Squaramide catalyzed enantioselective iodolactonization of allenoic acids

Renate Kristianslund, Marius Aursnes, Jørn Eivind Tungen, Trond Vidar Hansen

PII: S0040-4039(16)31338-7
DOI: http://dx.doi.org/10.1016/j.tetlet.2016.10.035
Reference: TETL 48205

To appear in: *Tetrahedron Letters*

Received Date: 19 August 2016
Revised Date: 5 October 2016
Accepted Date: 10 October 2016

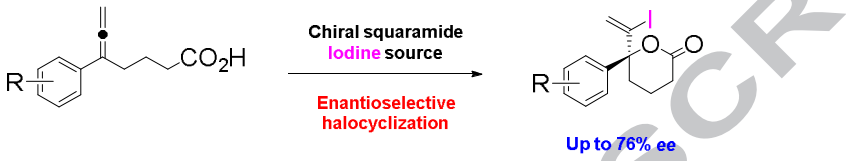
Please cite this article as: Kristianslund, R., Aursnes, M., Tungen, J.E., Hansen, T.V., Squaramide catalyzed enantioselective iodolactonization of allenoic acids, *Tetrahedron Letters* (2016), doi: http://dx.doi.org/10.1016/j.tetlet.2016.10.035

Graphical Abstract

Squaramide catalyzed enantioselective iodolactonization of allenoic acids

Renate Kristianslund, Marius Aursnes, Jørn Eivind Tungen, Trond Vidar Hansen

Leave this area blank for abstract info.



ELSEVIER

Tetrahedron Letters
journal homepage: www.elsevier.com

Squaramide catalyzed enantioselective iodolactonization of allenoic acids

Renate Kristianslund, Marius Aursnes, Jørn Eivind Tungen, Trond Vidar Hansen*

School of Pharmacy, Department of Pharmaceutical Chemistry, University of Oslo, PO Box 1068 Blindern, N-0316 Oslo, Norway

ARTICLE INFO

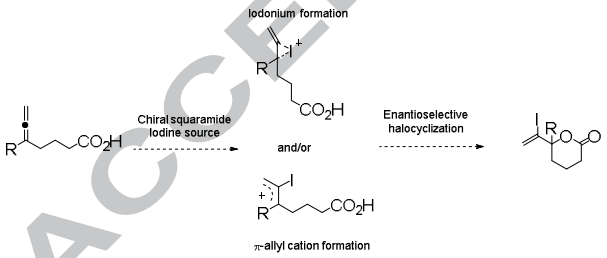
Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Squaramides
Iodolactonization
Allenoic acids
Stereoselective synthesis
H-bonding

ABSTRACT

An asymmetric iodolactonization reaction of allenoic acids has been extensively studied. Eight different chiral squaramides were prepared in a straightforward manner and investigated as organocatalysts. The reaction protocol is operationally simple to execute and proceeds with up to 76% enantiomeric excess. Several conditions, additives, catalysts and substrates have been investigated. The best results were observed with 3-((3,5-*bis*(trifluoromethyl)phenyl)amino)-4-(((1*R*,2*R*)-2-(dipentylamino)cyclohexyl)amino)-cyclobut-3-ene-1,2-dione as the catalyst.

Halocyclization reactions are useful synthetic transformations that have been applied to the synthesis of various natural products and bioactive compounds.[1] Recently, asymmetric versions have been developed for a wide variety of synthetic transformations, including halolactonizations,[2] cyclohaloaminations,[3] cyclohaloetherifications,[4] and other reactions involving halofunctionalizations.[5] Alkenes are most commonly employed, however, enynes have also been utilized for the formation of synthetically useful products.[6] Only very recently have allenes been investigated as substrates (Scheme 1).



Scheme 1. Outline of the iodocyclization of δ-1,1-disbustituted allenoic acids.

When we initiated our studies towards the development of an enantioselective iodolactonization protocol using allenoic acids, only a few studies had been reported.[7,8] Ma and co-workers reported the highly diastereoselective, substrate-controlled iodolactonization of such acids.[7] These studies revealed that the planar chirality of an allene is transferred to the iodolactone products.[7] Toste and co-workers disclosed a highly enantioselective bromocyclization of allenes.[8] This formal bromolactonization protocol was accomplished in the presence of a chiral dinuclear gold complex and/or chiral phosphate anions.[8] *N*-Bromolactams proved superior as the halogenating agent with up to 99% enantiomeric excess in several examples. However, when *N*-iodosuccinimide (NIS) was used for the synthesis of vinylic iodolactones, no asymmetry was induced.[8] In 2014, the group of Hennecke disclosed the first organocatalytic enantioselective bromolactonization protocol in the presence of a dimeric cinchona alkaloid derived catalyst.[9] These authors observed that the selectivity was variable; the highest *ee*-value was 72%. Of note, Hennecke and co-workers reported low selectivity in the presence of some trisimidazoline derived catalysts for the bromolactonization products.[9] Later in 2014, Murai, Shimizu and Fujioka reported the first enantioselective iodolactonization protocol using allenoic acids.[10] These authors reported that in the presence of iodine and an analogue of the trisimidazoline catalyst attempted by the Hennecke group, selectivity with up to 82% *ee* was observed for some cases.[10] Experiments supported that a π-allyl complex intermediate was most likely involved.[10]

Previously we disclosed highly enantioselective iodo-[11] and bromo-lactonization[12] protocols utilizing chiral squaramides, such as **1**-**8** (Fig. 1). The halolactone products were obtained in high to excellent yields with up to 96% *ee* for both reaction types.[11,12] Chiral squaramide derived catalysts have recently been employed in many asymmetric reactions.[13] This fact, combined with our interest in employing halolactones in natural product synthesis,[12,14] spurred our interest to investigate the asymmetric iodolactonization reactions of allenoic acids in the presence of catalysts **1**-**8** (Fig. 1). These efforts are communicated herein.

* Corresponding author. Tel.: +47-22-855-470; fax: +47-228 5-947; e-mail: t.v.hansen@farmasi.uio.no

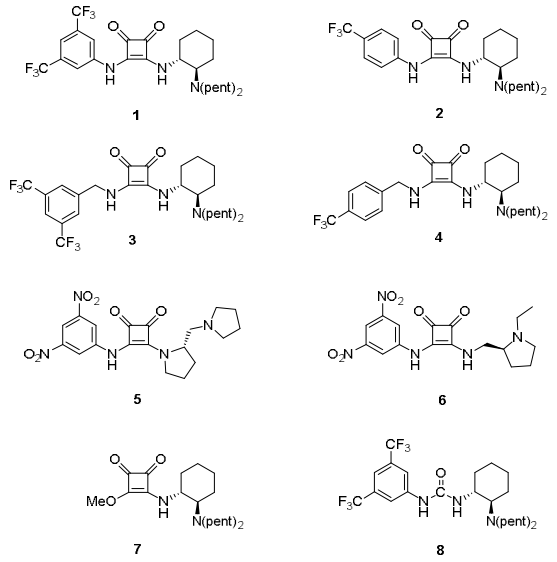
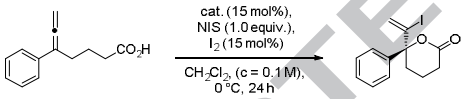


Figure 1. Squaramide catalysts investigated in this study.

We started our screening efforts by employing the squaramide catalysts **1-4**, NIS and I_2 in CH_2Cl_2 at 0 °C for the enantioselective iodolactonization reaction with **9a** as the model substrate. Based on our previous experience[11] and literature reports,[2c] the amounts of NIS and I_2 were 1.0 equivalent and 15 mol%, respectively. Pleasingly, under these conditions, the iodocyclization of allenoic acid **9a** afforded only the 5-*exo* cyclization product **10a**. However, the enantioselectivity was disappointingly low (*ee* = 9%) (Table 1, entry 1). The absolute configuration was established as (*S*) by comparison of the specific optical rotation values of **10a** with literature values.[10]

Table 1. Screening of squaramide catalysts **1-4** in the asymmetric iodolactonization reaction



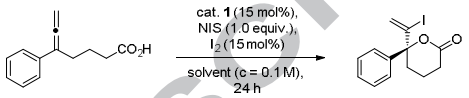
9a **10a**

Entry[a]	Catalyst	Yield (%)[b]	*Ee* (%)[c]
1	**1**	49	9
2	**2**	22	9
3	**3**	54	5
4	**4**	38	4

[a]Reactions performed on a 0.1 mmol scale of **9a**. [b]Isolated yield. [c]Determined by HPLC analysis using the commercial Chiralcel OD-H chiral column.

Product **10a** was also produced with similar low *ee*-values in the presence of catalysts **2-4** (Table 1, entries 2-4). In terms of both enantioselectivity and yield, catalyst **1** provided the best results. Previously, we have observed that altering the solvent and reaction conditions utilizing catalyst **1** in the iodolactonization of alkenoic acids[11] significantly enhanced the selectivity. Hence, we wanted to investigate if the selectivity in the iodocyclization of allene substrate **9a** was also amenable to such alterations (Table 2). The use of acetone, toluene, $CHCl_3$, EtOAc, THF or Et_2O at 0 °C resulted in very low asymmetric induction with varied yields (Entries 2-7). The best yield (52%) was observed using a 1:1 mixture of CH_2Cl_2:acetone as solvent (Entry 8). Reducing the temperature to -78 °C gave a slight increase in *ee* (12%) using CH_2Cl_2 as the solvent (Entry 9), while a 1:1 CH_2Cl_2:acetone mixture gave an even better selectivity. In this case, **10a** was formed with 42% *ee* in a modest 31% yield (Entry 10). EtOAc, acetone, THF, Et_2O or isopropanol all gave low enantiomeric excess of **10a** at -78 °C, with considerably varied yields (Entries 11-15). Of note, in toluene at -78 °C, (*R*)-configured **10a** was formed with 44% *ee* (Entry 16). The 1:1 solvent mixture of $CHCl_3$:hexane returned **10a** with 25% *ee* (Entry 17). Gratifyingly, a 1:1 mixture of $CHCl_3$:acetone improved the selectivity to 52% *ee*; in this case **10a** was obtained in low yield (Entry 18). Similar selectivity was seen using a 1:1 mixture of 1,2-dichloroethane:acetone (47% *ee*) (Entry 19).

Table 2. Screening of solvents in the asymmetric iodolactonization reaction.



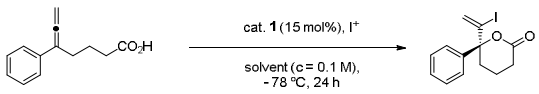
9a **10a**

Entry[a]	Solvent	Temp. (°C)	Yield (%)[b]	*Ee* (%)[c]
1	CH_2Cl_2	0	49	9
2	Acetone	0	33	3
3	Toluene	0	32	3
4	$CHCl_3$	0	34	7
5	EtOAc	0	33	9
6	THF	0	26	3
7	Et_2O	0	39	4
8	CH_2Cl_2/acetone (1:1)	0	52	6
9	CH_2Cl_2	- 78	8	12
10	CH_2Cl_2/acetone (1:1)	- 78	31	42
11	EtOAc	- 78	35	10
12	Acetone	- 78	8	18
13	THF	- 78	18	16
14	Et_2O	- 78	7	4
15	Isopropanol	- 78	12	9
16	Toluene	- 78	15	44[d]
17	$CHCl_3$/hexane (1:1)	- 78	8	25
18	$CHCl_3$/acetone (1:1)	- 78	19	52
19	1,2-Dichloroethane/acetone (1:1)	- 78	13	47

[a]Reactions performed on a 0.1 mmol scale of **9a**. [b]Isolated yield. [c]Determined by HPLC analysis using the commercial Chiralcel OD-H chiral column. [d]The (*R*)-enantiomer was formed as determined by HPLC analysis and specific optical rotation values.

We then investigated the importance of the iodine source (Table 3) with squaramide **1** as the catalyst, as this often influences the selectivity.[2c,11] The presence of both NIS and I_2 proved to be important, and the amount of iodine influenced both the yields and the *ee*-values (Entries 1-3). In the absence of I_2, the product was obtained in lower yield while the enantioselectivity remained unaltered (Entry 6), in comparison to using NIS together with 15 mol% I_2 (Entry 5). Using only iodine gave racemic **10a** (Entry 7), while increasing the amount of iodine compared to NIS diminished the selectivity (Entries 3, 8). The use of diiodohydantoine (DIH, Entry 4) gave a low yield with similar selectivity as NIS.

Table 3. Screening of I^+-source in the asymmetric iodolactonization reaction.



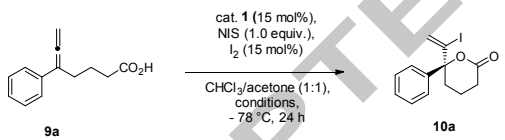
9a **10a**

Entry[a]	I^+ source	Solvent	Yield (%)[b]	*ee* (%)[c]
1	I_2 (5 mol%), NIS (1.0 equiv.)	$CHCl_3$/acetone (1:1)	12	48
2	I_2 (15 mol%), NIS (1.0 equiv.)	$CHCl_3$/acetone (1:1)	19	52
3	I_2 (65 mol%), NIS (1.0 equiv.)[d]	$CHCl_3$/acetone (1:1)	31	37
4	DIH (0.5 equiv.)	$CHCl_3$/acetone (1:1)	14	41
5	I_2 (15 mol%), NIS (1.0 equiv.)	CH_2Cl_2/acetone (1:1)	31	42
6	NIS (1.5 equiv.)	CH_2Cl_2/acetone (1:1)	15	43
7	I_2 (1.5 equiv.)	CH_2Cl_2/acetone (1:1)	14	0
8	I_2 (1.0 equiv.), NIS (1.0 equiv.)[e]	CH_2Cl_2/acetone (1:1)	28	9

[a]Reactions performed on a 0.1 mmol scale of **9a**. [b]Isolated yield. [c]Determined by HPLC analysis using the commercial Chiralcel OD-H chiral column. [d]Portionwise addition of I_2 over 96 hours. [e]72 h reaction time.

Since additives and altering the concentrations of the starting materials have also been reported to alter the enantioselectivity in the presence of chiral squaramides,[11,12] we performed some additional experiments (Table 4). Reducing the concentration of the substrate diminished the selectivity (Entry 1), while doubling the concentration returned similar results (Entry 2). The use of molecular sieves did not enhance the yield or the selectivity (Entry 3). Increasing the amount of catalyst (Entry 4), or the reaction time (Entry 5), as well as using additives (Entries 6-8), returned similar selectivities in the range of 35-50% *ee*. In all cases, the yields of **10a** were low.

Table 4. Screening of conditions in the asymmetric iodolactonization reaction.



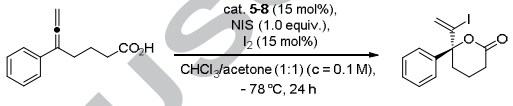
9a **10a**

Entry[a]	Conditions	Yield (%)[b]	*ee* (%)[c]
1	c = 0.025 M[d]	11	28
2	c = 0.20 M	22	48
3	3Å MS, 96 h[d, e]	15	41
4	100 mol% catalyst[e]	28	50
5	96 h[e]	18	45
6	2,6-di-*tert*-butylpyridine (2.5 equiv.)[e]	14	48
7	4-(*N*,*N*-dimethylamino)pyridine (0.1 equiv.), 96 h[e]	28	46
8	4-(*N*,*N*-dimethylamino)pyridine (1.0 equiv.), 72 h[e]	11	35

[a]Reactions performed on a 0.1 mmol scale of **9a**. [b]Isolated yield. [c]Determined by HPLC analysis using the commercial Chiralcel OD-H chiral column. [d]Reaction was performed using CH_2Cl_2/acetone (1:1). [e]Concentration of **9a** was 0.1 M.

The improved conditions were then applied with catalysts **5-8** (Table 5). All four catalysts were less selective than **1** (Entries 1-4), with only catalyst **8** able to induce any reasonable asymmetry in the product **10a** (Entry 4). In this case, **10a** was obtained in 45% *ee* and 19% isolated yield. To explore the substrate scope with respect to selectivity, several substrates were prepared and subjected to the improved conditions as described above (Table 6). The electronic properties of the substituents gave rise to differences in the selectivity. Electron-donating substituents in the *para*-position returned almost racemic products **10b** and **10c** (Entries 2, 3), while 3,5-dimethyl substitution provided **10d** in 37% *ee* (Entry 4). Substrates **9e** and **9f** with either a fluoro- or a chloro-substituent in the *para*-position, respectively, were next examined. Substrate **9e** gave similar results for product **10e** as for product **10a** (Entry 5), while an improvement with respect to enantioselectivity was observed using **9f**. In this case, the vinylic δ-iodolactone **10f** was obtained with 75% *ee* and 22% isolated yield. The *para*-CF_3-substituted substrate **9g** gave product **10g** with 69% *ee* (Entry 6). The nitro-group in the *para*-position gave the highest selectivity (76% *ee*), but a very poor yield was observed for product **10h** (< 5%). Similar poor yields were obtained for product **10i** which was formed with an enantiomeric excess of 53%.

Table 5. Screening of catalysts **5-8.**

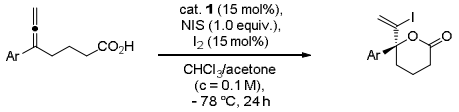


9a **10a**

Entry[a]	Catalyst	Yield (%)[b]	*ee* (%)[c]
1	**5**	24	0
2	**6**	21	3
3	**7**	15	0
4	**8**	19	45

[a]Reactions performed on a 0.1 mmol scale of **9a**. [b]Isolated yield. [c]Determined by HPLC analysis using the commercial Chiralcel OD-H chiral column.

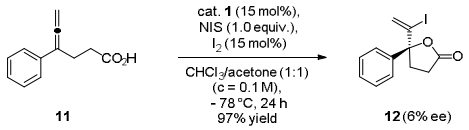
Table 6. Substrate scope of the asymmetric iodolactonization reaction.



Entry[a]	Ar (**9**, **10**)	Yield (%)[b]	*ee* (%)[c]
1	**9a**, **10a**: C_6H_5	19	52
2	**9b**, **10b**: 4-MeO-C_6H_4	81	5
3	**9c**, **10c**: 4-*tert*-Bu-C_6H_4	5	2
4	**9d**, **10d**: 3,5-Me_2-C_6H_3	11	37
5	**9e**, **10e**: 4-F-C_6H_4	14	50
6	**9f**, **10f**: 4-Cl-C_6H_4	22	75
7	**9g**, **10g**: 4-CF_3-C_6H_4	13	69
8	**9h**, **10h**: 4-NO_2-C_6H_4	< 5	76
9	**9i**, **10i**: 4-CN-C_6H_4	< 5	53

[a]Reactions performed on a 0.1 mmol scale of **9a**. [b]Isolated yield. [c]Determined by HPLC analysis using the commercial Chiralcel OD-H and Chiralpak AD-H chiral columns.

Next we tried the conditions in Table 6 with 4-phenylhexa-4,5-dienoic acid (**11**) as the substrate (Scheme 2). This produced the corresponding vinylic γ-iodolactone **12** in near quantitative yield, but with very poor enantiomeric excess (6%). These types of substrates are more difficult to engage in highly stereoselective reactions due to the rapid cyclization to the γ-iodolactones.[11,12,15]



Scheme 2. Organocatalyzed iodolactonization reaction with 4-phenylhexa-4,5-dienoic acid (**11**).

To summarize, we have investigated the enantioselective organocatalyzed iodolactonization reaction of aryl-substituted δ-unsaturated allenoic acids **9a-i** using eight different squaramides. Only low to modest enantiomeric excess of products **10a-i** were observed, with up to 76% *ee* in the best case. Unfortunately, these synthetically useful products were obtained in low yields due to the low conversions at -78 °C of all substrates investigated, except the *para*-methoxy substituted substrate **9b**.[16] Efforts towards improving both the enantioselectivity and the chemical yields are ongoing. Since chiral squaramides are easily available over a few steps, their application in enantioselective protocols will most likely continue to rise.[13] Along with prior demonstrations of highly enantioselective halocyclization reactions,[11,12] we hope that the initial results reported herein will stimulate further developments of organocatalyzed reactions for the preparation of synthetically useful vinylic iodolactones. Chiral squaramides have many advantages, such as their insensitivity to moisture and oxygen, low toxicity and ease of preparation from low cost starting materials.[13] Only recently have squaramide derived organocatalysts been employed for the synthesis of non-[12] and halogenated natural products.[17] Considering their large number,[17] enantioselective and catalytic processes using these types of catalysts will most likely be used for their preparation.

Acknowledgments

Helpful discussions with Associate Professor Anders Vik are appreciated. The Norwegian Research Council (FRIPRO-FRINATEK 230470) is gratefully acknowledged for scholarships to R. K. and M. A., while we thank the School of Pharmacy, University of Oslo, for a scholarship to J. E. T.

References and notes

1. (a) Laya, M. S.; Banerjee, A. K.; Cabrera, E. V. *Curr. Org. Chem.* **2009**, *13*, 720-730; (b) Snyder, S. A.; Treitler, D. S.; Brucks, A. P. *Aldrichimica Acta* **2011**, *44*, 27-40.
2. (a) Hennecke, U. *Chem. – Asian J.* **2012**, *7*, 456-465; (b) Nolsøe, J. M.; Hansen, T. V. *Eur. J. Org. Chem.* **2014**, 3051-3065; (c) Veitch, G. E.; Jacobsen, E. N. *Angew. Chem. Int. Ed.* **2010**, *49*, 7332-7335; (d) Chen, G.; Ma, S. *Angew. Chem., Int. Ed.* **2010**, *49*, 8306-8308; (e) Tan, C. K.; Zhou, L.; Yeung, Y.-Y. *Synlett* **2011**, 1335-1339; (f) Filippova, L.; Stenstrøm, Y.; Hansen, T. V. *Tetrahedron Lett.* **2014**, *55*, 419-422; (g) Arai, T.; Kojima, T.; Watanbe, O.; Itoh, T.; Kanoh, H. *ChemCatChem.* **2015**, *7*, 3234-3428; (h) Denmark, S. E.; Kuester, W. E.; Burk, M. T. *Angew. Chem., Int. Ed.* **2012**, *51*, 10938-10953; (i) Dobish, M. C.; Johnston, J. N. *J. Am. Chem. Soc.* **2012**, *134*, 6068-6071.
3. Examples of asymmetric haloaminocyclizations: (a) Bovino, M. T.; Chemler, S. R. *Angew. Chem., Int. Ed.* **2012**, *51*, 3923-3927; (b) Chen, J.; Zhou, L.; Yeung, Y.-Y. *Org. Biomol. Chem.* **2012**, *10*, 3808-3811; (c) Chen, F.; Tan C. K.; Yeung, Y.-Y. *J. Am. Chem. Soc.* **2013**, *135*, 1232-1235; (d) Alix, A.; Lalli, C.; Retailleau P.; Masson, G. R. *J. Am. Chem. Soc.* **2012**, *134*, 10389-10392; (e) Zhou, L.; Tay, D. W.; Chen, J.; Leung, G. Y. C.; Yeung, Y.-Y. *Chem. Commun.* **2013**, *49*, 4412-4414.
4. Examples of asymmetric cycloetherifications: (a) Tan, C. K.; Yu, W. Z.; Yeung, Y. *Chirality* **2014**, *26*, 328-343; (b) Zeng, X.; Miao, C.; Wang, S.; Xia, C.; Sun, W. *Chem. Commun.* **2013**, *49*, 2418-2420; (c) Hennecke, U.; Müller, C. H.; Fröhlich, R. *Org. Lett.* **2011**, *13*, 860-863; (d) Denmark, S. E.; Burk, M. T. *Org. Lett.* **2012**, *14*, 256-259; (e) Huang, D.; Wang, H.; Xue, F.; Guan, H.; Li, L.; Peng, X.; Shi, Y. *Org. Lett.* **2011**, *13*, 6350-6353.
5. (a) Zhang, W.; Zheng, S.; Liu, N.; Werness, J. B.; Guzei I. A.; Tang, W. *J. Am. Chem. Soc.* **2010**, *132*, 3664-3665; (b) Wilking, M.; Mueck-Lichtenfeld, C.; Daniliuc, C. G.; Hennecke, U. *J. Am. Chem. Soc.* **2013**, *135*, 8133-8136; (c) Rauniyar, V.; Lackner, A. D.; Hamilton, G. L.; Toste, F. D. *Science* **2011**, *334*, 1681-1684.
6. (a) Zhang, W.; Zheng, S.; Liu, N.; Werness, J. B.; Guzei, I. A.; Tang, W. *J. Am. Chem. Soc.* **2010**, *132*, 3664-3665; (b) Zhang, W.; Hu, X.; Xu, H.; Tang, W. *J. Am. Chem. Soc.* **2009**, *131*, 3832-3833.
7. (a) Jiang, X.; Fu, C.; Ma, S. *Chem. Eur. J.* **2008**, *14*, 9656-9664; (b) Lü, B. ; Jiang, X.; Fu, C.; Ma, S. *J. Org. Chem.* **2009**, *74*, 438-441; (c) Zhang, X.; Fu, C.; Yu, Y.; Ma, S. *Chem. Eur. J.* **2012**, *18*, 13501-13509.
8. Miles, D. H.; Marcos, V.; Toste, F. D. *Chem. Sci.* **2013**, *4*, 3427-3431.
9. Wilking, M.; Daniliuc, C. G.; Hennecke, U. *Synlett* **2014**, *25*, 1701-1704.
10. Murai, K.; Shimizu, N.; Fujioka, H. *Chem. Commun.* **2014**, *50*, 12530-12533.
11. Tungen, J. E.; Nolsøe, J. M. J.; Hansen, T. V. *Org. Lett.* **2012**, *14*, 5884-5887.
12. Aursnes, M.; Tungen, J. E.; Hansen, T. V. *J. Org. Chem.* **2016**, *81*,8287–8295 .
13. (a) Han, X.; Zhou, H.-B.; Dong, C. *Chem. Rec.* **2016**, *16*, 897-906; (b) Storer, R. I.; Aciro, C.; Jones, L. H. *Chem. Soc. Rev.* **2011**, *40*, 2330-2346;
14. (a) Primdahl, K. G.; Stenstrøm, Y.; Hansen, T. V.; Vik, A. *Chem. Phys. Lipids* **2016**, *196*, 1-4; (b) Filippova, L.; Aarum, I.; Ringdal, M.; Dahl, M. K.; Hansen, T. V.; Stenstrøm, Y. *Org. Biomol. Chem.* **2015**, *13*, 4680-4685; (c) Jacobsen, M. G.; Vik, A.; Hansen, T. V. *Tetrahedron Lett.* **2014**, *55*, 2842-2844; (d) Jacobsen, M. G.; Vik, A.; Hansen T. V. *Tetrahedron Lett*. **2012**, *53*, 5837-5839; (e) Vik, A.; Hansen, T. V. *Tetrahedron Lett.* **2011**, *52,* 1060-1062; (f) Vik, A.; Hansen, T. V.; Holmeide, A. K.; Skattebøl, L. *Tetrahedron Lett.* **2010**, *51,* 2852-2854; (g) Hansen, T. V.; Skattebøl. L. *Tetrahedron Lett.* **2004**, *45*, 2809-2811.
15. Gilmore, K.; Alabugin, I. V. *Chem. Rev.* **2011**, *111*, 6513-6556.
16. Conversion was determined to be < 60% by ^{1}H NMR-analyses; full conversion was observed for **9b**.
17. (a) Chung, W.; Vanderwal, C. D. *Angew. Chem., Int. Ed.* **2016**, *55*, 4396-4434; (b) Martin, T.; Padron, J. I.; Martin, V. S. *Synlett* **2013**, 12-32.

Copies of ^{1}H and ^{13}C NMR spectra and of chromatograms of HPLC analyses, as well as experimental procedures, are available at **[to be inserted by editorial office]**.

Highlights:

A highly regioselective synthesis of vinylic iodolactones is reported.

A robust, practical and operationally simple protocol for the preparation of chiral squaramide catalysts is demonstrated.

The reported organocatalyzed protocol renders the use of metals or special pre-cautions unnecessary.

The chiral catalysts investigated returned enantiomeric excess of up to 76%.

Useful vinylic iodolactones were obtained as products.