sub>2</sub>Cl<sub>2</sub>) afforded the title compound as an orange solid (60 mg, 0.064 mmol, 7.7% yield).  
<sup>1</sup>H NMR (501 MHz, CDCl<sub>3</sub>): δ = 8.50 (t, *J* = 1.9 Hz, 1 H), 8.40 (t, *J* = 1.7 Hz, 1 H), 7.98–7.92 (m, 4 H), 7.91–7.86 (m, 2 H), 7.84–7.76 (m, 6 H), 7.76–7.71 (m, 2 H), 7.62–7.57 (m, 4 H), 7.57–7.52 (m, 2 H), 7.52–7.44 (m, 2 H), 7.44–7.38 (m, 2 H), 7.34 (dddd, *J* = 9.9, 8.2, 6.5, 2.0 Hz, 6 H), 6.01 (dt, *J* = 11.1, 2.0 Hz, 1 H), 5.22 (d, *J* = 11.1 Hz, 1 H). MS (ESI<sup>−</sup>): *m/z* = 933 [M − H<sup>+</sup>]. HRMS (ESI<sup>−</sup>): *m/z* [M − H<sup>+</sup>] calcd for C<sub>43</sub>H<sub>33</sub>O<sub>12</sub>S<sub>6</sub><sup>−</sup>: 933.0302; found: 933.0302. Owing to the expected high symmetry of the anion, triethylamine was added and NMR spectra of this species in CDCl<sub>3</sub> were acquired.  
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ = 8.36 (s, 3 H), 7.70 (d, *J* = 7.8 Hz, 12 H), 7.33 (t, *J* = 7.4 Hz, 6 H), 7.19 (t, *J* = 7.7 Hz, 12 H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>): δ = 156.81, 142.11, 132.43, 128.47, 128.15, 125.14, 107.38. MS (ESI<sup>−</sup>): *m/z* = 933 [M − H<sup>+</sup>].
- (5) **General Procedure for Chiral Acid 2**  
A Schlenk flask was charged with solid (*S*)-4*H*-dinaphtho[2,1-*d*:1',2'-*f*] [1,3]dithiepine 3,3,5,5-tetraoxide (**S3**, 0.06 g, 0.15 mmol, 3.0 equiv) and perchlorate salt **3** (0.02 g, 0.05 mmol, 1.0 equiv). The solid mixture was partially dissolved in pyridine (2.0 mL) and a solution of NaOMe (0.26 g, 0.18 mmol, 3.5 equiv) in MeOH (0.033 mL, 5.4 M) was added.<sup>3a</sup> A clear, red solution was obtained and the reaction mixture was heated to 100 °C for 3 h. A dark red solution was obtained. All volatiles were removed under reduced pressure. Purification via flash column chromatography (silica, 0.25–10% gradient of MeOH in CH<sub>2</sub>Cl<sub>2</sub>) and acidification with aq. HCl (6 M) afforded the title compound as an orange solid (12 mg, 0.05 mmol, 19% yield).  
<sup>1</sup>H NMR (501 MHz, CDCl<sub>3</sub>): δ = 8.27 (d, *J* = 4.9 Hz, 1 H), 8.25 (dd, *J* = 3.9, 1.1 Hz, 3 H), 8.23 (s, 1 H), 8.21 (d, *J* = 3.5 Hz, 1 H), 8.19 (d, *J* = 3.6 Hz, 1 H), 8.08–7.94 (m, 9 H), 7.92 (d, *J* = 8.2 Hz, 1 H), 7.87 (d, *J* = 8.2 Hz, 1 H), 7.77–7.62 (m, 7 H), 7.59 (d, *J* = 8.8 Hz, 1 H), 7.48–7.31 (m, 6 H), 7.28 (d, *J* = 8.7 Hz, 1 H), 7.22 (dd, *J* = 8.9, 5.1 Hz, 3 H), 7.17 (t, *J* = 8.2 Hz, 2 H), 6.05 (dt, *J* = 10.5, 1.9 Hz, 1 H), 5.55 (d, *J* = 10.5 Hz, 1 H). MS (ESI<sup>−</sup>): *m/z* = 1227 [M − H<sup>+</sup>]. HRMS (ESI<sup>−</sup>): *m/z* [M − H<sup>+</sup>] calcd for C<sub>67</sub>H<sub>39</sub>O<sub>12</sub>S<sub>6</sub><sup>−</sup>: 1227.0771; found 1227.0771.
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