Organic LETTERS

Letter

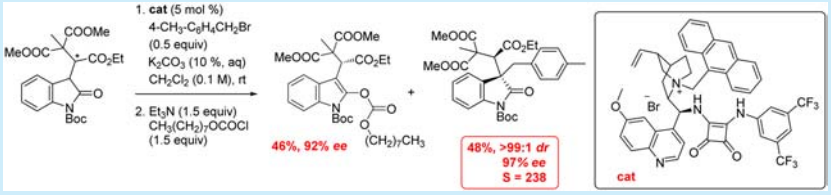
pubs.acs.org/OrgLett

Enantioselective Alkylative Kinetic Resolution of 2-Oxindole-Derived Enolates Promoted by Bifunctional Phase Transfer Catalysts

Emiliano Sorrentino and Stephen J. Connon*

Trinity Biomedical Sciences Institute, School of Chemistry, The University of Dublin, Trinity College, Dublin 2, Ireland

Supporting Information



ABSTRACT: The first strategy for bringing about highly enantioselective alkylative enolate kinetic resolutions using a simple phase-transfer protocol via S_N2 chemistry has been developed. In the presence of a new squaramide-based quaternized cinchona alkaloid-derived catalyst and aqueous base, benzyl, allyl, and propargyl halides react with racemic substituted oxindoles to generate densely functionalized products with the two contiguous stereocenters, one of which is an all-carbon quaternary.

Kinetic resolution (KR) is a powerful, time-honored tool for the preparation of enantiomerically enriched materials. A vast number of KR protocols (e.g., acylation, epoxidation, oxidation, reduction, ring opening, inter alia) exploiting reactions involving a diverse array of functional groups have been developed.[1] However, despite exhaustive research since the 1980s, the diastereoselective alkylation of enolates incorporating chiral auxiliaries and the KR of chiral enolates has been comparatively neglected.[2−7] To the best of our knowledge only two reports (both involving alkylation reactions) have appeared to date.[8,9] These reactions are also rare examples of KR processes which also generate a chiral center.[10]

In 1991, Simpkins et al. reported the noncatalytic KR of heterocyclic chiral enolates (such as that derived from **1**) via an alkylation reaction mediated by the chiral lithium amide **2**.[8] Although diastereomer **3** (Figure 1A) was the only product obtained, the *ee* was not reported and selectivity ($S = k_{fast}/k_{slow}$) was poor ($S = 4$).[11] A considerably more enantiodiscriminatory KR process was recently developed by Hou et al.,[9] who employed a chiral palladium complex to promote the asymmetric allylic alkylation of quinolone derivatives (**4**, Figure 1B).[12] The alkylated product (i.e., **6**) was obtained with absolute diastereocontrol with very high enantioselectivity (S up to 145).

Since the pioneering studies reported by Dolling et al.,[13] phase-transfer catalysis has become a practical methodology for the asymmetric alkylation of enolates generated *in situ*.[14] However, the KR of racemic chiral enolates (generated *in situ*) via phase-transfer-catalyzed alkylation reactions has been unexploited to date and, to the best of our knowledge, the only examples known are three isolated reactions reported by Dixon et al. (Figure 1C).[15,16] The 2-oxindole structural unit is found in a myriad of natural products and bioactive molecules.[17] Rather surpisingly, only three examples of the KR of 3-substituted 3-oxindoles are known, and none involve the KR of enolates.[18,19] Herein we present the development of an unprecedented KR of 2-oxindole

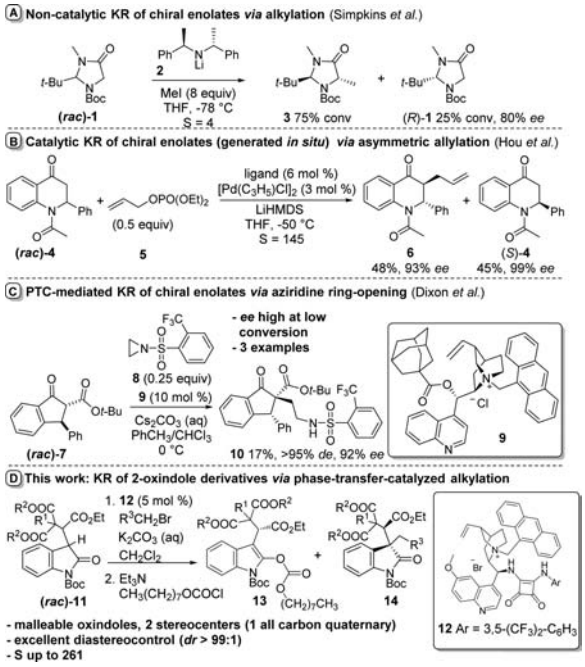


Figure 1. KR of chiral enolates.

derivatives (**11**) via an enolate alkylation reaction, promoted by a new squaramido-based bifunctional PTC (**12**), to afford 3,3′-disubstituted-2-oxindoles **14**.[20]

The formed products are densely functionalized and contain two contiguous stereocenters (one all-carbon quaternary). They can be obtained as single diastereomers (dr > 99:1), with

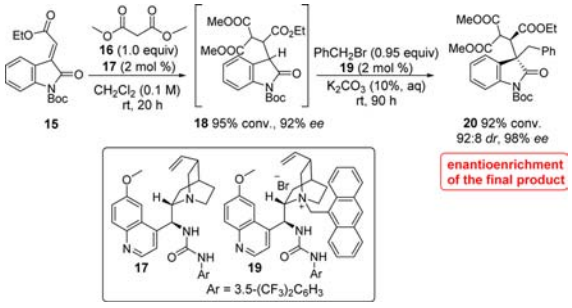
Received: August 12, 2016
Published: October 4, 2016

DOI: 10.1021/acs.orglett.6b02398
Org. Lett. 2016, 18, 5204−5207

enantioselectivity (S up to 261) often akin to that associated with KR catalyzed by efficient enzymatic systems (Figure 1D).

Our study began with an observation: in the search for new tandem catalytic processes, we found that bifunctional catalyst **17** was able to catalyze the asymmetric addition of malonate **16** to alkylidene oxindole **15**. The resulting Michael adduct **18**, formed in 92% *ee*, could be subsequently treated in the same pot with a small undercharge of benzyl bromide in the presence of aqueous base and the bifunctional PTC **19** to afford **20** in 98% *ee* (Scheme 1). The observed improvement in enantiomeric excess alerted us

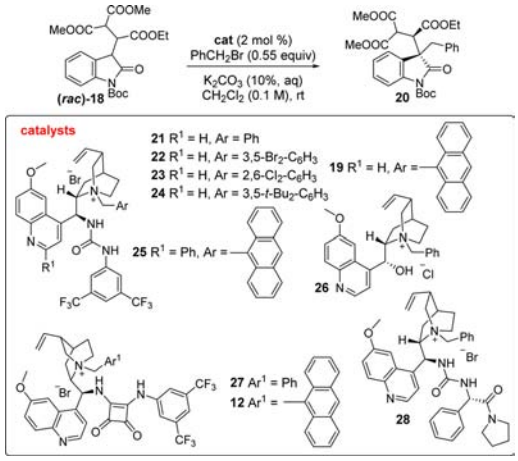
Scheme 1. Observed Enantioenrichment of a Chiral Nonracemic Oxindole by PTC-Catalyzed Enolate Alkylation



to the possibility of developing an efficient methodology for the KR of densely functionalized enolates derived from the ubiquitous 2-oxindole *motif*.

Triester (***rac*)-18** was treated with 0.55 equiv of benzyl bromide and a PTC (i.e., **19** and **21**−**28**) in a biphasic solvent system comprising CH_2Cl_2 and an aqueous carbonate base, to afford the alkylated derivative **20** (Table 1). Since the product possesses two stereogenic centers, the determination of the conversion-independent selectivity factor ($S = k_{fast}/k_{slow}$, $= \ln[1 - \mathrm{Conv}(1 + ee_{Prod})]/\ln[1 - \mathrm{Conv}(1 - ee_{Prod})]$) is not straightforward. Therefore, in these preliminary studies we utilized an approximate, simplified parameter S^*, based on conversion determined by ^{1}H NMR spectroscopy and the *ee* data associated with the major product enantiomer only, which served solely as a guide for catalyst design. The first catalyst evaluated was the urea-based bifunctional system **21**, first reported by Dixon,[21,22a] which promoted the KR of **18** with moderate enantioselectivity (entry 1). Modification of the *N*-benzyl substituent to incorporate electron-withdrawing groups (i.e., **22** and **23**) did not lead to an appreciable improvement in terms of selectivity (entries 2 and 3), while the use of catalyst **24**, bearing a bulky 3,5-di-*tert*-butylbenzyl moiety, led to considerably more enantioselective alkylation (entry 4). Further augmentation of the steric demand of this catalyst substituent by replacement of the benzyl group with an anthracenylmethyl unit allowed the resolution to occur with synthetically useful levels of selectivity ($S^* > 10$, i.e., **19**, entry 5). Installation of a phenyl ring at the C-2′ position of catalyst **19** (i.e., **25**) led to a dramatic diminution of selectivity (entry 6). Catalysts possessing weaker hydrogen-bond donors (i.e., **26** and **28**) promoted the formation of almost racemic products (entries 7 and 8). The squaramide hydrogen-bond donating substituent[22b] proved a useful addition to these systems. Catalyst **27** was able to promote the KR of **18** with an S^* of 6.9 (entry 9), which is twice the value obtained by employing the analogous urea-based catalyst **21** (compare entries 1 and 9). We therefore synthesized a new squaramido-analogue of the superior urea-based catalyst **19** (i.e., catalyst **12**). To our delight, when **12** was employed in the KR of **18**, slow yet highly enantioselective alkylation occurred

Table 1. Catalyst Evaluation



entry	cat.	t (h)	conv (%)[a]	dr[a]	*ee* (%)[b]	S^*[c]
1	**21**	90	46	85:15	42	3.4
2	**22**	103	44	83:17	26	2.1
3	**23**	70	34	89:11	47	3.5
4	**24**	47	47	88:12	63	7.5
5	**19**	73	42	88:12	75	12
6	**25**	70	16	81:19	34	2.2
7	**26**	69	50	87:13	9	1.3
8	**28**	69	40	80:20	17	1.5
9	**27**	190	55	84:16	56	6.9
10	**12**	208	14	90:10	92	28
11[d]	**12**	136	26	89:11	97	92

[a]Determined by ^{1}H NMR spectroscopy. [b]Determined by CSP-HPLC, refers to the major diastereomer. [c]S^* = approximate selectivity factor (ref 1a) calculated using the conversion determined by ^{1}H NMR spectroscopy and the *ee* of product **20**. [d]Catalyst **12** was employed at 5 mol % loading.

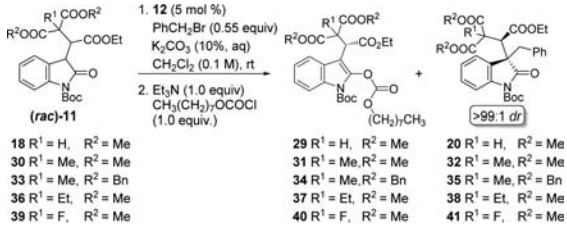
(entry 10). Increasing the loading to 5 mol % resulted in an outstanding S^* of 92 (entry 11).

Attention now turned to the question of the influence of the substrate's malonate ester unit on enantiocontrol (Table 2). In order to determine the *ee* of the unreacted starting materials (which are present as a pair of diastereomers inseparable by CSP-HPLC), the chiral center at the C-3 position was ablated *in situ* after alkylation by *O*-acylation with octyl chloroformate, to give **29**, **31**, **34**, and **40**. Starting with **18**, increasing the loading of catalyst **12** further to 10 mol % allowed the isolation of **20** in good yield and increased selectivity (entry 1).

Variation of the structure of the malonate unit led, in each case, to the formation of a single product diastereomer (dr > 99:1, entries 2−5), which allowed for the calculation of the true selectivity factor, S. The installation of a methyl group at the α-carbon (i.e., **30**) resulted in an extraordinary level of enantiodiscrimination (i.e., S = 205, entry 2). It is noteworthy that exchange of the methyl esters for more synthetically versatile benzyl analogues was also well tolerated from both activity and selectivity standpoints (entry 3). Surprisingly, the replacement of the α-methyl substituent with an ethyl group (entry 4) resulted in a less selective process (due in part to the simultaneous decomposition of the substrate **36**, via a retro-Michael elimination process); nevertheless, overall enantioselectivity remained high. Excellent levels of selectivity were also observed when 2-oxindole **39**, bearing an α-fluorine atom, was utilized in the KR protocol (entry 5). While all the alkylated products could be isolated with

DOI: 10.1021/acs.orglett.6b02398
Org. Lett. 2016, 18, 5204−5207

Table 2. Substrate Scope: 2-Oxindole Derivatives



entry	S.M.	t (h)	conv. (%)[a]	S.M. *ee* (%)[b]	prod. *ee* (%)[b]	S[c]
1[d]	**18**	183	45.1[e] (51, 43[f])	45	95[g]	98.0[h]
2	**30**	134	45.4 (47, 45)	81	98	205.8
3	**33**	115	41.7 (49, 42)	70	98	224.3
4	**36**	133	41.7[e] (n/d, 40)	n/d	92	42.0[i]
5	**39**	264	43[e] (54, 41)	18	95	70.0[i]

[a]Conversion was determined using CSP-HPLC, where conversion = 100 × $ee_{S.M.}/(ee_{S.M.} + ee_{Prod.})$; isolated yields of recovered starting material and product, respectively, in parentheses. [b]Determined by CSP-HPLC. [c]S = enantioselectivity (k_{fast}/k_{slow}; see ref 1a). [d]Catalyst **12** was employed at 10 mol % levels. [e]Determined by ^{1}H NMR spectroscopic analysis. [f]Combined yield of both diastereomers, 89:11 *dr* [g]Refers to the major product. [h]$S = S^*$. [i]S calculated using isolated yield of the alkylated product due to starting material racemization or decomposition.

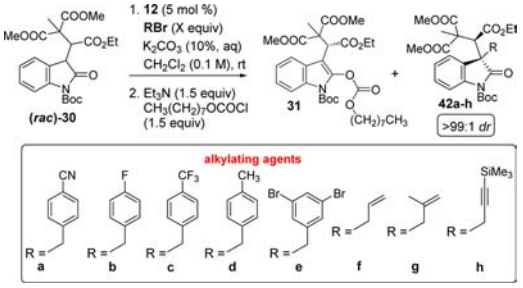
excellent *ee* at conversion close to 50%, the resolved 2-oxindole substrates undergo partial racemization *in situ* (due to retro-Michael/Michael processes; see Supporting Information).[23] The rate of this racemization is not of sufficient magnitude to facilitate efficient DKR. The notable exceptions were oxindoles **30** and **33**, which do not discernibly racemize.

A study of the KR of oxindole **30** employing a variety of alkyl halides was also undertaken (Table 3). Benzyl bromides incorporating either electron-withdrawing (**a**−**c**, entries 1−3) or electron-donating (**d**, entry 4) substituents all participated in highly enantiodiscriminatory KR processes, with S > 100. The dibromo derivative **e** also proved a useful substrate, allowing the isolation of the corresponding alkylated substrate in 45% yield and 96% *ee* (entry 5). Allylation is also possible: use of allyl bromide (**f**) allowed a slow yet extraordinarily selective KR to take place (S > 250, entry 6). Faster alkylation (at the expense of selectivity) occurs using increased loadings of **f**, with 1.5 equiv representing a good compromise between selectivity and yield (entries 7 and 8). The methodology also accommodates the more hindered methylallyl bromide (**g**), which can be reacted with **30** at 2 °C with excellent enantiocontrol (entry 9). Finally, highly selective propargylation of **30** using the protected propargyl bromide **h** was possible, with an S value of 89.6 (entry 10). These reactions all proceeded with total diastereocontrol.

In order to demonstrate that the stereoablation process (used primarily to allow facile evaluation of the enantiomeric excess of the unreacted starting material) is both reversible and does not result in erosion of enantiopurity, we treated a sample of the *O*-acylated material **31** (of known enantiomeric excess) with methanol in the presence of substoichiometric loadings of DMAP (Scheme 2) to generate **30** as an almost 1:1 diastereomeric mixture. This was then resubjected to *O*-acylation with octyl chloroformate (to facilitate analysis) to give **31** in unaltered *ee*.

In summary, highly tunable bifunctional phase transfer catalysts have been shown to promote the alkylative kinetic resolution of chiral enolates. Optimization studies identified both the catalyst's squaramide-based hydrogen-bond donating group and a bulky

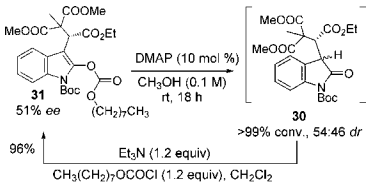
Table 3. Substrate Scope: Electrophilic Component



entry	R	X	t (h)	conv (%)[a]	**31** *ee* (%)[b]	**42** *ee* (%)[b]	S[c]
1	**a**	0.5	170	43.5 (48, 44)[d]	74	96	113.7
2	**b**	0.5	96	48.2 (49, 48)[d]	89	96	149.1
3	**c**	0.5	130	40.1 (52, 40)[d]	65	97	139.7
4	**d**	0.5	134	48.6 (46, 48)[d]	92	97	237.7
5	**e**	0.5	121	46.4 (49, 45)[d]	83	96	134.2
6	**f**	0.5	255	20.3 (79, 21)[e]	25	99	261.8
7	**f**	2.0	139	52.1 (48, 52)[e]	95	87	51.5
8	**f**	1.5	120	43.8 (49, 43)[d]	75	96	103.8
9[f]	**g**	2.0	163	39.9 (52, 40)[d]	65	98	172.3
10[g]	**h**	2.0	168	41.9 (54, 42)[d]	69	96	89.6

[a]Conversion was determined using CSP-HPLC, where conversion = 100 × $ee_{S.M.}/(ee_{S.M.} + ee_{Prod.})$. [b]Determined by CSP-HPLC. [c]S = enantioselectivity (k_{fast}/k_{slow}; see ref 1a). [d]Isolated yields of S.M. and Prod. [e]Determined by ^{1}H NMR spectroscopy. [f]Reaction performed at 2 °C. [g]Stereoablation carried out after column chromatography purification.

Scheme 2. Cleavage of 31 and Reprotection



chiral ammonium ion substituent as key units for the facilitation of effective catalysis. The process generates benzylated, allylated, and propargylated 2-oxindole units substituted with a densely functionalized side chain incorporating an ester at the α-position and a malleable malonate derivative β to the heterocycle. The level of enantio- and diastereocontrol obtained ranges from excellent to outstanding, with S factors in excess of 250 possible. The resolved starting materials can undergo racemization via a retro-Michael/Michael process; however this can be arrested through the installation of a methyl group at the β-carbon of the side chain. Studies to further exploit the synthetic potential of the catalytic alkylative kinetic resolution of enolates by bifunctional phase transfer catalysis are underway.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b02398.

Experimental procedures, analytical and crystallographic data (PDF)

DOI: 10.1021/acs.orglett.6b02398
Org. Lett. 2016, 18, 5204−5207

AUTHOR INFORMATION

Corresponding Author

*E-mail: connons@tcd.ie.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

Financial support from the European Research Council and Science Foundation Ireland (12/IA/1645) is gratefully acknowledged.

REFERENCES

(1) For selected reviews concerning kinetic resolution, see: (a) Kagan, H. B.; Fiaud, J. C. *Top. Stereochem.* **1988**, *18*, 249. (b) Vedejs, E.; Jure, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 3974. (c) Pellissier, H. *Adv. Synth. Catal.* **2011**, *353*, 1613.

(2) For the kinetic resolution of enolates via a silylation reaction, see: (a) Kim, H.-D.; Kawasaki, H.; Nakajima, M.; Koga, K. *Tetrahedron Lett.* **1989**, *30*, 6537. (b) Coggins, P.; Simpkins, N. S. *Synlett* **1992**, *1992*, 313. (c) Koga, K.; Odashima, K. *Yakugaku Zasshi* **1997**, *117*, 800.

(3) For the kinetic resolution of enolates involving Michael addition reactions, see: (a) Davies, S. G.; Garner, A. C.; Long, M. J. C.; Morrison, R. M.; Roberts, P. M.; Savory, E. D.; Smith, A. D.; Sweet, M. J.; Withey, J. M. *Org. Biomol. Chem.* **2005**, *3*, 2762. (b) Ley, S. V.; Dixon, D. J.; Guy, R. T.; Rodriguez, F.; Sheppard, T. D. *Org. Biomol. Chem.* **2005**, *3*, 4095.

(4) For the kinetic resolution of enolates via aldol chemistry, see: (a) Paterson, I.; McClure, C. K.; Schumann, R. C. *Tetrahedron Lett.* **1989**, *30*, 1293. (b) Chen, L.; Luo, S.; Li, J.; Li, X.; Cheng, J.-P. *Org. Biomol. Chem.* **2010**, *8*, 2627.

(5) For the kinetic resolution of enolates via hydroxylation reactions, see: Davis, F. A.; Kumar, A. *J. Org. Chem.* **1992**, *57*, 3337.

(6) For examples of parallel kinetic resolution involving enolates, see: Bocknack, B. M.; Wang, L.-C.; Krische, M. J. *Proc. Natl. Acad. Sci. U. S. A.* **2004**, *101*, 5421.

(7) For examples of dynamic kinetic resolution involving enolates, see: (a) Wang, J.; Xie, H.; Li, H.; Zu, L.; Wang, W. *Angew. Chem., Int. Ed.* **2008**, *47*, 4177. (b) Yu, C.; Zhang, Y.; Song, A.; Ji, Y.; Wang, W. *Chem. - Eur. J.* **2011**, *17*, 770. (c) Yang, W.; Yang, Y.; Du, D.-M. *Org. Lett.* **2013**, *15*, 1190.

(8) Coggins, P.; Simpkins, N. S. *Synlett* **1991**, *1991*, 515.

(9) Lei, B.-L.; Ding, C.-H.; Yang, X.-F.; Wan, X.-L.; Hou, X.-L. *J. Am. Chem. Soc.* **2009**, *131*, 18250.

(10) For examples see ref 9 and: (a) Martin, V. S.; Woodard; Katsuki, S. S. T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237. (b) Ohkuma, T.; Koizumi, M.; Muñiz, K.; Hilt, G.; Kabuto, C.; Noyori, R. *J. Am. Chem. Soc.* **2002**, *124*, 6508. (c) Naasz, R.; Arnold, L. A.; Minnaard, A. J.; Feringa, B. L. *Angew. Chem., Int. Ed.* **2001**, *40*, 927. (d) Jurkauskas, V.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 2892. (e) Suarez, A.; Downey, C. W.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 11244. (f) Peschiulli, A.; Procuranti, B.; O' Connor, C. J.; Connon, S. J. *Nat. Chem.* **2010**, *2*, 380.

(11) Simpkins et al. also reported the kinetic resolution of a single substrate via an alkylation reaction: Rodeschini, V.; Simpkins, N. S.; Wilson, C. *J. Org. Chem.* **2007**, *72*, 4265.

(12) A similar protocol was recently reported by Hou et al.: Lei, B.-L.; Zhang, Q.-S.; Yu, W.-H.; Ding, Q.-P.; Ding, C.-H.; Hou, X.-F. *Org. Lett.* **2014**, *16*, 1944.

(13) Dolling, U.; Davis, P.; Grabowski, E. J. J. *J. Am. Chem. Soc.* **1984**, *106*, 446.

(14) For selected reviews concerning asymmetric phase-transfer catalysis, see: (a) Ooi, T.; Maruoka, K. *Angew. Chem., Int. Ed.* **2007**, *46*, 4222. (b) Hashimoto, T.; Maruoka, K. *Chem. Rev.* **2007**, *107*, 5656. (c) Maruoka, K. *Org. Process Res. Dev.* **2008**, *12*, 679. (d) Jew, S.; Park, H. *Chem. Commun.* **2009**, 7090. (e) Shirakawa, S.; Maruoka, K. *Angew. Chem., Int. Ed.* **2013**, *52*, 4312. (f) Novacek, J.; Waser, M. *Eur. J. Org. Chem.* **2013**, *2013*, 637. (g) Liu, S.; Kumatabara, Y.; Shirakawa, S. *Green Chem.* **2016**, *18*, 331. (h) Kaneko, S.; Kumatabara, Y.; Shirakawa, S. *Org. Biomol. Chem.* **2016**, *14*, 5367.

(15) Moss, T. A.; Barber, D. M.; Kyle, A. F.; Dixon, D. J. *Chem. - Eur. J.* **2013**, *19*, 3071.

(16) Few reports detailing KR catalyzed by PTCs have appeared; for examples, see: (a) Hummelen, J. C.; Wynberg, H. *Tetrahedron Lett.* **1978**, *19*, 1089. (b) Annunziata, R.; Cinquini, M.; Colonna, S. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2422. (c) Julia, S.; Ginebreda, A.; Guixer, J. *J. Chem. Soc., Chem. Commun.* **1978**, 742. (d) Julia, S.; Ginebreda, A.; Guixer, J.; Tomas, A. *Tetrahedron Lett.* **1980**, *21*, 3709. (e) Ooi, T.; Kato, D.; Inamura, K.; Ohmatsu, K.; Maruoka, K. *Org. Lett.* **2007**, *9*, 3945. (f) Frisch, K.; Jørgensen, K. A. *Org. Biomol. Chem.* **2007**, *5*, 2966. (g) Ohmatsu, K.; Hamajima, Y.; Ooi, T. *J. Am. Chem. Soc.* **2012**, *134*, 8794. (h) Dong, S.; Liu, X.; Zhu, Y.; He, P.; Lin, L.; Feng, X. *J. Am. Chem. Soc.* **2013**, *135*, 10026. (i) Ohmatsu, K.; Ando, Y.; Ooi, T. *J. Am. Chem. Soc.* **2013**, *135*, 18706. (j) Shirakawa, S.; Wu, X.; Maruoka, K. *Angew. Chem., Int. Ed.* **2013**, *52*, 14200.

(17) For selected reviews concerning the synthesis of 2-oxindole derivatives, see: (a) Galliford, C. V.; Scheidt, K. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 8748. (b) Trost, B.; Brennan, M. *Synthesis* **2009**, *2009*, 3003. (c) Zhou, F.; Liu, Y.-L.; Zhou, J. *Adv. Synth. Catal.* **2010**, *352*, 1381. (d) Dalpozzo, R.; Bartoli, G.; Bencivenni, G. *Chem. Soc. Rev.* **2012**, *41*, 7247. (e) Ball-Jones, N. R.; Badillo, J. J.; Franz, A. K. *Org. Biomol. Chem.* **2012**, *10*, 5165. (f) Hong, L.; Wang, R. *Adv. Synth. Catal.* **2013**, *355*, 1023. (g) Cheng, D.; Ishihara, Y.; Tan, B.; Barbas, C. F. *ACS Catal.* **2014**, *4*, 743.

(18) (a) Lu, S.; Poh, S. B.; Siau, W.-Y.; Zhao, Y. *Angew. Chem., Int. Ed.* **2013**, *52*, 1731. (b) Yang, Y.; Moinodeen, F.; Chin, W.; Ma, T.; Jiang, Z.; Tan, C.-H. *Org. Lett.* **2012**, *14*, 4762. (c) Brittain, W. D. G.; Buckley, B. R.; Fossey, J. S. *Chem. Commun.* **2015**, *51*, 17217.

(19) Ooi et al. have employed 2-oxindole derivatives as pronucleophiles for the PTC-mediated ring opening KR of aziridines; see: Ohmatsu, K.; Ando, Y.; Ooi, T. *J. Am. Chem. Soc.* **2013**, *135*, 18706.

(20) The absolute configuration of compounds of general structure **14** was assigned by analogy to the absolute configuration of **42c**, which was determined using XRD analysis (see Supporting Information).

(21) Johnson, K. M.; Rattley, M. S.; Sladojevich, F.; Barber, D. M.; Nunez, M. G.; Goldys, A. M.; Dixon, D. J. *Org. Lett.* **2012**, *14*, 2492.

(22) See also: (a) Li, M.; Woods, P. A.; Smith, M. D. *Chem. Sci.* **2013**, *4*, 2907. (b) Wang, B.; He, Y.; Fu, X.; Wei, Z.; Lin, Y.; Duan, H. *Synlett* **2015**, *26*, 2588.

(23) For experiments concerning the stability of **30** under the reaction conditions, see the Supporting Information. For selected reviews concerning kinetic resolution, see: (a) Kagan, H. B.; Fiaud, J. C. *Top. Stereochem.* **1988**, *18*, 249. (b) Vedejs, E.; Jure, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 3974. (c) Pellissier, H. *Adv. Synth. Catal.* **2011**, *353*, 1613.

DOI: 10.1021/acs.orglett.6b02398
Org. Lett. 2016, 18, 5204−5207