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Brønsted Acid Catalyzed Asymmetric Silylation of Biaryl Diols

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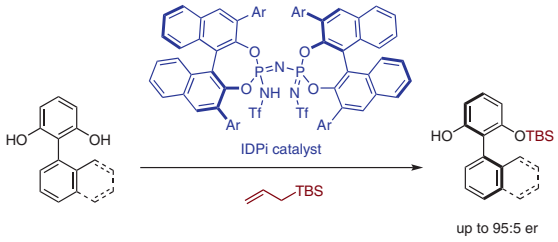

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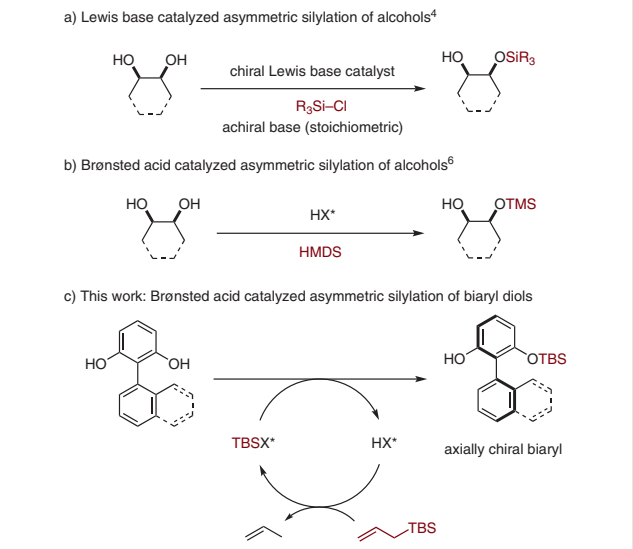
Abstract We report a Brønsted acid catalyzed enantioselective silylation of biaryl diols with an allylsilane as a silicon source. This process enables facile access to enantioenriched biaryl silyl ethers with an axial stereogenicity. A control experiment supports a mechanism proceeding by desymmetrization followed by kinetic resolution.

Key words Brønsted acid, imidodiphosphorimidate, silylation, axial chirality, desymmetrization, kinetic resolution

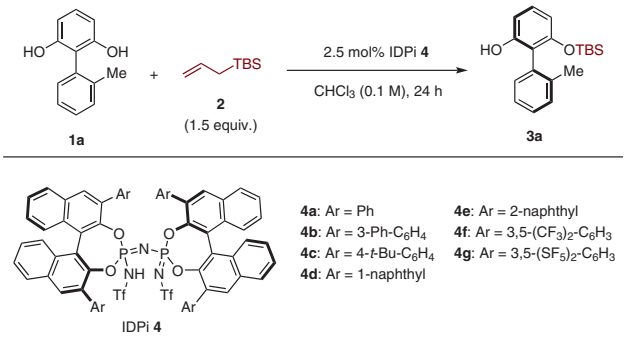
The silylation of alcohols is a commonly used protecting group operation in chemical synthesis.[1] Since the first enantioselective variant reported by Ishikawa,[2] several catalytic enantioselective approaches have been developed during the past two decades.[3] The majority of these methods use a chiral Lewis base catalyst in conjunction with a stoichiometric amount of an achiral base and a silyl chloride (Scheme 1a).[4] Transition-metal-catalyzed silylations of alcohols with hydrosilanes via kinetic resolution have also been developed.[5] Recently, we reported a Brønsted acid catalyzed enantioselective silylation of alcohols with hexamethyldisilazane (HMDS) (Scheme 1b).[6] Inspired by our studies on silicon–hydrogen exchange reactions, we recently found that strong and confined imidodiphosphorimidate (IDPi) Brønsted acids catalyze the enantioselective silylation of phenol derivatives with allylsilanes.[7] We envisioned that our silylation strategy could be applied to biaryl diols to yield axially chiral biaryl silyl ethers. Indeed, we herein report a Brønsted acid catalyzed atroposelective silylation of biaryl diols (Scheme 1c).



Scheme 1 Catalytic asymmetric silylation of alcohols

We commenced our investigation by examining the silylation of biaryl diol **1a** in the presence of different IDPi catalysts **4** and allyl(*tert*-butyl)dimethylsilane (**2**) (Table 1). Catalyst **4a** afforded the desired mono-silylated product, but with poor enantioselectivity (54:46 er; entry 1). While catalysts **4b–e** revealed low enantioselectivities (54:46 to 62:38 er; entries 2–5), catalyst **4f** resulted in promising enantioselectivity (71:29 er; entry 6). A modification of the *m*,*m*-substituents on the 3,3′-phenyl groups of the BINOL backbone from trifluoromethyl to pentafluorosulfanyl further enhanced the enantioselectivity (77:23 er; entry 7). At –50 °C, the reaction proceeded with 86:14 er (entry 8). Finally, high enantioselectivity was achieved by increasing the amount of allylsilane **2** (95:5 er; entry 9).

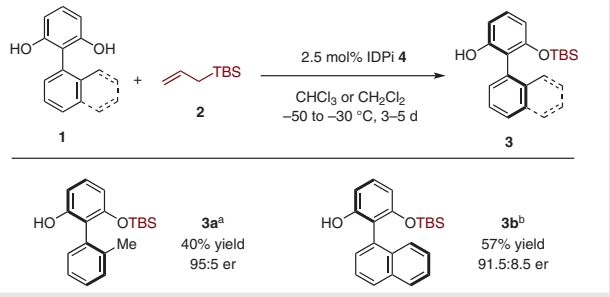
Table 1 Optimization of the Reaction Conditions[a]



Entry	IDPi	Temp (°C)	Conv. (%)	er
1	**4a**	rt	70	54:46
2	**4b**	rt	67	54:46
3	**4c**	rt	70	61:39
4	**4d**	rt	71	56:44
5	**4e**	rt	55	62:38
6	**4f**	rt	66	71:29
7	**4g**	rt	70	77:23
8[b]	**4g**	–50	70	86:14
9[b,c]	**4g**	–50	full	95:5

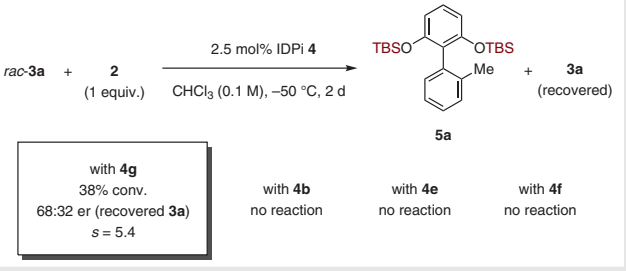
[a] Reactions were performed with substrate **1a** (0.025 mmol), allylsilane **2** (1.5 equiv.) and IDPi **4** (2.5 mol%) in $CHCl_3$ (0.25 mL); conversions (conv.) were determined by ^1H NMR analysis with dibromomethane as an internal standard; enantiomeric ratios (er) were measured by HPLC analysis.
[b] Reaction time: 5 days.
[c] 2 equivalents of **2** were used.

We next conducted the reactions on a 0.1 mmol scale (Scheme 2). The reaction of **1a** gave the desired product **3a** without loss of enantioselectivity. Employing naphthyl substrate **1b** required catalyst **4b** to furnish product **3b** with high enantioselectivity (91.5:8.5 er). The absolute configuration of **3b** was determined by comparing experimental and computational circular dichroism (CD) spectra (see the Supporting Information for details).[8]



Scheme 2 Asymmetric silylation of biaryl diols. Reactions were performed on a 0.1 mmol scale. [a] Reaction was conducted with catalyst **4g** and allylsilane **2** (2 equiv.) in $CHCl_3$ (0.1 M) at –50 °C for 5 days. [b] Reaction was conducted with catalyst **4b** and allylsilane **2** (1.5 equiv.) in CH_2Cl_2 (0.2 M) at –30 °C for 3 days.

We performed a control experiment that confirmed that a kinetic resolution takes place during a second silylation (Scheme 3). Upon subjecting racemic mono-silylated product **3a** to Brønsted acid catalyzed silylation conditions, bis-silylated product **5a** was obtained and the remaining **3a** showed an er of 68:32. This result is consistent with the desymmetrizing silylation of **1a** to initially provide the enantioenriched mono-silylated product **3a**, the enantioselectivity of which is further improved in the second silylation via kinetic resolution. Although several catalysts (**4b**, **4e**, and **4f**) were further examined for the kinetic resolution, they did not afford the bis-silylated product **5a**.



Scheme 3 Control experiment

In summary, we have developed a Brønsted acid catalyzed asymmetric silylation of biaryl diols that provides access to axially chiral biaryl silyl ethers.[9] A simple mechanistic investigation has revealed that the reaction proceeds via a desymmetrization–kinetic resolution sequence. Efforts to develop other useful silylation methods are currently underway in our laboratory. During our studies, Professor Martin Oestreich kindly shared a manuscript with us describing his independent and advanced investigation of the same transformation.[10] Our own studies on the asymmetric silylation of biaryl diols have since been terminated at the reported stage.

Conflict of Interest

The authors declare no conflict of interest.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/a-2100-1575.

References and Notes

(1) Greene, T. W.; Wuts, P. G. M. *Protection for the Hydroxyl Group, Including 1,2- and 1,3-Diols*, In *Protective Groups in Organic Synthesis, 3rd ed*; John Wiley & Sons: New York, **1999**, 17–245.
(2) Isobe, T.; Fukuda, K.; Araki, Y.; Ishikawa, T. *Chem. Commun.* **2001**, 243.
(3) (a) Xu, L.-W.; Chen, Y.; Lu, Y. *Angew. Chem. Int. Ed.* **2015**, *54*, 9456. (b) Seliger, J.; Oestreich, M. *Chem. Eur. J.* **2019**, *25*, 9358.
(4) (a) Zhao, Y.; Rodrigo, J.; Hoveyda, A. H.; Snapper, M. L. *Nature* **2006**, *443*, 67. (b) Zhao, Y.; Mitra, A. W.; Hoveyda, A. H.; Snapper, M. L. *Angew. Chem. Int. Ed.* **2007**, *46*, 8471. (c) Sheppard, C. I.; Taylor, J. L.; Wiskur, S. L. *Org. Lett.* **2011**, *13*, 3794. (d) Manville, N.; Alite, H.; Haeffner, F.; Hoveyda, A. H.; Snapper, M. L. *Nat. Chem.* **2013**, *5*, 768.
(5) (a) Weickgenannt, A.; Mewald, M.; Muesmann, T. W. T.; Oestreich, M. *Angew. Chem. Int. Ed.* **2010**, *49*, 2223. (b) Dong, X.; Weickgenannt, A.; Oestreich, M. *Nat. Commun.* **2017**, *8*, 15547. (c) Dong, X.; Kita, Y.; Oestreich, M. *Angew. Chem. Int. Ed.* **2018**, *57*, 10728. (d) Seliger, J.; Dong, X.; Oestreich, M. *Angew. Chem. Int. Ed.* **2019**, *58*, 1970.
(6) (a) Hyodo, K.; Gandhi, S.; van Gemmeren, M.; List, B. *Synlett* **2015**, *26*, 1093. (b) For an example of asymmetric silylation of alcohols using BINOL-based polyether catalyst, see: Park, S. Y.; Lee, J.-W.; Song, C. E. *Nat. Commun.* **2015**, *6*, 7512.
(7) (a) Kaib, P. S. J.; Schreyer, L.; Lee, S.; Properzi, R.; List, B. *Angew. Chem. Int. Ed.* **2016**, *55*, 13200. (b) Schreyer, L.; Properzi, R.; List, B. *Angew. Chem. Int. Ed.* **2019**, *58*, 12761. (c) Zhou, H.; Bae, H. Y.; Leutzsch, M.; Kennemur, J. L.; Bécart, D.; List, B. *J. Am. Chem. Soc.* **2020**, *142*, 13695. (d) Zhou, H.; Han, J. T.; Nöthling, N.; Lindner, M. M.; Jenniches, J.; Kühn, C.; Tsuji, N.; Zhang, L.; List, B. *J. Am. Chem. Soc.* **2022**, *144*, 10156. (e) Zhou, H.; Properzi, R.; Leutzsch, M.; Belanzoni, P.; Bistoni, G.; Tsuji, N.; Han, J. T.; Zhu, C.; List, B. *J. Am. Chem. Soc.* **2023**, *145*, 4994.
(8) Li, X. C.; Ferreira, D.; Ding, Y. *Curr. Org. Chem.* **2010**, *14*, 1678.
(9) **Silylation of Biaryl Diols; General Procedure**
A GC vial equipped with a Teflon-coated magnetic stir bar was charged with catalyst **4** (2.5 mol%), biaryl diol **1** (0.1 mmol) and solvent ($CHCl_3$ or CH_2Cl_2), and the resulting mixture was cooled to –50 or –30 °C in a cryostat. After 10 min, allylsilane **2** (2 or 1.5 equiv.) was slowly added and the reaction mixture was stirred for 3–5 d at the same temperature. After complete conversion as indicated by TLC, the reaction was quenched with trimethylamine. The solvent was removed in vacuo and the mixture was purified by column chromatography on silica gel to afford the desired silyl ether **3**.
(S)-6-((tert-Butyldimethylsilyl)oxy)-2′-methyl-[1,1′-biphenyl]-2-ol [(S)-3a]
Yield: 12.6 mg (40%); white solid; $[\alpha]_D^{25}$ –25.5 (c 0.53, $CHCl_3$). ^1H NMR (501 MHz, CD_2Cl_2): δ = 7.34–7.24 (m, 3 H), 7.16 (dd, J = 7.4, 1.7 Hz, 1 H), 7.12 (t, J = 8.2 Hz, 1 H), 6.60 (dd, J = 8.2, 1.0 Hz, 1 H), 6.50 (dd, J = 8.1, 1.0 Hz, 1 H), 4.75 (s, 1 H), 2.12 (s, 3 H), 0.65 (s, 9 H), 0.07 (s, 3 H), –0.06 (s, 3 H). ^{13}C NMR (126 MHz, CD_2Cl_2): δ = 154.4, 154.0, 139.2, 132.7, 131.5, 130.9, 129.1, 128.8, 126.5, 120.2, 111.7, 108.5, 25.3, 19.8, 18.0, –4.3, –4.6. EI-HRMS: m/z $[M]^{+\bullet}$ calcd for $C_{19}H_{26}O_2Si$: 314.1695; found: 314.1697. HPLC (IA-3, heptane/isopropanol = 95:5, 0.5 mL/min, 298 K, 220 nm): t_{R1} = 8.6 min, t_{R2} = 10.8 min; er = 95:5.
(10) Zhu, M.; Jiang, H.-J.; Sharanov, I.; Irran, E.; Oestreich, M. *Angew. Chem. Int. Ed.* **2023**, *62*, in press DOI: 10.1002/anie.202304475.