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Ring-Opening/Expansion Rearrangement of Cycloprop[2,3]inden-1-ols Catalyzed by *p*-Toluenesulfonic Acid

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Abstract: A divergent approach to generate either 1-hydroxymethylindenes (which could then be converted to benzofulvenes through a dehydration reaction) or naphthalenes by the rearrangement of cycloprop[2,3]inden-1-ols is reported. The effect of the cyclopropyl ring substitution pattern on ring-opening/expansion rearrangements of the substrates was systemically studied.

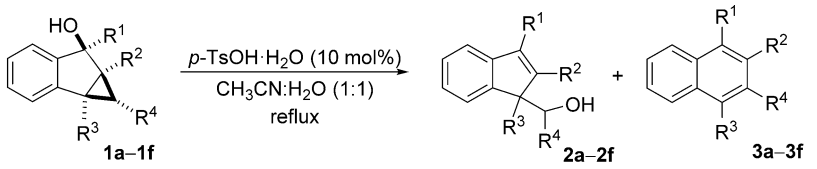
Keywords: benzofulvenes; naphthalenes; rearrangement; ring-expansion; ring-opening

Investigation of methods to synthesize benzofulvenes or isomeric naphthalenes is currently an active area of research owing to the special properties displayed by compounds with these aromatic core structures in the fields of materials science, organometallics, and medicinal chemistry.[1,2] Substantial effort has been devoted to the construction of these two motifs by means of cyclization and annulation reactions, as well as transition metal-mediated coupling reactions.[3,4] Although constructing benzofulvenes or naphthalenes *via* rearrangement of strained rings is an unconventional strategy, it has been shown to be a valid and sometimes more efficient alternative to standard methods for preparing these target molecules.[5] For example, Huang and Yang reported that the reaction of alkylidenecyclopropanes with acyl chlorides in the presence of aluminum chloride affords benzofulvene derivatives in good to excellent yields.[5c] Liu et al. used a novel $Eu(OTf)_3$-catalyzed ring-expansion rearrangement of trimethylsilyl-substituted cycloprop-[2,3]inden-1-ol to synthesize substituted naphthalenes.[5h,j] Shi et al. reported a Lewis acid-catalyzed rearrangement of vinylcyclopropenes to produce either naphthalene or indene skeletons, depending on the choice of the Lewis acid.[5i] The importance of the benzofulvene and naphthalene skeletons and the dearth of syntheses of these structures *via* rearrangements of strained rings make additional research in this area desirable.

According to reports from the Răzuş group and the Friedrich group, treatment of substituted *endo*-cycloprop[2,3]inden-1-ols or their 3,5-dinitrobenzoate esters in buffered or acidic organic-aqueous solutions results in the epimerization of the hydroxy groups or hydrolysis of the esters.[6] Although the primary interest of these researchers was to investigate the possible antihomoaromaticity of the cycloprop[2,3]inden-1-yl cation, they observed the formation of small amounts of naphthalenes. Inspired by these pioneering studies and owing to our interest in ring-opening rearrangements of cyclopropyl carbinols,[7] in this study, we synthesized a series of substituted cycloprop[2,3]inden-1-ols and investigated their rearrangements. We found that the rearrangements of cycloprop[2,3]inden-1-ols catalyzed by $TsOH{\cdot}H_2O$ led to 1-hydroxymethylindenes (which could then be converted to benzofulvenes through a dehydration reaction) or naphthalenes depending on the substituent at the C-3 position of the substrate.

endo-Cycloprop[2,3]inden-1-ols were prepared by reduction of indenone, Simmons–Smith cyclopropanation, oxidation of the hydroxy group, and addition of a nucleophile to the resulting ketone.[8] In previous studies, we showed that under refluxing conditions, water can act as a mildly acidic catalyst to promote organic reactions traditionally catalyzed by Brønsted or Lewis acids.[7,9] We found that treatment of cycloprop[2,3]inden-1-ol **1a** in refluxing water led to epimerization of the C-1 carbon, a result that was in agreement with previous experimental results.[6b] However, when **1a** was refluxed in 1:1 (v/v) CH_3CN/H_2O containing a catalytic amount of $TsOH{\cdot}H_2O$, 1-hydroxymethylindene **2a** was formed by attack of a water molecule at C-10 (Table 1, entry 1).[10] Substrate **1b**, in which the substituent at C-2 (the R^2

Table 1. Substituent effects on the reactions of *endo*-cycloprop[2,3]inden-1-ols.[a]

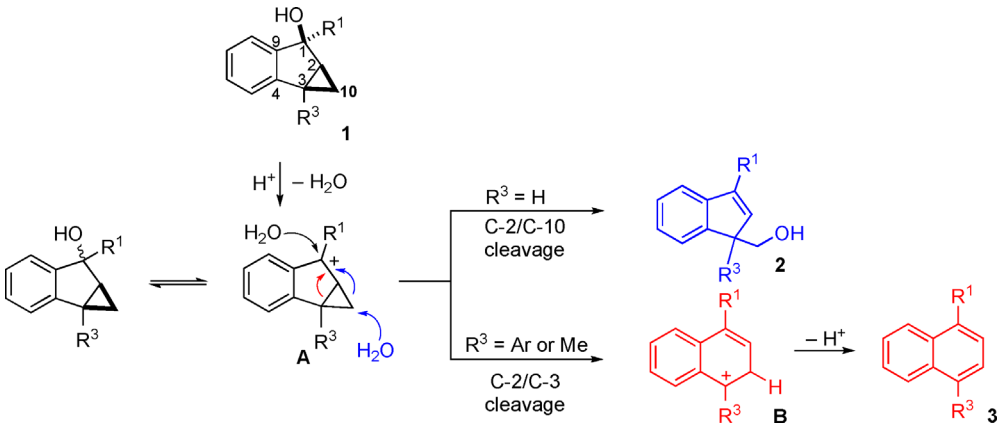


Entry	Substrate	R^1	R^2	R^3	R^4	Time [h]	**2** [%]	**3** [%]
1	**1a**	Ph	H	H	H	2	94	0
2	**1b**	Ph	Me	H	H	1	94	0
3	**1c**	Ph	H	Me	H	2	4	70
4	**1d**	Ph	H	Ph	H	1	0	96
5	**1e**	H	H	Ph	H	6	0	81
6	**1f**	Ph	H	H	Me	0.5	91	0

[a] *Reaction conditions:* substrates (0.5 mmol) were treated with TsOH·H_2O (10 mol%) in 1:1 (v/v) CH_3CN/H_2O at refluxing temperature. Isolated yields are given.

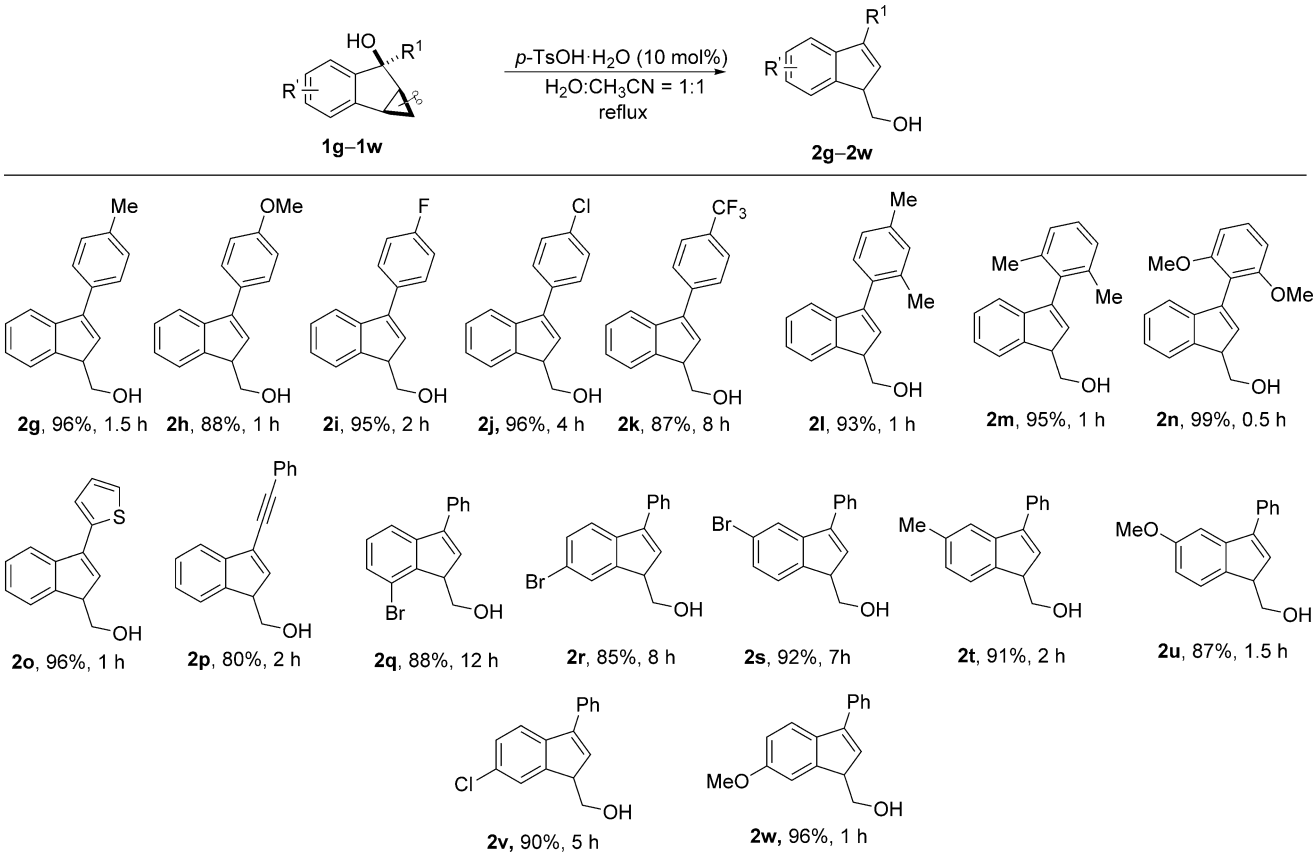
group) was changed from a hydrogen atom to a methyl group, reacted similarly but required a shorter reaction time (entry 2). When the substituent at C-3 (the R^3 group) was changed from a hydrogen atom to a methyl group, selectivity for naphthalene formation was observed; substituted naphthalene **3c** was obtained in 70% yield, along with only 4% of 1-hydroxymethylindene product **2c** (entry 3). Changing R^3 of **1c** from a methyl group to a phenyl group resulted in exclusive formation of the corresponding substituted naphthalene (**3d**, entry 4). Substrate **1e** (R^3 = Ph, R^1 = H) afforded naphthalene **3e**, but the reaction took longer than the reaction of **1d** (entry 5). Substrate **1f**, in which R^4 of **1a** was changed from a hydrogen atom to a methyl group, gave 1-hydroxymethylindenes **2f** (entry 6) and the rearrangement reaction was faster than the reaction of **1a**.

Experimental results obtained in our lab and reported in the literature show that under neutral or mildly acidic conditions, C-1 of cycloprop[2,3]inden-1-yl cation **A** undergoes a hydrolytic reaction that results in the formation of the *exo*-cycloprop[2,3]inden-1-ol products (Scheme 1).[6b] Olah and co-workers studied charge delocalization in cycloprop[2,3]inden-1-yl cation **A** by means of ^{13}C NMR[11] and found that there was more charge delocalization at C-10 and less at C-3 of the cyclopropyl ring caused by the antihomoaromatic effect.[6a] These results explain the nucleophilic attack of water at C-10 and cleavage of the C-2/C-10 bond, as well as the fact that the reactions of **1b** and **1f** were faster than the reaction of **1a** when C-2 or C-10 was substituted with a methyl group. However, when R^3 was an alkyl or aryl group, cyclopropyl ring expansion *via* cleavage of the C-2/C-3 bond,



Scheme 1. Mechanism for the formation of 1-hydroxymethylindene and naphthalene products.

Table 2. Synthesis of 1-hydroxymethylindenes *via* ring-opening rearrangements of *endo*-cycloprop[2,3]inden-1-ols **1**.[a]



[a] Substrates (0.5 mmol) were treated with TsOH·H_2O (10 mol%) in 1:1 (v/v) CH_3CN/H_2O (10 mL) at refluxing temperature. Isolated yields are given.

which transforms cation **A** to benzylic and tertiary cation **B**, becomes more favorable. Deprotonation of cation **B** provides naphthalene products **3**.

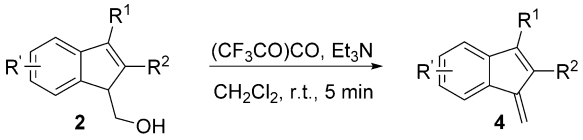
We investigated the generality of this ring-opening rearrangement by varying the substituent at C-1 (Table 2). Aryl-substituted substrates **1g**–**1o**, which have electron-donating or electron-withdrawing groups at various positions on the aromatic ring, showed good reactivities and afforded 1-hydroxymethylindenes **2g**–**2o** in good to excellent yields. In addition, the reaction of propargylic alcohol **1p** afforded ring-opening product **2p** in 80% yield. 1-Hydroxymethylindenes **2q**–**2w**, which have substituents at various positions on the aromatic ring of the indene moiety, were also obtained in high yields.

The 1-hydroxymethylindenes could be readily transformed into benzofulvenes by treatment with trifluoroacetic anhydride and triethylamine in dichloromethane (Table 3).

We found that ring-expansion rearrangements of C-3 substituted cycloprop[2,3]inden-1-ols **5** afforded aryl-substituted naphthalenes **6** in higher yields in toluene than in CH_3CN/H_2O solution (Table 4, entries 1 and 2). Using this method, we could also obtain 1,3- and 1,4-asymmetrically substituted biarylnaphthalenes (entries 3–8), which are challenging to synthesize *via* coupling-based strategies.[4b,c,j,k]

In summary, we have elucidated the effects of substituents on the cyclopropane ring in the *p*-toluenesul-

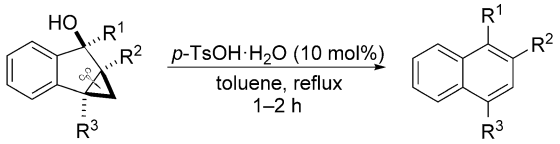
Table 3. Transformation of 1-hydroxymethylindenes to benzofulvenes.[a]



Entry	Substrate	Product	Yield [%]
1	**2a**	**4a**	92
2	**2b**	**4b**	85
3	**2k**	**4k**	97
4	**2m**	**4m**	92
5	**2s**	**4s**	91
6	**2u**	**4u**	87

[a] Substrates (0.5 mmol) were treated with $(CF_3CO)_2O$ (1.2 equiv.) and Et_3N (3.0 equiv.) in CH_2Cl_2 (5 mL). Isolated yields are given.

Table 4. Synthesis of substituted naphthalenes *via* ring-expansion rearrangements of cycloprop[2,3]inden-1-ols.[a]



5a–5h 6a–6h

Entry	Substrate	$R^1/R^2/R^3$	Yield of **6** [%]
1	**5a**	H/H/4-OMeC_6H_4	97
2	**5b**	H/H/4-ClC_6H_4	99
3	**5c**	H/Ph/Ph	98
4	**5d**	H/*t*-Bu/Ph	95
5	**5e**	4-MeC_6H_4/H/Ph	92
6	**5f**	4-$CF_3C_6H_4$/H/Ph	92
7	**5g**	C_4H_3S/H/Ph	91
8	**5h**	4-MeC_6H_4/H/4-ClC_6H_4	98

[a] Substrates (0.5 mmol) were treated with TsOH·H_2O (10 mol%) in refluxing toluene (5 mL). Isolated yields are given.

fonic acid-catalyzed ring-opening or ring-expansion rearrangements of cycloprop[2,3]inden-1-ols, which provided an efficient alternative method for preparation of various substituted benzofulvenes and naphthalenes.

Experimental Section

General Procedure for the Ring-Opening/Expansion Rearrangements of *endo*-Cycloprop[2,3]inden-1-ol 1 or 5

To a round-bottom flask (25 mL) containing cycloprop[2,3]inden-1-ol **1** (0.5 mmol, 1.0 equiv.) was added CH_3CN/H_2O (v/v = 1:1, 10 mL) (or 5 mL of toluene for **5**), and then to the solution was added *p*-TsOH·H_2O (10 mol%). The flask was fitted with a condenser, stirred at the indicated temperature, and monitored by TLC. Upon consumption of the starting material, the resulting solution was cooled to room temperature and then a saturated aqueous solution of $NaHCO_3$ was added to the mixture which was then extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, then concentrated under vacuum to give the crude product, which was purified by flash column chromatography (elution: PE:EA = 3:1 for **2** or PE for **6**) to afford the desired product **2** or **6**.

General Procedure for the Transformation of 1-Hydroxymethylindenes 2 to Benzofulvenes 4

To a round-bottom flask (10 mL) containing alcohol **2** (0.5 mmol, 1.0 equiv.) was added CH_2Cl_2 (5.0 mL), and then to the solution was added trifluoroacetic anhydride (0.6 mmol, 1.2 equiv.) and Et_3N (1.5 mmol, 3.0 equiv.) at room temperature. The reaction was stirred at room temperature and monitored by TLC. Upon consumption of the starting material, the resulting solution was diluted with CH_2Cl_2. The mixture was washed with water, and then the aqueous layer was extracted with CH_2Cl_2. The organic layer was washed with brine, dried over $MgSO_4$, then concentrated under vacuum to give the crude product, which was purified by flash column chromatography (elution: PE) to afford the desired product **4**.

Acknowledgements

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References

[1] For syntheses of benzofulvenes, see: a) T. M. Londergan, C. J. Teng, W. P. Weber, *Macromolecules* **1999**, *32*, 1111; b) T. Nakano, K. Takewaki, T. Yade, Y. Okamoto, *J. Am. Chem. Soc.* **2001**, *123*, 9182; c) T. Nakano, T. Yade, *J. Am. Chem. Soc.* **2003**, *125*, 15474; d) A. S. Felts, B. S. Siegel, S. M. Young, C. W. Moth, T. P. Lybrand, A. J. Dannenberg, L. J. Marnett, K. Subbaramaiah, *J. Med. Chem.* **2008**, *51*, 4911; e) M. J. Walters, A. L. Blobaum, P. J. Kingsley, A. S. Felts, G. A. Sulikowski, L. J. Marnett, *Bioorg. Med. Chem. Lett.* **2009**, *19*, 3271; f) Y. Kosaka, K. Kitazawa, S. Inomata, T. Ishizone, *ACS Macro Lett.* **2013**, *2*, 164; g) C. Martinelli, A. Cardone, V. Pinto, M. M. Talamo, M. L. D′arienzo, E. Mesto, E. Schingaro, F. Scordari, F. Naso, R. Musio, G. M. Farinola, *Org. Lett.* **2014**, *16*, 3424.

[2] For syntheses of naphthalenes, see: a) C. B. de Koning, A. L. Rousseau, W. A. L. van Otterlo, *Tetrahedron* **2003**, *59*, 7; b) Y. Chen, S. Yekta, A. K. Yudin, *Chem. Rev.* **2003**, *103*, 3155; c) M. Berthod, G. Mignani, G. Woodward, M. Lemaire, *Chem. Rev.* **2005**, *105*, 1801; d) J. M. Brunel, *Chem. Rev.* **2005**, *105*, 857; e) D. Parmar, E. Sugiono, S. Raja, M. Rueping, *Chem. Rev.* **2014**, *114*, 9047; f) W. Jiang, Y. Li, Z.-H. Wang, *Acc. Chem. Res.* **2014**, *47*, 3135; g) S.-L. Suraru, F. Würthner, *Angew. Chem. Int. Ed.* **2014**, *53*, 7428.

[3] For representative publications on the construction of benzofulvenes. see: a) P. R. Schreiner, M. Prall, V. Lutz, *Angew. Chem.* **2003**, *115*, 5935; *Angew. Chem. Int. Ed.* **2003**, *42*, 5757; b) S. V. Kovalenko, S. Peabody, M. Manoharan, R. J. Clark, I. V. Alabugin, *Org. Lett.* **2004**, *6*, 2457; c) S. W. Peabody, B. Breiner, S. V. Kovalenko, S. Patil, I. V. Alabugin, *Org. Biomol. Chem.* **2005**, *3*, 218; d) S. Ye, K. Gao, H. Zhou, X. Yang, J. Wu, *Chem. Commun.* **2009**, 5406; e) P. Cordier, C. Aubert, M. Malacria, E. Lacôte, V. Gandon, *Angew. Chem.* **2009**, *121*, 8913; *Angew. Chem. Int. Ed.* **2009**, *48*, 8757; f) F. W. Patureau, T. Besset, N. Kuhl, K. Glorius, *J. Am. Chem. Soc.* **2011**, *133*, 2154; g) C. M. Sousa, J. Berthet, S. Delbaere, P. J. Coelho, *J. Org. Chem.* **2014**, *79*, 5781; h) S. Muthusamy, M. Sivaguru, *Org. Lett.* **2014**, ***16***, 4248; i) B. Guo, L. Zheng, L. Zhang, R. Hua, *J. Org. Chem.* **2015**, *80*, 8430.

[4] For representative publications on the construction of substituted naphthalenes: a) E. Yoshikawa, K. V. Radhakrishnan, Y. Yamamoto, *J. Am. Chem. Soc.* **2000**, *122*, 7280; b) N. Asao, K. Takahashi, S. Lee, T. Kasahara, Y. Yamamoto, *J. Am. Chem. Soc.* **2002**, *124*, 12650; c) G. S. Viswanathan, M. Wang, C.-J. Li, *Angew. Chem.* **2002**, *114*, 2242; *Angew. Chem. Int. Ed.* **2002**, *41*, 2138; d) Q. Huang, R. C. Larock, *J. Org. Chem.* **2003**, *68*, 7342; e) D. Yue, N. Della Cá, R. C. Larock, *J. Org. Chem.* **2006**, *71*, 3381; f) A. S. Paraskar, A. R. Reddy, A. Patra, Y. H. Wijsboom, O. Gidron, L. J. W. Shimon, G. Leitus, M. Bendikov, *Chem. Eur. J.* **2008**, *14*, 10639; g) S. Akai, T. Ikawa, S. Takayanagi, Y. Morikawa, S. Mohri, M. Tsubakiyama, M. Egi, Y. Wada, Y. Kita, *Angew. Chem.* **2008**, *120*, 7787; *Angew. Chem. Int. Ed.* **2008**, *47*, 7673; h) A. A. Cant, L. Roberts, M. F. Greaney, *Chem. Commun.* **2010**, *46*, 8671; i) C. Feng, T.-P. Loh, *J. Am. Chem. Soc.* **2010**, *132*, 17710; j) S. J. Ryan, L. Candish, D. W. Lupton, *J. Am. Chem. Soc.* **2011**, *133*, 4694; k) D. J. Kang, J. Kim, S. Oh, P. H. Lee, *Org. Lett.* **2012**, *14*, 5636; l) P. Gandeepan, C.-H. Cheng, *Org. Lett.* **2013**, *15*, 2084; m) S.-Y. Wang, Z. Chai, Y. Wei, X.-C. Zhu, S.-L. Zhou, S.-W. Wang, *Org. Lett.* **2014**, *16*, 3592; n) Y.-X. Liu, J. Guo, Y. Liu, X.-Y. Wang, Y.-S. Wang, X.-Y. Jia, G.-F. Wei, L.-Z. Chen, J.-Y. Xiao, M.-S. Cheng, *Chem. Commun.* **2014**, *50*, 6243; o) G. Naresh, R. Kant, T. Narender, *Org. Lett.* **2015**, *17*, 3446.

[5] a) M. Shi, L.-X. Shao, J.-M. Lu, Y. Wei, K. Mizuno, H. Maeda, *Chem. Rev.* **2010**, *110*, 5883; b) M. Shi, J.-M. Lu, Y. Wei, L.-X. Shao, *Acc. Chem. Res.* **2012**, *45*, 641; c) X. Huang, Y.-W. Yang, *Org. Lett.* **2007**, *9*, 1667; d) J.-M. Lu, Z.-B. Zhu, M Shi, *Chem. Eur. J.* **2009**, *15*, 963; e) Y. Nishii, T. Yoshida, H. Asano, K. Wakasugi, J. Morita, Y. Aso, E. Yoshida, J. Motoyoshiya, H. Aoyama, Y. Tanabe, *J. Org. Chem.* **2005**, *70*, 2667; f) T. Hamura, T. Suzuki, T. Matsumoto, K. Suzuki, *Angew. Chem.* **2006**, *118*, 6442; *Angew. Chem. Int. Ed.* **2006**, *45*, 6294; g) L.-X. Shao, Y.-P. Zhang, M.-H. Qi, M. Shi, *Org. Lett.* **2007**, *9*, 117; h) A. C. Glass, B. B. Morris, L. N. Zakharov, S.-Y. Liu, *Org. Lett.* **2008**, *10*, 4855; i) Z.-B. Zhu, Y. Wei, M. Shi, *Chem. Eur. J.* **2009**, *15*, 7543; j) A. C. Glass, S. Klonoski, L. N. Zakharov, S.-Y. Liu, *Chem. Commun.* **2011**, *47*, 286; k) J. Aponte-Guzmán, J. E. Taylor, Jr., E. Tillman, S. France, *Org. Lett.* **2014**, *16*, 3788.

[6] a) E. C. Friedrich, D. B. Taggart, M. A. Saleh, *J. Org. Chem.* **1977**, *42*, 1437; b) A. C. Răzuş, V. Wertheimer, A. M. Glatz, Z. S. Away, F. Badea, *Rev. Roum. Chim.* **1981**, *26*, 457.

[7] P.-F. Li, C.-B. Yi, J. Qu, *Org. Biomol. Chem.* **2015**, *13*, 5012.

[8] All starting materials were prepared according to previously reported procedures.

[9] a) F.-Z. Zhang, Y. Tian, G.-X. Li, J. Qu, *J. Org. Chem.* **2015**, *80*, 1107; b) P.-F. Li, H.-L. Wang, J. Qu, *J. Org. Chem.* **2014**, *79*, 3955.

[10] A survey of other Brønsted acids, Lewis acids, and solvents revealed that the optimal reaction conditions were as follows: 10 mol% $TsOH{\cdot}H_2O$ in 1:1 (v/v) CH_3CN/H_2O. See the Supporting Information for details.

[11] G. A. Olah, G. Liang, S. P. Jindal, *J. Org. Chem.* **1975**, *40*, 3259.