Nitrosoarenes

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An Efficient Approach to Chiral Allyloxyamines by Stereospecific Allylation of Nitrosoarenes with Chiral Allylboronates**

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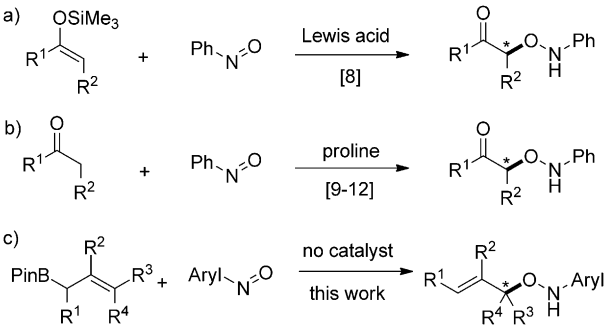
Abstract: *A novel and efficient approach to allyloxyamines by the allylation of nitrosoarenes with α-chiral allylboronates is described. C–O bond formation occurs with high stereospecificity and the product allyloxyamines are easily transformed into valuable chiral building blocks such as isoxazolidines and allylic alcohols. The reaction features complete regioselectivity (O-selectivity), high E/Z selectivity, and excellent chirality transfer.*

Nitrosobenzene was first prepared by Baeyer at the end of the 19th century.[1] Since then, nitrosoarenes and other nitroso derivatives have become highly useful building blocks in organic synthesis.[2] Nitroso compounds are reactive substrates which undergo various valuable reactions such as [3,3] sigmatropic rearrangements,[3] ene reactions,[4] cycloaddition reactions,[2d,5] and aldol-type reactions.[6] In recent years, a growing number of reports have presented nitrosobenzene as a versatile electrophile in catalytic enantioselective aldol-type reactions. Nitrosoarenes can either react at the oxygen or at the nitrogen atom depending on the activation mode, but commonly products derived from *N*-attack are obtained.[7] Momiyama and Yamamoto first reported *O*-selective nucleophilic attack of silyl enol ethers to nitrosobenzene with Lewis acids as catalysts (Scheme 1a).[8] Along these lines, the research groups of MacMillan,[9] Zhong,[10] Hayashi,[11] and Yamamoto[12] independently disclosed the enantioselective *O*-nitroso aldol reactions of various aldehydes with nitrosobenzene by using proline as a catalyst (Scheme 1b). Although much progress has been made on stereo- and *O*-regioselective reactions with nitrosoarenes as electrophiles, transformations are restricted to nitroso aldol reactions.

As a continuation of our studies on the exploration of the reactivity of nitrosoarenes towards allylic nucleophiles[13] we investigated the stereoselective *O*-allylboration of nitrosoarenes to give allyloxyamines (Scheme 1c). These products should be valuable building blocks for organic synthesis. To date only two reports on this type of reaction have appeared.[14] Whereas triallylborane reacts at N and O unselectively,[14a] the corresponding allylation with allylboronates was reported to give allylic alcohols derived from *O*-allylation and subsequent N–O bond cleavage as major products.[14b] In both cases stereoselective nitrosoarene allylations using α-chiral allyl boron compounds were not addressed. The following questions have to be answered: a) Can the reaction be controlled to provide products of *O*-allylation regioselectively while keeping the N–O bond intact, b) does the reaction occur stereospecifically, and c) can the geometry of the newly formed double bond (*E*/*Z*) be controlled?



Scheme 1. Stereoselective *O*-nitroso aldol reaction and *O*-nitroso allylboration.

The direct allylation of aldehydes and imines has evolved into a highly efficient method for the enantioselective formation of a C–C bond.[15] Of the allyl metal species, allyl boronates have found particular attention.[16] Encouraged by the many successful examples on the use of α-chiral allylboronates in stereospecific allylations,[17] we studied the reaction of readily prepared racemic **2a** with nitrosopyridine **1a** to afford allyloxyamine **3a** (Table 1).

The reaction was conducted by using a slight excess of **2a** (1.2 equiv) in THF at room temperature for 2 h, and **3a** was obtained in 35% yield (entry 1). Azoxy compound **4a** and 2-methyl-3-nonen-5-ol derived from the reaction of nitrosopyridine **1a** with **3a** were formed in this and all following transformations as side products.[14b] **4a** was the major product in the presence of NaOH (entry 2). The addition of acetic acid or H_2O led to an improvement of the yield (entries 3 and 4). The yield was further improved upon switching to alcohols as the solvents, with MeOH affording the best result (63%, entries 5–7). This is likely due to in situ hydrolysis of the allylboration product to **3a** in alcoholic solvents. **3a** reacts slower than the intermediate allylborate with **1a** to afford **4a**.[18] The addition of 1 equiv of H_2O afforded the same result (entry 8). Other aprotic solvents such as CH_2Cl_2, toluene, or CH_3CN provided worse results (entries 9–11). The formation

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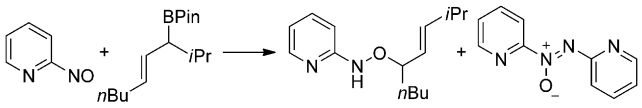
Table 1: Reaction of **1a** with **2a** under different conditions.[a]

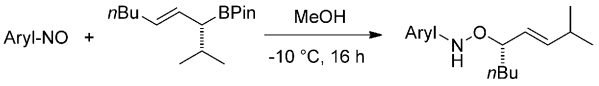


1a **2a** **3a** **4a**

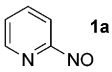
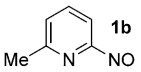
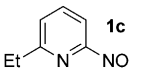
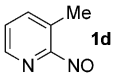
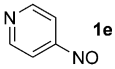
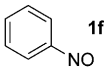
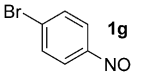
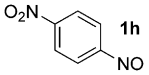
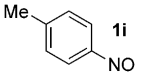
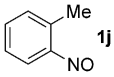
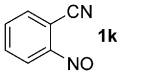
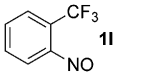
Entry	Solvent	Additive (1 equiv)	**3a** yield [%][b]	**4a** yield [%][b]
1	THF	–	35	22[c]
2	THF	NaOH	<5	34
3	THF	AcOH	45	17
4	THF	H_2O	45	20
5	*n*PrOH	–	58	15
6	MeOH	–	63	16[d]
7	*i*PrOH	–	51	16
8	MeOH	H_2O	57	21
9	CH_2Cl_2	–	48	15
10	toluene	–	21	21
11	CH_3CN	–	27	24
12[e]	MeOH	–	75	12
13[f]	**MeOH**	**–**	**86**[g]	**6**
14	MeOH	–	<5	82[h]

[a] Reaction conditions: **1a** (0.2 mmol) and **2a** (0.24 mmol) in the given solvent (3.0 mL) at room temperature for 2 h. [b] Yield determined by ^{1}H NMR spectroscopy. [c] 2-Methyl-3-nonen-5-ol formed in 18% yield. [d] 2-Methyl-3-nonen-5-ol formed in 10% yield. [e] Reaction conducted at 0°C for 6 h. [f] Reaction conducted at −10°C for 16 h. [g] Yield of isolated product, $E/Z = >20:1$. [h] Run with **1a** (0.4 mmol) and **2a** (0.2 mmol). 2-Methyl-3-nonen-5-ol isolated in 30% yield.

Table 2: Stereospecificity and variation of the nitrosoarene.[a]



1a-l **2a** (94% *ee*) **3a-l**

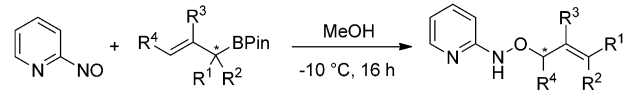
Entry	Aryl-NO	Product	E/Z[b]	Yield [%][c]	*ee* [%][d]
1		**3a**	>20:1	82	93
2		**3b**	>20:1	60	92
3		**3c**	>20:1	73	93
4		**3d**	–	n.d.	–
5		**3e**	>20:1	71	92
6		**3f**	6:1	74	93
7		**3g**	10:1	46	93
8		**3h**	>20:1	55	90
9		**3i**	3:1	51	90
10		**3j**	–	n.d.	–
11		**3k**	17:1	26	91
12		**3l**	–	n.d.	–

[a] Reaction conditions: **1** (0.2 mmol) and **2** (0.24 mmol) in MeOH (3.0 mL) at −10°C for 16 h. [b] Ratio determined by ^{1}H NMR analysis of the isolated products. [c] Yield of isolated product ($E+Z$). [d] *ee* value of **2a** and products determined by HPLC or GC analysis (see the Supporting Information). n.d. = not detected.

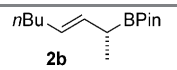
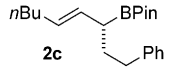
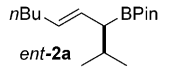
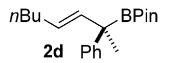
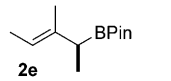
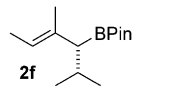
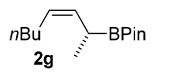
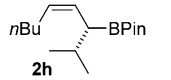
of **4a** was largely suppressed at lower temperatures (entries 12 and 13). The yield of isolated **3a** was 86% when the reaction was carried out at −10°C for 16 h (entry 13). The use of 2 equiv **1a** with respect to **2a** led to **4a** being obtained in 82% yield, with no **3a** identified in the crude reaction mixture (entry 14).

We tested the stereospecificity of the allylboration of **1** with **2a** and also studied the effect of the aryl substituent of the nitrososoarene on the reaction outcome under the optimized reaction conditions (Table 2). Enantioenriched **2a** was prepared according to a literature procedure.[17e] Pleasingly, the reaction of (*R*)-**2a** provided (*S*)-**3a** with excellent stereospecificity (entry 1).[19] Excellent chirality transfer was also obtained with the 6-alkyl-substituted nitrosopyridines **1b** and **1c**, although the yield was slightly decreased (**3b**, **3c**, entries 2 and 3). Installing a methyl group at the *ortho*-position of the nitroso functionality (see **1d**) fully suppressed the allylboration, likely for steric reasons (entry 4). Moving the N atom of the pyridine ring to the *para* position (see **1e**) gave **3e** in good yield (71%) and excellent stereoselectivity (entry 5). Nitrosobenzene **1f** provided **3f** in good yield, excellent enantiospecificity, but significantly lower E/Z selectivity (entry 6), thus indicating the importance of the pyridine N atom in the nitroso component. High E/Z selectivity was restored upon introducing an electron-withdrawing *para* substituent. The *p*-bromo and *p*-nitro congeners **1g** and **1h** reacted with high stereoselectivity but moderate yield (entries 7 and 8). It seems that the E/Z selectivity is influenced by the electronics of the nitrosoarene. Indeed, *p*-methylnitrosobenzene **1i** provided **3i** with low E/Z selectivity (entry 9). *o*-Methylnitrosobenzene **1j** and the *o*-trifluoromethyl derivative **1l** did not react with **2a**, likely for steric reasons (entries 10 and 12). With a cyano group as an *ortho*-substituent, **3k** was obtained in a low yield (entry 11). Based on these studies we conclude that electron-poor nitrosoarenes react with excellent stereoselectivity and substituents *ortho* to the nitroso functionality lower the reactivity. We do not currently understand why electron-richer nitrosoarenes react with low E/Z selectivity. Kinetic experiments revealed that *p*-nitronitrosobenzene reacts faster than nitrosobenzene, which shows that the Lewis basicity of the N atom in the nitrosoarene is less important for the allylboration than the electrophilicity of the N=O moiety (see the Supporting Information). The best result in terms of reactivity and selectivity was obtained with 2-nitrosopyridine.

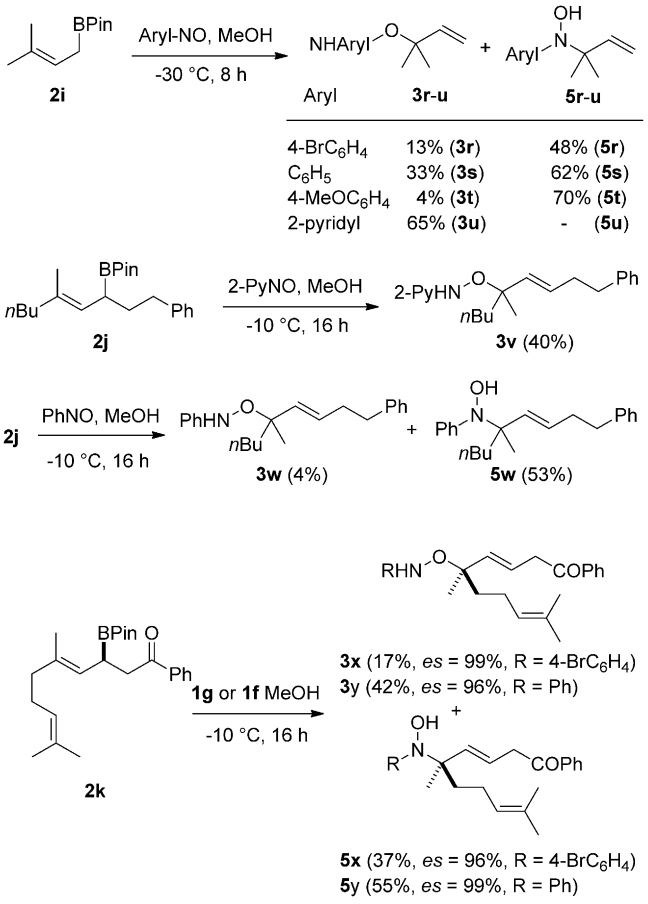
Table 3: Reaction of **1a** with various α-chiral allyl boronates.[a]



1a **2a-h** **3a,m-q**

	Allyl boronate	*ee* [%]	Product	*E*/*Z*[b]	Yield [%][c]	*ee* [%]
1	 **2b**	91	**3m**	1.6:1	95	90(*S*,*E*)[d]
2	 **2c**	94	**3n**	4:1	95	94(*S*,*E*)
3	 *ent*-**2a**	88	*ent*-**3a**	>20:1	76	88(*R*)
4	 **2d**	97	**3o**	20:1	42	95(*R*)
5	 **2e**	87	**3p**	2:1	64	87(*S*,*Z*) 87(*R*,*E*)
6	 **2f**	93	**3q**	9:1	14	93(*R*,*Z*) 93(*S*,*E*)
7	 **2g**	90	*ent*-**3m**	15:1	64	89(*R*)
8	 **2h**	96	*ent*-**3a**	>20:1	13	94(*R*)

[a] Reaction conditions: **1** (0.2 mmol) and **2** (0.24 mmol) in MeOH (3.0 mL) at −10 °C for 16 h. [b] Ratio determined by ^{1}H NMR analysis of the isolated products. [c] Yield of isolated product (*E* + *Z*). [d] *ee* value of the *E* isomer was determined after cyclization to **6m**, see below.

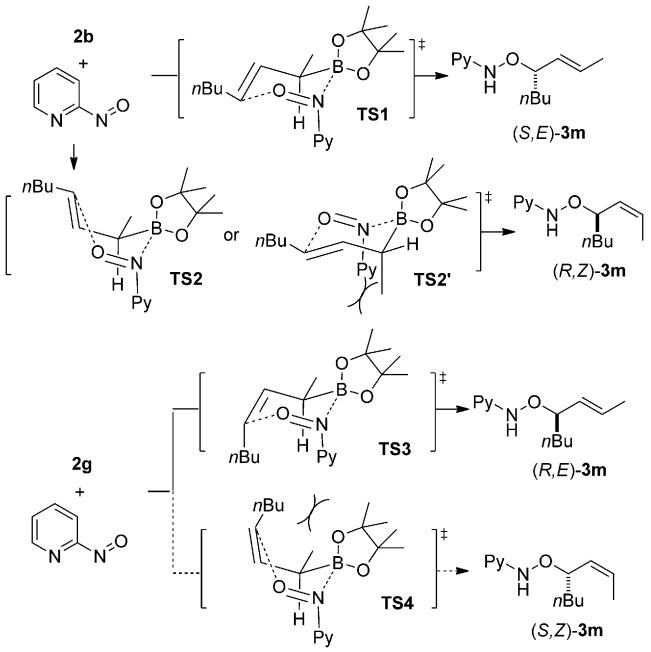


Scheme 2. Formation of fully substituted C centers.

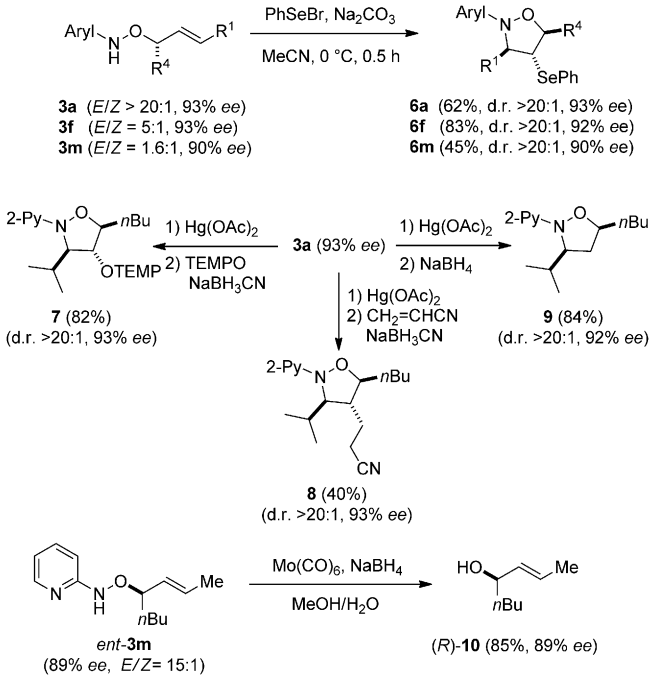
We next explored the scope by varying the α-chiral allylboronate using **1a** as the electrophile (Table 3). The size of the α substituent R^1 strongly influences the *E*/*Z* selectivity, but the enantiospecificity is unaffected. With the methyl and phenethyl derivatives **2b** and **2c**, **3m** and **3n** were obtained in excellent yield and stereospecificity with *E*/*Z* selectivities of 1.6:1 and 4:1, respectively (entries 1 and 2). Enantiomeric products can be obtained by using an enantiomeric boronate (entry 3). A slightly lower yield was achieved with the sterically more hindered allylboronate **2d**, but the selectivity remained high (entry 4). Boronate **2e** bearing a β-methyl substituent gave a low *E*/*Z* selectivity but excellent enantiospecificity for both isomers (see **3p**, entry 5). As expected, *E*/*Z* selectivity increased with the larger isopropyl congener **2f** (see **3q**, entry 6). The (*Z*)-allylic boronates **2g** and **2h** afforded *ent*-**3m** and *ent*-**3a** with high *E* selectivity. In contrast to the *E* isomer **2b**, where a low *E*/*Z* selectivity was achieved with the α-methyl-substituted boronate, the *Z*-allylboronate **2g** reacted with high selectivity (*E*/*Z* = 15:1, entry 7). Yields were lower for the *Z*-allylboronates and it is apparent that the *Z* congeners deliver products of opposite absolute configuration (entries 7 and 8).

We then tested γ,γ-disubstituted allylboronates. Surprisingly, the allylation of **1g** with **2i** provided *N*-allylation product **5r** as the major compound (48%) along with 13% of **3r** (Scheme 2). Higher yields for the *N*-allylation were achieved with more-electron-rich nitroso derivatives (see **5s**, **5t**). However, 2-nitrosopyridine delivered only the *O*-allylation product **3u** (65%). We do not currently understand the reversal of the N,O regioselectivity. Along these lines, **2j** resulted in *O*-allylation with 2-nitrosopyridine (**3v**, 40%) and mainly *N*-allylation with PhNO (**5w**, 53%). To study the enantiospecificity we tested **2k**,[20] which did not react with 2-nitrosopyridine. However, the allylation of nitrosoarene **1g** with **2k** gave the *N*-allylation product **5x** as the major compound (37%) with high enantiospecificity (*es*). An improved yield of the *N*-allylation product was achieved with nitrosobenzene (see **5y**).

Based on the model to explain the stereochemistry of the allylboration of aldehydes[15,16] and considering the stereochemical outcome of the nitrosoarene allylations, we suggest the following model to explain the observed stereochemistry (Scheme 3). *E*-allylboronates, as exemplified by **2b**, preferably react via a six-membered chair-type transition state **TS1**, in which the Lewis basic N atom of the nitroso functionality activates the allylboronate through B–N interaction.[21] The α substituent occupies a pseudoequatorial position, thereby determining the *E* selectivity and absolute configuration. The *Z* isomer (*R*,*Z*)-**3m** is likely formed via the boat transition state **TS2**. Alternatively, the higher energy chair **TS2′** might



Scheme 3. Suggested mechanism.



Scheme 4. Follow-up reactions.

also be considered, where the α substituent is axially oriented. For larger α substituents such as *i*Pr (see **2a**) the *Z* products are not formed. The *Z*-allylboronates exemplified by **2g** likely react via **TS3** to the major product (*R*,*E*)-**3m**. As expected, the *E*/*Z* selectivity for *Z*-allylboronates is far higher. The severe threefold 1,3-diaxial interactions makes a chair TS unlikely and we, therefore, suggest the boat **TS4** leading to the small amounts of (*S*,*Z*)-**3m** observed in the experiment.

To show the potential of the method we investigated follow-up reactions. Since isoxazolidines are valuable heterocycles, the electrophilic cyclization of allyloxyamines **3** was studied. We found that cyclization of **3a** with PhSeBr[22] proceeded in CH_3CN to give isoxazolidine **6a** in good yield and excellent diastereoselectivity (Scheme 4). Interestingly, PhSeBr-induced cyclization of **3f** and **3m**, which were used as *E*/*Z* mixtures of isomers, afforded **6f** and **6m** with very high *trans*/*trans* selectivity in moderate to good yield. We assume that only the *E* isomer undergoes the selenocyclization, as reflected by the significantly lower yield obtained in the transformation of **3m** to **6m** and the high diastereoselectivity.

Treatment of the allyloxyamine **3a** with $Hg(OAc)_2$ afforded the cyclized mercury acetate which was further transformed directly.[23] Reduction with $NaBH_3CN$ in the presence of acrylonitrile as a radical acceptor afforded **8** with excellent *trans*/*trans* diastereoselectivity, whereas reduction with $NaBH_4$ gave isoxazoldine **9** (84%) as a single diastereoisomer, thereby revealing that 1,3-induction in the initial $Hg(OAc)_2$-mediated cyclization was complete.[24] We also found that the intermediate mercury hydride reacts efficiently with 2,2,6,6-tetramethylpiperidine-*N*-oxyl (TEMPO)[25] to give TEMPO adduct **7** in good yield and complete *trans*/*trans* diastereoselectivity. The N–O bond in these isoxazolidines can be readily cleaved under mild conditions,[5d] as shown for the transformation of *ent*-**3m** to chiral allylic alcohol (*R*)-**10** ($[\alpha]_D^{20} = -7.0$ ($c = 0.46$, EtOH)). This known alcohol was used for the assignment of the absolute configuration ((*S*)-**10**), 96% *ee*, $[\alpha]_D^{23} = +7.2$ ($c = 0.36$, EtOH)[26]).

In summary, we have presented highly stereoselective *O*-allylation of aryl nitroso compounds with chiral allylboronates to provide the corresponding allyloxyamines. The products are obtained with excellent stereospecificity and in most cases very high *E*/*Z* selectivity. Our method further expands the high value of readily available α-chiral allylboronates for asymmetric synthesis. A model to explain the stereochemical outcome of the nitrosoarene allylborations is suggested and the products obtained are highly valuable synthetic intermediates, as shown by various efficient follow-up reactions.

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[1] A. Baeyer, *Ber. Dtsch. Chem. Ges.* **1874**, *7*, 1638–1640.
[2] a) P. Zuman, B. Shah, *Chem. Rev.* **1994**, *94*, 1621–1641; b) H. Yamamoto, N. Momiyama, *Chem. Commun.* **2005**, 3514–3525; c) H. Yamamoto, *Tetrahedron* **2013**, *69*, 4503–4515; d) B. S. Bodnar, M. J. Miller, *Angew. Chem. Int. Ed.* **2011**, *50*, 5630–5647; *Angew. Chem.* **2011**, *123*, 5746–5764.
[3] a) A. Zakarian, C.-D. Lu, *J. Am. Chem. Soc.* **2006**, *128*, 5356–5357; b) A. Jabbari, K. N. Houk, *Org. Lett.* **2006**, *8*, 5975–5978.
[4] a) W. Adam, O. Krebs, *Chem. Rev.* **2003**, *103*, 4131–4146; b) M. Baidya, H. Yamamoto, *Synthesis* **2013**, 1931–1938.
[5] a) Y. Yamamoto, H. Yamamoto, *Eur. J. Org. Chem.* **2006**, 2031–2043; b) C. K. Jana, A. Studer, *Angew. Chem. Int. Ed.* **2007**, *46*, 6542–6544; *Angew. Chem.* **2007**, *119*, 6662–6664; c) C. K. Jana,

A. Studer, *Chem. Eur. J.* **2008**, *14*, 6326 – 6328; d) C. K. Jana, S. Grimme, A. Studer, *Chem. Eur. J.* **2009**, *15*, 9078 – 9084; e) I. Chatterjee, C. K. Jana, M. Steinmetz, S. Grimme, A. Studer, *Adv. Synth. Catal.* **2010**, *352*, 945 – 948; f) S. Chakrabarty, I. Chatterjee, L. Tebben, A. Studer, *Angew. Chem. Int. Ed.* **2013**, *52*, 2968 – 2971; *Angew. Chem.* **2013**, *125*, 3041 – 3044; g) S. Chakrabarty, I. Chatterjee, B. Wibbeling, C. G. Daniliuc, A. Studer, *Angew. Chem. Int. Ed.* **2014**, *53*, 5964 – 5968; *Angew. Chem.* **2014**, *126*, 6074 – 6078.

[6] J. M. Janey, *Angew. Chem. Int. Ed.* **2005**, *44*, 4292 – 4300; *Angew. Chem.* **2005**, *117*, 4364 – 4372.

[7] a) J. W. Lewis, P. L. Myers, J. A. Ormerod, *J. Chem. Soc. Perkin Trans. 1* **1972**, 2521 – 2524; b) T. Sasaki, Y. Ishibashi, M. Ohno, *Chem. Lett.* **1983**, 863 – 866; c) W. Oppolzer, O. Tamura, *Tetrahedron Lett.* **1990**, *31*, 991 – 994.

[8] a) N. Momiyama, H. Yamamoto, *Angew. Chem. Int. Ed.* **2002**, *41*, 2986 – 2988; *Angew. Chem.* **2002**, *114*, 3112 – 3114; b) N. Momiyama, H. Yamamoto, *J. Am. Chem. Soc.* **2003**, *125*, 6038 – 6039.

[9] S. P. Brown, M. P. Brochu, C. J. Sinz, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2003**, *125*, 10808 – 10809.

[10] G. Zhong, *Angew. Chem. Int. Ed.* **2003**, *42*, 4247 – 4250; *Angew. Chem.* **2003**, *115*, 4379 – 4382.

[11] Y. Hayashi, J. Yamaguchi, K. Hibino, M. Shoji, *Tetrahedron Lett.* **2003**, *44*, 8293 – 8296.

[12] N. Momiyama, H. Torii, S. Saito, H. Yamamoto, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5374 – 5378.

[13] I. Chatterjee, R. Fröhlich, A. Studer, *Angew. Chem. Int. Ed.* **2011**, *50*, 11257 – 11260; *Angew. Chem.* **2011**, *123*, 11453 – 11456.

[14] a) Y. N. Bubnov, D. G. Pershin, A. L. Karionova, M. E. Gurskii, *Mendeleev Commun.* **2002**, *12*, 202 – 203; b) R. E. Kyne, M. C. Ryan, L. T. Kliman, J. P. Morken, *Org. Lett.* **2010**, *12*, 3796 – 3799.

[15] a) *Houben-Weyl*, *Vol. E21b* (Eds.: G. Helmchen, R. W. Hoffmann, J. Mulzer, E. Schaumann), Thieme, Stuttgart, **1995**, pp. 1357 – 1602; b) Y. Yamamoto, N. Asao, *Chem. Rev.* **1993**, *93*, 2207 – 2293; c) S. E. Denmark, J. Fu, *Chem. Rev.* **2003**, *103*, 2763 – 2794; d) S. Lou, P. N. Moquist, S. E. Schaus, *J. Am. Chem. Soc.* **2007**, *129*, 15398 – 15404; e) P. Jain, J. C. Antilla, *J. Am. Chem. Soc.* **2010**, *132*, 11884 – 11886; f) R. Alam, A. Das, G. Huang, L. Eriksson, F. Himo, K. J. Szabo, *Chem. Sci.* **2014**, *5*, 2732 – 2738.

[16] a) "Allylboron Reagents": W. R. Roush in *Houben-Weyl*, *Vol. E21b* (Eds.: G. Helmchen, R. W. Hoffmann, J. Mulzer, E. Schaumann), Thieme, Stuttgart, **1995**, p. 1410; b) W. R. Roush, S. Chemler in *Modern Carbonyl Chemistry* (Ed.: J. Otera), Wiley-VCH, Weinheim, **2000**, p. 403; c) J. W. J. Kennedy, D. G. Hall in *Boronic Acids* (Ed.: D. G. Hall), Wiley-VCH, Weinheim, **2005**, chap. 6, pp. 241.

[17] a) R. W. Hoffmann, *Pure Appl. Chem.* **1988**, *60*, 123 – 130; b) R. W. Hoffmann, G. Niel, A. Schlapbach, *Pure Appl. Chem.* **1990**, *62*, 1993 – 1998; c) G. Y. Fang, V. K. Aggarwal, *Angew. Chem. Int. Ed.* **2007**, *46*, 359 – 362; *Angew. Chem.* **2007**, *119*, 363 – 366; d) M. Althaus, A. Mahmood, J. R. Suárez, S. P. Thomas, V. K. Aggarwal, *J. Am. Chem. Soc.* **2010**, *132*, 4025 – 4028; e) J. L. Y. Chen, H. K. Scott, M. J. Hesse, C. L. Willis, V. K. Aggarwal, *J. Am. Chem. Soc.* **2013**, *135*, 5316 – 5319; f) M. J. Hesse, S. Essafi, C. G. Watson, J. N. Harvey, D. Hirst, C. L. Willis, V. K. Aggarwal, *Angew. Chem. Int. Ed.* **2014**, *53*, 6145 – 6149; *Angew. Chem.* **2014**, *126*, 6259 – 6263.

[18] The reaction of **3a** with **1a** in MeOH at 0 °C for 2 h provided **4a** in 38 % yield. Allylboration and hydrolysis are faster than further reaction to **4a**. In THF, **3a** does not react at room temperature with **1a**. However, the allylboration product, generated in situ upon treatment of **3a** with NaH and PinBO*i*Pr, reacted efficiently at 0 °C for 2 h with nitrosopyridine (1 equiv) to afford **4a** (60 %) and 2-methyl-3-nonen-5-ol (65 %, see the Supporting Information).

[19] The absolute configuration was assigned by transforming **3m** by N-O cleavage to the corresponding known alcohol, see below. All other compounds were assigned in analogy.

[20] H.-S. Sim, X. Feng, J. Yun, *Chem. Eur. J.* **2009**, *15*, 1939 – 1943.

[21] The HOMO of nitroso components is the out of phase combination of the lone pairs at N and O, and is orthogonal to the LUMO (N=O π^*). For HNO, coefficients at N and O are similar, see A. G. Leach, K. N. Houk, *Chem. Commun.* **2002**, 1243 – 1255. Depending on the Lewis acid, either N or O interaction is possible. Nitrosobenzene was suggested to interact with BF_3 at the nitrogen atom, see K. D. Otley, J. A. Ellman, *J. Org. Chem.* **2014**, *79*, 8296 – 8303.

[22] B. Janza, A. Studer, *Synthesis* **2002**, 2117 – 2123.

[23] B. Giese, K. Heuck, *Chem. Ber.* **1981**, *114*, 1572 – 1575.

[24] Y. Yamamoto, T. Komatsu, K. Maruyama, *J. Org. Chem.* **1985**, *50*, 3115 – 3121.

[25] a) T. Vogler, A. Studer, *Synthesis* **2008**, 1979 – 1993; b) L. Tebben, A. Studer, *Angew. Chem. Int. Ed.* **2011**, *50*, 5034 – 5068; *Angew. Chem.* **2011**, *123*, 5138 – 5174; c) S. Wertz, A. Studer, *Green Chem.* **2013**, *15*, 3116 – 3134.

[26] H. Ohmiya, Y. Makida, T. Tanaka, M. Sawamura, *J. Am. Chem. Soc.* **2008**, *130*, 17276 – 17277.

