Kinetic Resolution

International Edition: DOI: 10.1002/anie.201700977
German Edition: DOI: 10.1002/ange.201700977

Kinetic Resolution of 2-Substituted Indolines by *N*-Sulfonylation using an Atropisomeric 4-DMAP-*N*-oxide Organocatalyst

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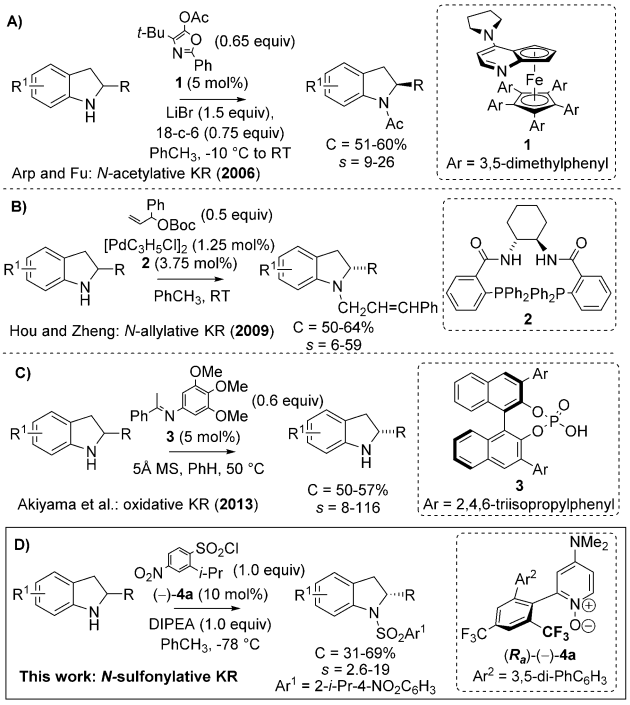
Abstract: *The first catalytic kinetic resolution by N-sulfonylation is described. 2-Substituted indolines are resolved (s = 2.6–19) using an atropisomeric 4-dimethylaminopyridine-N-oxide (4-DMAP-N-oxide) organocatalyst. Use of 2-isopropyl-4-nitrophenylsulfonyl chloride is critical to the stereodiscrimination and enables facile deprotection of the sulfonamide products with thioglycolic acid. A qualitative model that accounts for the stereodiscrimination is proposed.*

The global demand for enantiomerically pure alcohols and amines is steadily increasing[1] and kinetic resolution (KR) of racemates provides a useful and scalable approach to accessing such compounds.[2,3] Whilst several efficient non-enzymatic methods for the Lewis base (LB) catalyzed[4] KR of alcohols via acylation,[5] silylation,[5,6–9] phosphorylation[5,10,11] and sulfonylation[5,8,12] have been developed, analogous protocols for the KR of amines are less common.[5,13,14] This situation mainly reflects the challenge in achieving efficient catalysis, as most amines are themselves significantly Lewis basic.[5,13]

Optically active 2-substituted and 2,3-disubstituted indolines[15] occur in many natural products,[16] drugs,[17] and drug candidates.[18] This and the proximity of the moderately Lewis basic indoline nitrogen to the C2/C3 stereogenic centers, makes them attractive for KR[19] via LB-catalyzed *N*-functionalization. So far, only Arp and Fu[20] have achieved this, using planar chiral LB catalyst **1** to effect KR via *N*-acylation (Scheme 1 A), although others, notably Hou and Zheng[21] and Akiyama et al.,[22] have reported non-acylative KRs (Scheme 1 B,C). Asymmetric hydrogenation of indoles also provides efficient access to this type of indoline.[23]

Our laboratory has developed atropisomeric 3-aryl-4-DMAP derivatives as LB catalysts for the acylative KR of *sec*-alcohols[24] and amines.[25] Recently, we also reported a comparative study of amines vs. *N*-oxides as catalysts for the acylation, sulfonylation and silylation of alcohols, revealing that *N*-oxides are generally more efficient catalysts for sulfonylation and silylation.[26] Cognisant that 4-DMAP-*N*-oxide promotes the sulfonylation of aniline with benzene sulfonyl chloride around 20-fold faster than 4-DMAP.[27] we envisioned that a suitable chiral pyridine-*N*-oxide derivative would catalyze sulfonylative KR of indolines. Herein, we report the development of such a process employing an atropisomeric 2-aryl-4-DMAP-*N*-oxide catalyst (**4**) with 2-isopropyl-4-nitrophenylsulfonyl chloride as the sulfonylating agent (Scheme 1 D).



Scheme 1. Comparison of previous KRs of indolines with this work.[21,22].

The challenge of achieving chirality transfer via an sulfonyloxypyridinium salt intermediate during *N*-oxide-catalyzed sulfonylation as compared to via an acylpyridinium salt intermediate during pyridine-catalzed acylation (i.e. **I** vs. **II**, Scheme 2 A), accrues from two key differences. Firstly, there is an additional rotatable bond between the pyridine ring and the electrophilic sulfur atom (cf. the carbonyl carbon atom). Secondly, the trajectory of the incoming nucleophile relative to the S–O bond in the asynchronous S_N2 transition state is linear (cf. the Bürgi–Dunitz trajectory towards the C=O

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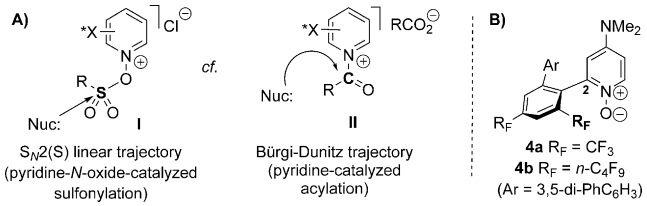


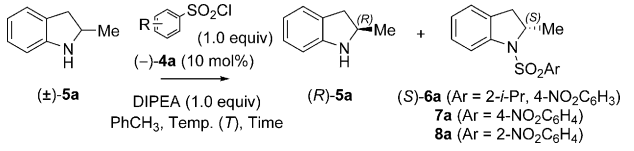
Scheme 2. A) Schematic comparison of reaction trajectories for sulfonylation vs. acylation. B) Structures of atropisomeric catalysts **4a** and **4b**.

bond).[28] Our design of catalysts **4a** and **4b** incorporated an atropisomeric axis at the 2-position of the pyridine to address these challenges, as well as an electron deficient 2,4-bis(perfluoroalkyl)phenyl motif to impart high reactivity by analogy with achiral congeners as catalysts for *O*-phosphorylation (Scheme 2B).[29]

We began our investigations using the bis-trifluoromethyl catalyst (−)-**4a** and (±)-2-methylindoline (**5a**, Table 1, see the Supporting Information for full details). Initial evaluation of the sulfonylating agent revealed that 4-nitrophenylsulfonyl chloride (4-NsCl) was reactive but unselective whereas 2-NsCl was similarly reactive and delivered $s = 1.3$ at 0 °C (entries 1 and 2, Table 1). Lowering the reaction temperature resulted in increased selectivity[3] ($s = 5.7$ at −78 °C, entries 3–5, Table 1). Encouraged by these results and aiming to combine a bulky 2-substituent capable of relaying stereochemical information[30] with favorable reactivity imparted by the nitro group, we next investigated the use of 2-isopropyl-6-NsCl and 2-isopropyl-4-NsCl as sulfonylating agents. Whilst the former proved unreactive (entries 10 and 11, Table 1), the latter resulted in a significant increase in selectivity at −78 °C ($s = 13.8$, entry 7, Table 1). We also examined the performance of bis-perfluorobutyl catalyst (+)-**4b** under these conditions; this catalyst promoted reaction of the opposite indoline enantiomer as expected but the reaction was slower and offered no advantage in terms of selectivity ($s = 8.2$ after 24 h, entries 8 and 9, Table 1). The efficiency of several additives commonly used in LB-catalyzed KRs were also evaluated,[23b,c,31] but to no avail (see the Supporting Information).

Next, we evaluated the substrate scope of this sulfonylative KR (Table 2). 2-Alkyl- and 2-siloxymethylindolines were found to undergo sulfonylative KR with good selectivity ($s = 10.1$–17.2, entries 1–6, Table 2). 2-Alkyl-5-substituted indolines were also resolved efficiently (entries 9–11, Table 2), although 2-Me-5-OMe indoline **5k** was resolved with the lowest selectivity ($s = 4.8$), likely because of the relatively high nucleophilicity of this derivative due to conjugation between the OMe and NH groups. Similarly, the 6-NMe_2 derivative **5l** displayed high reactivity but low selectivity ($s = 2.6$, entry 12, Table 2). Unfortunately, sterically encumbered 2-Ph and 2-CO_2Me substituted indoline derivatives proved unreactive both under standard conditions and at elevated temperature (entries 7 and 8, Table 2). 7-Substituted indolines also proved unreactive, presumably due to steric hindrance of the reactive nitrogen center (data not shown). Preparative sulfonylative KR of 2-methylindoline was performed using catalyst (−)-**4a**, affording similar selectivity and conversion after 3 h as the analytical run ($s = 11.6$, C = 61 %, *cf.* entry 1, Table 2). The enantioenriched sulfonylated product (2*R*)-**6a** underwent facile deprotection with thioglycolic acid[33] and DBU in MeCN (93 %) with no detectable erosion

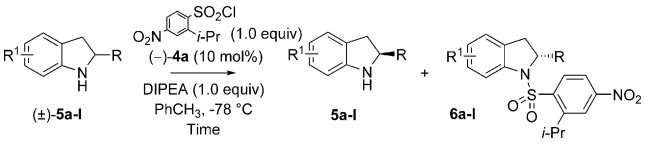
Table 1: Optimization of *N*-sulfonylative KR of (±)-2-methylindoline **5a**.



Entry	Cat.	R	*T* [°C]	*t* [h]	Conv. [%][a]	*s*[a]
1	(−)-**4a**	4-NO_2	0	4	100	N.D.
2	(−)-**4a**	2-NO_2	0	3	60	1.3
3	(−)-**4a**	2-NO_2	−40	4	53	1.4
4	(−)-**4a**	2-NO_2	−60	3	23	1.9
5	(−)-**4a**	2-NO_2	−78	3	15	5.7
6	(−)-**4a**	2-*i*-Pr, 4-NO_2	−60	3	54	8.9
7	(−)-**4a**	2-*i*-Pr, 4-NO_2	−78	3	**52**	**13.8**[b]
8	(+)-**4b**	2-*i*-Pr, 4-NO_2	−78	3	< 5	N.D.[c]
9	(+)-**4b**	2-*i*-Pr, 4-NO_2	−78	24	48	8.2[c]
10	(−)-**4a**	2-*i*-Pr, 6-NO_2	−78	3	0	N.D.
11	(−)-**4a**	2-*i*-Pr, 6-NO_2	r.t.	3	0	N.D.

[a] Conversions and *s* values calculated from chiral HPLC data. Absolute configuration of recovered starting materials **5a** established as (2*R*) by comparison with literature data, see the Supporting Information.
[b] There is no detectable conversion in the absence of catalyst under these optimized conditions. [c] Gives enantiomeric starting material and product to those depicted [that is, (*S*)-**5a** and (*R*)-**6a**]. N.D. = not determined.

Table 2: Evaluation of scope of indoline sulfonylative KR.



Entry (substrate)	R	R^1	*t* [h]	Conv. [%][a]	*s*[a,b]
1 (**5a**)	Me	H	3	52	13.8(*R*)[c]
2 (**5b**)	CH_2OTES	H	6	34	14.8
3 (**5c**)	CH_2OTIPS	H	5	33[d]	10.1[e]
4 (**5d**)	CH_2OTBS	H	5	47[d]	17.2(*S*)
5 (**5e**)	*i*-Pr	H	6	40	16.2(*S*)[e]
6 (**5f**)	*n*-Bu	H	3	56	12.9(*R*)
7 (**5g**)	Ph	H	4	< 1	N.D.
8 (**5h**)	CO_2Me	H	4	< 1	N.D.
9 (**5i**)	Me	5-Cl	2	46	13.8(*R*)
10 (**5j**)	Me	5-Me	6	41	11.0(*R*)[e]
11 (**5k**)	Me	5-OMe	1	52	4.8
12 (**5l**)	Me	6-NMe_2	2	69	2.6

[a] Conversions and *s* values calculated from chiral HPLC data.
[b] Indicated absolute configurations are of recovered starting materials established by comparison with literature data, see the Supporting Information. Note: Although the CIP designations vary, all entries using catalyst (−)-**4a** give the configuration depicted. [c] Same experiment as Table 1, entry 7. [d] Conversion measured by ^{1}H NMR, *s* determined by chiral HPLC of starting material or product. [e] Catalyst (+)-**4a** was used and gave enantiomeric starting material or product to those depicted. N.D. = not determined.

of its enantiopurity. Concomitantly, catalyst (−)-**4a** was recovered quantitatively as a single enantiomer (see the Supporting Information).

The absolute configuration of the dextrorotatory enantiomer of catalyst **4a** was assigned by comparison of its optical rotation value and electronic and vibrational circular dichroism (ECD and VCD) spectra with those computed by DFT.[34] All three datasets led to (+)-**4a** being assigned the (S_a) configuration.[32] The VCD data was most compelling as the match in the 1000–1250 cm^{-1} region was largely independent of conformation (Figure 1).

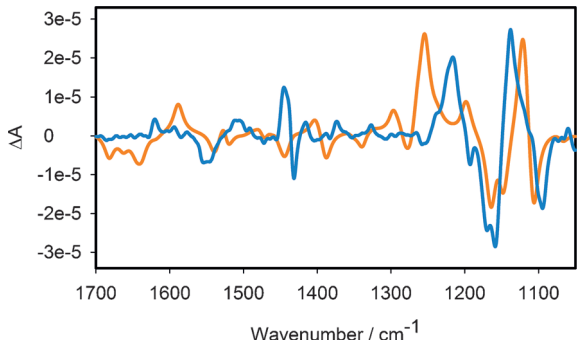
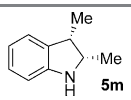
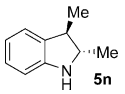
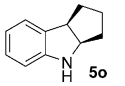
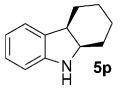
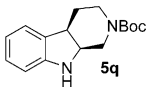


Figure 1. Experimental VCD spectrum for (+)-**4a** (blue) and computed VCD spectrum for (S_a)-**4a** (orange) [at the ωB97XD/Def2-TZVPP/SCRF = chloroform level, weighted by the Boltzmann conformer populations calculated using B3LYP+D3BJ/6-311G(2df,p)/SCRF = chloroform free energies].[32] For further details see the Supporting Information.

The lowest-energy potentially stereodiscriminating conformer of the chiral sulfonyloxypyridinium salt **9a**, derived from (+)-**4a**/2-isopropyl-4-NsCl, as computed by DFT, was used to construct a qualitative model to rationalize the sense and scope of the indoline KR reactions (Figure 2A,B). This conformer provides a chiral "pocket" for which the phenyl ring of the arylsulfonate forms the base, the 2-isopropyl group of the arylsulfonate forms one side (element A), and the terphenyl group of the catalyst forms the other side (element B, Figure 2C). The approach of the indoline nitrogen lone pair to the $\sigma^*_{S\text{-}O}$ orbital such that the C2/C3 positions can avoid clashing with elements A/B then leads to the preferred sulfonylation of (2*R*)-**5a** as shown in Figure 2C. The 2-substituents of indolines **5a–f** are presumably able to rotate to avoid a steric clash with element B, allowing them to be resolved efficiently (entries 2–6, Table 2). By contrast, the less flexible 2-Ph and 2-CO_2Me substituents in indolines **5g** and **5h** (entries 7 and 8, Table 2) cannot avoid clashing with element B, making them poor substrates for KR. 7-Substituted indolines are also poor substrates for this resolution due to steric interactions with element A.

This qualitative model predicts that 2,3-disubstituted indolines will require *cis*-stereochemistry for efficient KR and that *trans* derivatives will resolve poorly as one alkyl group would necessarily protrude into element B. To test these hypotheses, we investigated the sulfonylative KR of *cis* and *trans* 2,3-dimethylindolines **5m** and **5n** and tricyclic indolines **5o–q** (Table 3).

Table 3: Sulfonylative KR of 2,3-disubstituted indolines **5m–q**.

Entry	Cat.	Substrate	*t* [h]	Conv. [%][a]	*s*[a,b]
1	(+)-**4a**	 **5m**	3	62	9.7(2*S*,3*S*)
2	(+)-**4a**	 **5n**	3	6	2.1
3	(−)-**4a**	 **5o**	3	35	7.2
4	(−)-**4a**	 **5p**	2	37	11.7(4a*R*,9a*R*)
5	(−)-**4a**	 **5q**	4	54[c]	19.0

[a] Conversions and *s* values calculated from chiral HPLC data.
[b] Absolute configurations of unreacted starting material established by comparison with literature data, see the Supporting Information.
[c] Conversion measured by ^{1}H NMR, *s* determined by chiral HPLC of starting material or product.

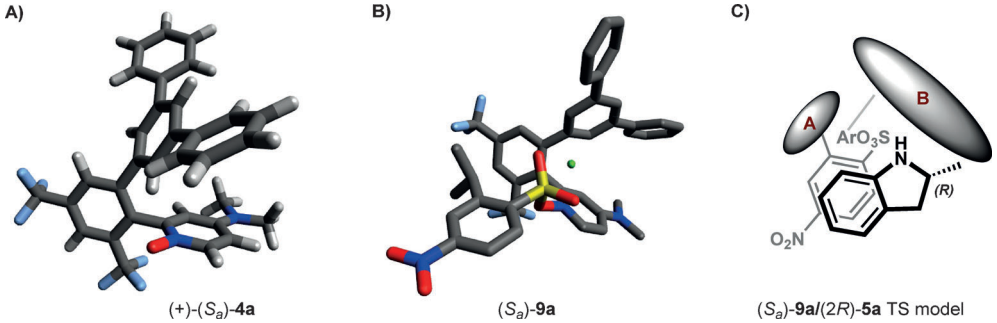


Figure 2. A) Lowest free energy conformer of catalyst (+)-**4a** with S_a configuration by DFT at the B3LYP+D3BJ/6-311G(2df,p)/SCRF = chloroform level (see the Supporting Information).[32] B) Lowest free energy, potentially stereodiscriminating conformer of chiral sulfonyloxypyridinium salt (S_a)-**9a** (H atoms removed for clarity) by DFT at the B3LYP+D3BJ/6-311++G(2df,p)/SCRF = toluene level (see the Supporting Information).[32] C) Qualitative model for stereodiscrimination illustrated for the reactive (2*R*) enantiomer of indoline **5a** with the (+)-**4a** derived sulfonyloxypyridine salt (S_a)-**9a**.

As predicted, *cis*-2,3-dimethylindoline undergoes efficient KR ($s = 9.7$, entry 1, Table 3) whereas the analogous *trans* derivative is a poor substrate ($s = 2.1$, entry 2, Table 3). Given the prevalence of the tricyclic indoline motif in natural products,[19a,35] we were pleased to find that these substrates also undergo efficient KR with good selectivity ($s = 7.2$–18.9, entries 3–5, Table 3). Congruent with the model,

increasing the aliphatic ring size resulted in increased selectivity (cf. entries 3 and 4, Table 3) and *N*-Boc-β-carboline provided the highest selectivity yet obtained in this *N*-sulfonylative KR ($s = 19.0$, entry 5, Table 3).

In summary, we have developed the first protocol for catalytic KR of amines by sulfonylation and demonstrated its utility for the preparation of enantiomerically enriched 2-substituted and 2,3-disubstituted indolines. The use of an atropisomeric 2-aryl-4-DMAP-*N*-oxide catalyst **4a** in combination with a 2-substituted-4-nitrophenylsulfonyl chloride is crucial for achieving enantioselectivity and allows for facile deprotection of the sulfonamide products using thioglycolic acid. A qualitative model has been developed to rationalize the substrate scope and to aid further development, which is ongoing in our laboratory.

Acknowledgements

We thank the EPSRC, the Institute of Chemical Biology (ICB, Imperial College London) and the SCI (Messel Scholarship, J.I.M.) for funding. We also thank Aaron Trowbridge, Zhennan Liu, Mihaela Pop, Lisa Barbaro, Si Jia Lee and Christian Nielsen (all Imperial College London) for preliminary supporting studies.

Conflict of interest

The authors declare no conflict of interest.

Keywords: asymmetric catalysis · indoline · kinetic resolution · organocatalysis · sulfonylation

[1] M. Breuer, K. Ditrich, T. Habicher, B. Hauer, M. Keßeler, R. Stürmer, T. Zelinski, *Angew. Chem. Int. Ed.* **2004**, *43*, 788 – 824; *Angew. Chem.* **2004**, *116*, 806 – 843.
[2] E. Vedejs, M. Jure, *Angew. Chem. Int. Ed.* **2005**, *44*, 3974 – 4001; *Angew. Chem.* **2005**, *117*, 4040 – 4069.
[3] H. B. Kagan, J. C. Fiaud, *Top. Stereochem.* **1988**, *18*, 249 – 330.
[4] S. E. Denmark, G. L. Beutner, *Angew. Chem. Int. Ed.* **2008**, *47*, 1560 – 1638; *Angew. Chem.* **2008**, *120*, 1584 – 1663.
[5] For recent reviews, see: a) J. I. Murray, Z. Heckenast, A. C. Spivey, in *Lewis Base Catal. Org. Synth.*, Wiley-VCH, Weinheim, **2016**, pp. 457 – 526; b) A. C. Spivey, S. Arseniyadis, in *Compr. Enantioselective Organocatalysis*, Wiley-VCH, Weinheim, **2013**, pp. 1225 – 1284; c) C. E. Müller, P. R. Schreiner, *Angew. Chem. Int. Ed.* **2011**, *50*, 6012 – 6042; *Angew. Chem.* **2011**, *123*, 6136 – 6167; d) S. France, D. J. Guerin, S. J. Miller, T. Lectka, *Chem. Rev.* **2003**, *103*, 2985 – 3012.
[6] L. Wang, R. K. Akhani, S. L. Wiskur, *Org. Lett.* **2015**, *17*, 2408 – 2411.
[7] N. Manville, H. Alite, F. Haeffner, A. H. Hoveyda, M. L. Snapper, *Nat. Chem.* **2013**, *5*, 768 – 774.
[8] X. Sun, H. Lee, S. Lee, K. L. Tan, *Nat. Chem.* **2013**, *5*, 790 – 795.
[9] A. Weickgenannt, M. Mewald, M. Oestreich, *Org. Biomol. Chem.* **2010**, *8*, 1497 – 1504.
[10] S. Han, S. J. Miller, *J. Am. Chem. Soc.* **2013**, *135*, 12414 – 12421.
[11] J. I. Murray, A. C. Spivey, R. Woscholski, *Chem. Biol.* **2013**, *6*, 175 – 184.
[12] K. W. Fiori, A. L. A. Puchlopek, S. J. Miller, *Nat. Chem.* **2009**, *1*, 630 – 634.
[13] For a review of amine KR, see: V. P. Krasnov, D. A. Gruzdev, G. L. Levit, *Eur. J. Org. Chem.* **2012**, 1471 – 1493.
[14] For recent organocatalytic amine KRs, see: a) N. Mittal, K. M. Lippert, C. K. De, E. G. Klauber, T. J. Emge, P. R. Schreiner, D. Seidel, *J. Am. Chem. Soc.* **2015**, *137*, 5748 – 5758; b) B. Wanner, I. Kreituss, O. Gutierrez, M. C. Kozlowski, J. W. Bode, *J. Am. Chem. Soc.* **2015**, *137*, 11491 – 11497; c) I. Kreituss, K.-Y. Chen, S. H. Eitel, J.-M. Adam, G. Wuitschik, A. Fettes, J. W. Bode, *Angew. Chem. Int. Ed.* **2016**, *55*, 1553 – 1556; *Angew. Chem.* **2016**, *128*, 1579 – 1582; d) I. Kreituss, J. W. Bode, *Acc. Chem. Res.* **2016**, *49*, 2807 – 2821; e) S. Das, N. Majumdar, C. K. De, D. S. Kundu, A. Döhring, A. Garczynski, B. List, *J. Am. Chem. Soc.* **2017**, *139*, 1357 – 1359.
[15] a) D. Liu, G. Zhao, L. Xiang, *Eur. J. Org. Chem.* **2010**, 3975 – 3984; b) A. Awata, T. Arai, *Angew. Chem. Int. Ed.* **2014**, *53*, 10462 – 10465; *Angew. Chem.* **2014**, *126*, 10630 – 10633.
[16] W. Zi, Z. Zuo, D. Ma, *Acc. Chem. Res.* **2015**, *48*, 702 – 711.
[17] a) B. M. Bechle, M. T. Didiuk, E. L. Fritzen, R. S. Garigipati, WO2006032987 A1, **2006**; b) F. R. Goodman, G. B. Weiss, M. E. Hurley, *Cardiovasc. Drug Rev.* **1985**, *3*, 57 – 69.
[18] a) R. R. Poondra, N. N. Kumar, K. Bijian, M. Prakesch, V. Campagna-Slater, A. Reayi, P. T. Reddy, A. Choudhry, M. L. Barnes, D. M. Leek, M. Daroszewska, C. Lougheed, B. Xu, M. Schapira, M. A. Alaoui-Jamali, P. Arya, *J. Comb. Chem.* **2009**, *11*, 303 – 309; b) Z. Gan, P. T. Reddy, S. Quevillon, S. Couve-Bonnaire, P. Arya, *Angew. Chem. Int. Ed.* **2005**, *44*, 1366 – 1368; *Angew. Chem.* **2005**, *117*, 1390 – 1392; c) K. C. Nicolaou, A. J. Roecker, J. A. Pfefferkorn, G.-Q. Cao, *J. Am. Chem. Soc.* **2000**, *122*, 2966 – 2967.
[19] a) S. Anas, H. B. Kagan, *Tetrahedron: Asymmetry* **2009**, *20*, 2193 – 2199; b) V. Gotor-Fernández, P. Fernández-Torres, V. Gotor, *Tetrahedron: Asymmetry* **2006**, *17*, 2558 – 2564; c) V. P. Krasnov, G. L. Levit, I. M. Bukrina, I. N. Andreeva, L. S. Sadretdinova, M. A. Korolyova, M. I. Kodess, V. N. Charushin, O. N. Chupakhin, *Tetrahedron: Asymmetry* **2003**, *14*, 1985 – 1988.
[20] F. O. Arp, G. C. Fu, *J. Am. Chem. Soc.* **2006**, *128*, 14264 – 14265.
[21] X. L. Hou, B. H. Zheng, *Org. Lett.* **2009**, *11*, 1789 – 1791.
[22] a) K. Saito, Y. Shibata, M. Yamanaka, T. Akiyama, *J. Am. Chem. Soc.* **2013**, *135*, 11740 – 11743; b) K. Saito, T. Akiyama, *Angew. Chem. Int. Ed.* **2016**, *55*, 3148 – 3152; *Angew. Chem.* **2016**, *128*, 3200 – 3204.
[23] a) Z. Yang, F. Chen, Y. He, N. Yang, Q.-H. Fan, *Angew. Chem. Int. Ed.* **2016**, *55*, 13863 – 13866; *Angew. Chem.* **2016**, *128*, 14067 – 14070; b) T. Touge, T. Arai, *J. Am. Chem. Soc.* **2016**, *138*, 11299 – 11305; c) C. Li, J. Chen, G. Fu, D. Liu, Y. Liu, W. Zhang, *Tetrahedron* **2013**, *69*, 6839 – 6844; d) Y.-C. Xiao, C. Wang, Y. Yao, J. Sun, Y.-C. Chen, *Angew. Chem. Int. Ed.* **2011**, *50*, 10661 – 10664; *Angew. Chem.* **2011**, *123*, 10849 – 10852; e) R. Kuwano, *Heterocycles* **2008**, *76*, 909 – 922; f) Y.-G. Zhou, *Acc. Chem. Res.* **2007**, *40*, 1357 – 1366; g) F. Glorius, *Org. Biomol. Chem.* **2005**, *3*, 4171 – 4175.
[24] Y. Wei, A. C. Spivey, M. Mahesh, E. Larionov, H. Zipse, *J. Am. Chem. Soc.* **2012**, *134*, 9390 – 9399 and references therein.
[25] S. Arseniyadis, M. Mahesh, P. McDaid, T. Hampel, S. G. Davey, A. C. Spivey, *Collect. Czech. Chem. Commun.* **2011**, *76*, 1239 – 1253.
[26] J. I. Murray, A. C. Spivey, *Adv. Synth. Catal.* **2015**, *357*, 3825 – 3830.
[27] V. A. Savelova, I. A. Belousova, L. M. Litvinenko, A. A. Yakoveta, *Dokl. Chem.* **1984**, *274*, 1393 – 1398.
[28] a) I. M. Gordon, H. Maskill, M.-F. Ruasse, *Chem. Soc. Rev.* **1989**, *18*, 123 – 151; b) T. W. Bentley, *Int. J. Mol. Sci.* **2015**, *16*, 10601 – 10623.

[29] J. I. Murray, R. Woscholski, A. C. Spivey, *Chem. Commun.* **2014**, *50*, 13608 – 13611.
[30] For key discussions of related stereochemical relays, see: a) J. Clayden, N. Vassiliou, *Org. Biomol. Chem.* **2006**, *4*, 2667 – 2678; b) D. Seebach, A. K. Beck, *Tak. Times* **2006**, *157*, 34 – 40; c) K. Mikami, M. Shimizu, H.-C. Zhang, B. E. Maryanoff, *Tetrahedron* **2001**, *57*, 2917 – 2951.
[31] For examples of additive use, see: a) S. Arai, S. Bellemin-Laponnaz, G. C. Fu, *Angew. Chem. Int. Ed.* **2001**, *40*, 234 – 236; *Angew. Chem.* **2001**, *113*, 240 – 242; b) C. K. De, E. G. Klauber, D. Seidel, *J. Am. Chem. Soc.* **2009**, *131*, 17060 – 17061; c) K. Arnold, B. Davies, D. Hérault, A. Whiting, *Angew. Chem. Int. Ed.* **2008**, *47*, 2673 – 2676; *Angew. Chem.* **2008**, *120*, 2713 – 2716; d) M. Binanzer, S. Y. Hsieh, J. W. Bode, *J. Am. Chem. Soc.* **2011**, *133*, 19698 – 19701; e) V. B. Birman, H. Jiang, X. Li, L. Guo, E. W. Uffman, *J. Am. Chem. Soc.* **2006**, *128*, 6536 – 6537; f) B. S. Fowler, P. J. Mikochik, S. J. Miller, *J. Am. Chem. Soc.* **2010**, *132*, 2870 – 2871.
[32] J. I. Murray, N. J. Flodén, A. Bauer, N. D. Fessner, D. L. Dunklemann, O. Bob-Egbe, H. S. Rzepa, A. C. Spivey, Imperial College HPC Data Repository, **2016**, https://doi.org/10.14469/hpc/1774.
[33] T. Fukuyama, C.-K. Jow, M. Cheung, *Tetrahedron Lett.* **1995**, *36*, 6373 – 6374.
[34] V. P. Nicu, A. Mándi, T. Kurtán, P. L. Polavarapu, *Chirality* **2014**, *26*, 525 – 531.
[35] D. G. I. Kingston, *J. Nat. Prod.* **2009**, *72*, 507 – 515.

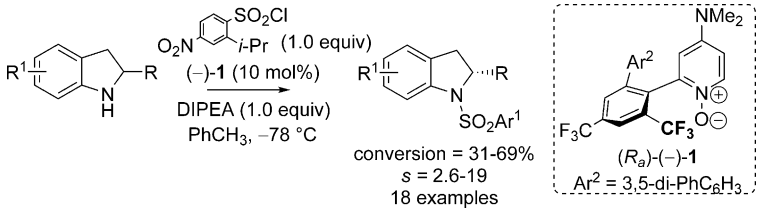
Manuscript received: January 27, 2017
Revised: March 27, 2017
Final Article published: ■■ ■■, ■■■■

Communications

Kinetic Resolution

J. I. Murray, N. J. Flodén, A. Bauer, N. D. Fessner, D. L. Dunklemann, O. Bob-Egbe, H. S. Rzepa, T. Bürgi, J. Richardson, A. C. Spivey* ———— ■■■■–■■■■

Kinetic Resolution of 2-Substituted Indolines by *N*-Sulfonylation using an Atropisomeric 4-DMAP-*N*-oxide Organocatalyst



A practical (re)solution: The kinetic resolution of 2-substituted indolines by catalytic *N*-sulfonylation is reported using an atropisomeric 4-dimethylaminopyridine-*N*-oxide organocatalyst (see scheme). Vibrational cicrcular dichroism is used to assign the absolute configuration of the catalyst and a qualitative model that accounts for the stereodiscrimination is proposed.

