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Oxoammonium-mediated allylsilane-ether coupling reaction

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Abstract:	A new C(sp ³)-H functionalization reaction consisting in the oxidative α -allylation of allyl- and benzyl- methyl ethers has been developed. The C-C coupling could be carried out under mild conditions thanks to the use of cheap and green oxoammonium salts. The scope of the reaction was studied over 27 examples, considering the nature of the substituents on the two coupling partners.
Response to Reviewers:	<p>Object: Author's answer to Referees Comments of manuscript ejoc.202100026, submitted to European Journal of Organic Chemistry</p> <p>Dear Dr. Chen,</p> <p>Thank you very much for handling this submission and for being open to reconsider the resubmission of a revised version of it. We carefully read your comments as well as those of the two reviewers, and we are now submitting a new version of the manuscript for your reconsideration.</p> <p>Circumstantiated answers to the points addressed by the reviewers are listed here below.</p> <p>Reviewer #1</p> <p>Comment "It would seem that the methodology needs more work before publication. Isolated yields of the products are modest at best, although it seems that consumption of the starting material is complete. This suggests issues isolating the product and also a number of competing off-target reactions taking place. In my mind, the work is of limited synthetic value until these issues are addressed. I believe that further investigation and optimization is necessary. This could also provide further insight into the transformation and add value to a revised version."</p> <p>AnswerWe are aware that the yields of the transformation studied are acceptable, though not excellent. Considerable work has been done to obtain the optimal conditions. In many instances the yields are of synthetic utility, and purification always allowed to obtain pure products. Furthermore, the present reaction is an original transformation. Hopefully, new future studies by us and others will allow to further improve the yields.</p> <p>Comment "a method for preparing the oxoammonium salt itself is presented. There are other routes to this salt and they should at least be cited, if not mentioned in the text."</p> <p>AnswerAll the methods to prepare the oxoammonium salts we are aware of have been cited.</p>

	<p>Reviewer #2</p> <p>Comment "This mechanism goes back to a clearly flawed proposal by C.-J. Li for DDQ-mediated ether oxidations, and it must no longer be propagated. Ethers simply do not have a sufficiently low oxidation potential to form radical cations with organic oxidants. The better source of an electron would be the arene system, though this is still most likely a hydride transfer process. The authors should consult a couple papers in the literature for computational studies on oxoammonium ion-mediated hydride abstraction (J. Org. Chem. 2015, 80, 8150) and the energetic profile of electron transfer processes compared to hydride abstractions (J. Am. Chem. Soc. 2017, 139, 17935). It is essential that this incorrect mechanism not be continually proposed for the field to move forward."</p> <p>Answer We warmly thank the reviewer to have brought to our attention this problem. We have now corrected the mechanism. One of the suggested references (Ref 14a) was already quoted in the original version, and we added the second cited one (Ref 14b) in the revised version.</p> <p>Comment "I suspect that the secondary ether simply did an SN1 reaction faster than a hydride transfer due to the stability of the intermediate cation and the steric effects near the abstractable hydride."</p> <p>Answer The reviewer's suspect is more than legitimate. Since an SN1 mechanism would take place independently of the presence of the oxammonium salt, we repeated the coupling experiment, putting to react ether 2o with the allyl silane in the absence of the oxo-ammonium salt. As this extra test gave no reaction, we can safely rule out the SN1 mechanism. The execution of this extra test has been added in the new version.</p> <p>Comment "Additionally, while the Supporting Information generally describes the procedures well and the spectra show impressively clean products, there is no information about reaction times. Given the electronic differences between some of the substrates, readers would be appreciative of knowing how structural features influence kinetics. This should also be discussed briefly in the text."</p> <p>Answer The reaction times are now carefully indicated in the new version of the Supporting Information. The most relevant reaction times have also been added in the text of the revised version.</p> <p>Editor's comments</p> <p>The file format, graphics, Supporting Information, have been adjusted as requested. Table of Contents and Twitter addresses appear now at the end of the main manuscript, above of the reference section.</p> <p>In conclusion, the new version of the manuscript has been revised where modifications were suggested. The files "EurJOC_Cozzi_Oxoam_main_2021-02-08_rev" and "EurJOC_Cozzi_Oxoam_SI_2021-02-08_rev.docx" have now been uploaded. In the former file, text selected in yellow has been added or modified with respect to the original version.</p> <p>We hope that this new version of the manuscript fulfills the requirements for publication in European Journal of Organic Chemistry, and look forward to hearing from you at your earliest convenience.</p> <p>With my best regards</p> <p>Giovanni Poli</p>
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Oxoammonium-mediated allylsilane-ether coupling reaction

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Dedicated to Professor Franco Cozzi in honor of his 70th birthday

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Supporting information for this article is given via a link at the end of the document.

Abstract: A new C(sp³)-H functionalization reaction consisting in the oxidative α -allylation of allyl- and benzyl- methyl ethers has been developed. The C-C coupling could be carried out under mild conditions thanks to the use of cheap and green oxoammonium salts. The scope of the reaction was studied over 27 examples, considering the nature of the substituents on the two coupling partners.

Introduction

Metal-catalyzed C(sp³)-H functionalizations allow the preparation of increasingly complex scaffolds in a reduced number of steps,^[1] which is in accordance with some of the “green chemistry” principles. Though metal catalysis has proven to be very effective,^[2] metal-free protocols are not less interesting, and may offer complementary reactivities. Among the organic reagents capable of effecting oxidative C(sp³)-H functionalization through formal hydride abstraction (Figure 1), 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) has been very often used for the α -functionalization of amines and ethers.^[3]

Figure 1. Examples of oxidizing agents used for C(sp³)-H functionalization by formal hydride abstraction.

Although DDQ has allowed to accomplish a great number of synthetically relevant transformations,^[4] this reagent is rather toxic,^[5] and the development of alternative green and user-friendly oxidants is highly desirable. Conversely, oxoammonium salts, and in particular, those derived from TEMPO (TEMPO⁺X[−], *alias* T⁺X[−], **1a-1e** or 4-AcNHTEMPO⁺BF₄[−] **1f**) show a very low toxicity, and lend themselves as ideal and green agents for oxidative C-H bond functionalizations.^[6] Most of the studies carried out on oxidative C-C bond formation with these oxoammonium salts focused on the direct α -C(sp³)-H functionalization

of amines.^[7] On the other hand, the development of the corresponding direct α -C(sp³)-H functionalization of ethers has progressed more slowly, probably due to the energetically less accessible oxidation potential needed to generate oxocarbenium ions, as opposed to iminium ions. As a matter of fact, only a limited number of oxoammonium promoted transformations involving the α -C(sp³)-H functionalization of ethers (essentially benzyl-, allylethers and isochromanes) has been so far reported.^[8]

In the frame of our current interest in C-C coupling reactions, we focused our recent research investigations on the oxidative allylsilane-ether coupling reaction. Such a C-C coupling was pioneered by Hayashi and Mukaiyama in 1987, who used DDQ as the oxidizing agent in the presence of catalytic amounts of LiClO₄ (Scheme 1, equation 1).^[9] This transformation represents an oxidative variant of the Hosomi-Sakurai allylation (Scheme 1, equation 2),^[10] and it has been so far reported only in very limited examples, always using DDQ as the oxidant.^[11]

Scheme 1. Previous works related to the oxoammonium-mediated allylsilane-ether coupling reaction, and the actual work.

Previous work

Hayashi-Mukaiyama (1987), ref. 9

Hosomi-Sakurai (1976), ref. 10a

Bailey (2009); Leadbeater (2015), refs. 12

This work

In view of the reported ability of TEMPO⁺ reagents to oxidize allyl ethers to the corresponding carbonyl compounds in the presence of water (Scheme 1, equation 3),^[12] we envisaged to replace water with an allyl nucleophile, with the aim to end-up with a green and synthetically useful oxoammonium-mediated allylation reaction (Scheme 1, equation 4).

Results and Discussion

We started our investigation by choosing the allylation of cinnamyl methyl ether **2a** as model reaction, and adopting reaction conditions analogous to those reported by Leadbeater^[12b] in the oxoammonium-promoted oxidation of allylethers to the corresponding aldehydes, replacing water by an allylsilane [freshly prepared T⁺BF₄[−] (**1a**),^[13] then dichloromethane (0.2M) and allyltrimethylsilane (2.0 equiv.), at 45°C in a sealed tube]. Gratifyingly, reacting allyltrimethylsilane (2.0 equiv.) with the oxoammonium salt **1a**, gave the desired homoallyl ether **4aa** in 61% yield after 1h (Table 1, entry 1), together with some traces of cinnamaldehyde **5**. The mechanism of this reaction is expected to involve hydride transfer from the ether to T⁺BF₄[−] to generate an oxocarbenium ion and TEMPOH (step a),^[14] which are likely to be in equilibrium with the corresponding mixed acetal adduct (step b). Finally, an S_E2' addition of the allylsilane to the oxocarbenium ion is expected to form the final homoallyl ether (Scheme 2). Worthy of note, as an allyl silane is expected to react with T⁺BF₄[−], the kinetics of generation of the oxocarbenium ion has to be sensibly higher than that of the subsequent coupling.

Scheme 2. Plausible mechanism of the oxoammonium-mediated allylsilane-ether coupling reaction.

While decreasing the amount of allyltrimethylsilane to 1.5 and 1.2 equivalents diminished the yield of **4aa** without decreasing the yield of cinnamaldehyde **5**, further increase in the loading of the nucleophile to 2.5, 3.0 or 4.0 equivalents did not give extra improvements in the yield (see Supporting Information).

We then studied the influence of the solvent and we found that, of all the solvents tested (dichloromethane, 1,2-dichloroethane, acetonitrile, chloroform, methyl-*tert*-butylether,

1,4-dioxane, toluene, diethyl ether, HFIP, acetone), dichloromethane gave the best results. In addition, changing the concentration (0.17M, 0.25M, 0.5M and 1M) did not improve the result (see Supporting Information).

Performing the reaction at room temperature, and stopping the experiment after 1h gave a lower conversion of **2a**, a lower yield of **4aa**, as well as a higher yield of cinnamaldehyde **5**. No desired product **4aa** was formed in 1h when the reaction was carried out at 0°C (Table 1, entry 3).

Oxoammonium salts bearing other counter-anions [triflate (**1b**), bistriflimide (**1c**), hexafluorophosphate (**1d**) and chloride (**1e**)^[15]] were also tested. However, none of them gave better yields in **4aa** than T⁺BF₄[−] (Table 1, entries 4-7). The better efficiency of the oxoammonium salt bearing the tetrafluoroborate counter-anion with regard to the others may be due to its better solubility in dichloromethane at 45°C. Bobbitt's salt **1f** was found to be insoluble in dichloromethane and did not provide any conversion of the substrate **2a** in this solvent (Table 1, entry 8).

We then inspected the nature of the allylation reagent. Replacing allyltrimethylsilane for allyltributylstannane^[16] did not afford the desired product **4aa** (Table 1, entry 9) but only trace amounts of O-allylTEMPO. Furthermore, treating **2a** with T⁺BF₄[−] in dichloromethane at 45°C in a sealed tube for 1h before the introduction of allyltrimethylstannane — to avoid the possible undesired reaction between allyltrimethylstannane and the oxoammonium salt — afforded **4aa** in 25% yield, together with several unidentified byproducts (Table 1, entry 10). Using allyltriethoxysilane afforded only cinnamaldehyde **5** in a low yield (Table 1, entry 11). Finally, treating **2a** with T⁺BF₄[−] (1.2 equiv.) in dichloromethane at 45°C in a sealed tube for 1h before the introduction of allyltrimethylsilane (2.0 equiv.) afforded a roughly equimolar mixture of the desired homoallylether **4aa** and cinnamaldehyde **5** in low yields (Table 1, entry 12).

For the sake of comparison, other hydride abstracting reagents were also tested. In the event, tritylium tetrafluoroborate generated only allyltriphenylmethane in 31% yield (Table 1, entry 13), and essentially the same result was obtained by mixing **2a** with tritylium tetrafluoroborate for 1h before introducing allyltrimethylsilane (Table 1, entry 14). The use of DDQ gave mainly cinnamaldehyde **5** (Table 1, entry 15). In the end, no other hydride abstracting reagent proved to be more efficient than the oxoammonium salt T⁺BF₄[−] for our model transformation.

However, further tests using different batches of T⁺BF₄[−] under our optimized reaction conditions revealed some irreproducibility issues, the yield of **4aa** oscillating between 35 and 61%, with proportionally increasing amounts of cinnamaldehyde. Since the protocol we followed to prepare T⁺BF₄[−]^[8a] is performed in water, we suspected that precipitation from this solvent (see Supporting information) may be the cause of the formation of trace amounts of undesired TEMPOH·HBF₄ in the reagent. To solve this problem, we developed a water-free protocol to prepare T⁺BF₄[−], employing a purification technique that excluded the presence of residual TEMPOH·HBF₄.^[17]

Table 1. Optimization of the reaction conditions.

entry ^[a]	Z	Hydride abstractor	T (°C)	Conversion (%) ^[b]	Yield 4aa (%) ^[b]	Yield 5 (%) ^[b]
1	SiMe ₃	1a	45	93	61	9
2	SiMe ₃	1a	rt	86	48	18
3	SiMe ₃	1a	0	64	0	48
4	SiMe ₃	1b	45	90	21	0
5	SiMe ₃	1c	45	85	20	8
6	SiMe ₃	1d	45	>99	37	14
7	SiMe ₃	1e	45	25	0	17
8	SiMe ₃	1f	45	0	0	0
9	Sn(<i>n</i> -Bu) ₃	1a	45	43	0	0
10 ^[c]	Sn(<i>n</i> -Bu) ₃	1a	45	>99	25	0
11 ^[d]	Si(OEt) ₃	1a	45	>99	0	28
12 ^[c]	SiMe ₃	1a	45	>99	28	31
13	SiMe ₃	Ph ₃ CBF ₄	45	>99	0	0
14 ^[c]	SiMe ₃	Ph ₃ CBF ₄	45	>99	0	0
15	SiMe ₃	DDQ	45	>99	12	67

[a] Typical reaction conditions: **2a** (0.5 mmol), **3a** (2.0 equiv.), **1a-1f** (1.2 equiv.), solvent (2.5 mL), were heated at 45°C in a sealed tube, 1h. [b] Yields were determined by quantitative NMR analysis, using benzoic acid as the internal standard. [c] Substrate **2a** and **1a** were stirred for 1h at 45°C in a sealed tube before introducing the allylating reagent. [d] The reaction was heated under stirring for 2.5h; rt: room temperature; DDQ: 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone.

After several trials, we found that treating TEMPO with HF₄B·OEt₂ (1.1 equiv.) at 0°C in CHCl₃ for 1h, followed by addition of PhI(OAc)₂ (1.0 equiv.),^[18] gave, after further 2h stirring, the desired water-free oxoammonium salt **1a** in 94% yield. Chloroform revealed to be the solvent of choice, as it well dissolves TEMPO, TEMPOH·HBF₄, as well as PhI, without dissolving T⁺BF₄[−]. Gratifyingly, use of T⁺BF₄[−] obtained from this new water-free protocol in the above allylation reaction gave the desired product **4aa** with reproducible 56-59% isolated yields (Scheme 3) (See Supporting information).

Scheme 3. New water-free based protocol to T⁺BF₄[−].

With the optimized reaction conditions in hand, the scope of the reaction was then evaluated, starting with examination of the nature of the ether function linked to the cinnamyl structure (

Scheme 4, top left box). Cinnamyl methyl ether **2a** provided the desired allylated product **4aa** in 57% isolated yield, and scale-up of this reaction to 10 mmol gave 61% yield. Ethyl and *iso*-propyl ethers **2b** and **2c** gave the corresponding allylated products **4ba** and **4ca** in 28% and 44% yield, respectively. On the other hand, *tert*-butyl ether **2d** provided cinnamaldehyde **5** in 72% yield, and only traces amount of the desired allylated compound **4da**. The anhydrous formation of the aldehyde **5** from the *t*-butyl ether **2d** can be accounted for on the basis of a competitive Me₃C–O bond breaking from the oxocarbenium ion intermediate, to form *t*-butyl cation, which in turn will undergo an E1 elimination to isobutene.^[19] The fact that this alternative reactivity appears only in the case of the *t*-butyl ether **2d** suggests that the balance “allylation vs C–O bond breaking” is rather delicate and very much dependent on the stabilization of the carbocation resulting from the C–O bond breaking (Scheme 5).

Scheme 4. Influence of the substitution at the aromatic ring and at the alkene moiety on cinnamyl methyl ether substrates.

[a] Typical reaction conditions: **2a-p** (0.5 mmol), **3a** (2.0 equiv.), **1a** (1.2 equiv.), CH₂Cl₂ (2.5 mL), 45°C in a sealed tube, 1–5 h. [b] reaction performed on a 0.28 mmol scale. [c] Cinnamaldehyde **5** was isolated with 72% yield. [d] No conversion was observed after 24 h of reaction. Trace amounts of allylTEMPO were detected by ¹H NMR.

Scheme 5. Allylation vs C–O bond breaking as a function of the nature of the ether.

Treatment of cinnamyl acetate **2e** under the above optimized reactions left the substrate unchanged. This absence of reactivity is in line with the fact that the oxocarbenium ion intermediate is destabilized by the acetate function.^[14a] Substitution at the aromatic ring was then evaluated (

Scheme 4, bottom left and top right boxes). The presence of electron poor substituents on the aromatic ring was tolerated, as shown by the formation of the *p*-bromophenyl, *p*-nitrophenyl and *p*-trifluoromethyl adducts **4fa**, **4ga** and **4ha** in moderate to good yields. The substitution at the *ortho*, *meta* and *para* positions on the aromatic ring was then evaluated with the *p*-, *o*-, and *m*-tolyl derivatives, which gave the corresponding allylated adducts **4ja**, **4ka**, and **4la** in 46%, 51%, and 35% yield, respectively. A methylenedioxy bridge on the aromatic ring allowed also to obtain the corresponding allylation product **4ia** in 58% yield.

The geometry and the substitution of the alkene moiety was also investigated (

Scheme 4, bottom right box). In the event, the trisubstituted alkene **2m** generated the expected homoallyl ether **4ma** in 34%

yield with a small loss of the *E/Z* ratio (88:12 starting from > 99:1 for **2m**). The 1,1-disubstituted alkene 2-phenyl-3-methoxypropene **2n** was unreactive. Interestingly, treatment of (*E*)-1,3-diphenyl-3-methoxypropene **2o** with our optimized reaction conditions afforded the demethoxylated 1,5-diene **6** in 87% isolated yield (Scheme 6).

Scheme 6. Reductive allylation of (*E*)-1,3-diphenyl-3-methoxypropene.

Thus, it appears that on passing from primary to secondary allylic ethers, isohypsic allylation (methoxy departure) competes with oxidative allylation (hydrogen departure) of the substrate. This behavior parallels the Lewis acid catalyzed allylation of allyl ethers.^[20] Such a reactivity change may be due to the fact that substrate **2o** is more prone to undergo hydride abstraction from the methyl moiety at the α' position (blue path) than from the allylic / benzylic α position (red path). The resulting intermediate **B** may then release formaldehyde to generate the very delocalized 1,3-diphenylallyl cation **C**, which reacts with the allyl silane affording diene **6**. Repetition of the above experiment in the absence of the oxoammonium salt **1a**, performed as a blank test, gave no conversion, thus ruling out an S_N1 mechanism for such a reactivity (Scheme 7). *In situ* spectrometric mass analysis (see SI for details) detected the presence of intermediates **B** and **C**, thus supporting the proposed mechanism.

Scheme 7. Oxidative vs isohypsic allylation as a function of the nature of the starting allylic substrate: a mechanistic proposal.

Substitutions other than the 2-arylpropenyl moiety were than considered for the starting allylic ether (Scheme 8). Thus, methyl ether **2p**, bearing a highly conjugated phenylpentadienyl substituent gave the corresponding adduct **4pa** in 38% yield. (*E*)-2-Dodeceny methyl ether **2q** could be also allylated, providing the corresponding allylated product **4qa** in 41% yield.

The ethers **2r** and **2s** deriving from O-methylation of the monoterpenes (-)-myrtenol and (-)-perillyl alcohol afforded the corresponding allylated products **4ra** and **4sa** as 63:37 and 54:46 diastereoisomeric mixtures and in 68% and 56% yield, respectively.

Scheme 8. Scope of the reaction with alkyl- and alkenyl-substituted allyl methylethers.

[a] typical reaction conditions: **2p-2s** (0.5 mmol), **3a** (2.0 equiv.), **1a** (1.2 equiv.), Solvent (2.5 mL), 45°C in a sealed tube, 45 min-2h.

The allylation of benzylic methyl ethers was then tested (Scheme 9).^[21] When benzyl methylether **7a** was treated with allyl silane under the same reaction conditions as previously used for allylic substrates, the reaction turned out to be rather sluggish, and an overnight period was necessary to obtain full conversion. Furthermore, the resulting allylated product **8aa** was very volatile, and only a spectroscopic (¹H-NMR) yield of 47% could be determined.

The methyl ether bearing a *p*-trifluoromethyl group on the aryl ring **7b** gave a very low conversion (15%) after 24h reaction, and the allylated compound **8ba** was isolated with a very low yield (8%). This result may be in line with the lower reactivity of

the electron-poor substrate, which is less prone to hydride abstraction. Allylation of 2-(methoxymethyl)naphthalene **7c** and piperonyl methyl ether **7d** were more successful, affording the corresponding allylated products **8ca** and **8da** in 60% and 53% isolated yields. In the case of 1-methoxy-4-(methoxymethyl)benzene **7e**, the desired product **8ea** was isolated in 22% yield (43% ¹H-NMR), accompanied by a little amount (5%) of the isohypsic allylation product, homoallyl anisole **9**, whose formation may be explained as in the case of the conversion of **2o** into **6** (*vide supra*). Switching to benzyl and methoxymethyl (MOM) protection of the para located phenol function gave better yields [(57%), 32%], [(69%), 57%] of the respective allylated products **8fa** and **8ga**. Finally, the bis-MOM-protected catechol ether **7h** coming from demethylvanillin could be converted in only **6h** into the allylated methylether **8ha** in 64% isolated yield.

Scheme 9. Scope of the reaction with benzylic methyl ethers.

[a] typical reaction conditions: **7a-7h** (0.5 mmol), **3a** (2.0 equiv.), **1a** (1.2 equiv.), Solvent (2.5 mL), 45°C in a sealed tube, 6-24h. [b] Yields: spectroscopic yields, in parentheses, were determined by quantitative ¹H NMR using benzoic acid as an internal standard; isolated yields are out of parentheses. [c] Conversion was only 13%. [d] *p*-homoallylanisole **9** was also isolated in 5% yield.

The scope of the reaction as a function of the substitution of the allylsilane was then undertaken, starting with an allylsilane substituted at position 2 (Scheme 10). Accordingly, reaction between cinnamyl methyl ether **2a** and 2-((trimethylsilyl)methyl)-allyl acetate **3b** gave the corresponding adduct **4ab** in 61% yield. Reaction of piperonyl methyl ether **7d** with **3b** gave the allylated adduct **8db** in 55% yield. Reaction of **2a** with cinnamyltrimethylsilane **3c**^[22] gave **4ac** in 69% yield as a 69:31 mixture of diastereoisomers. Analogously, reaction of **7d** with **3c** afforded the corresponding adduct **8dc** in 58% and as 74:26 *syn/anti* diastereoisomeric ratio.^[23]

Not unexpectedly, the *syn* preference found in the C-H allylation of the benzylic ether **7d** parallels the *syn* diastereoselectivity observed in the acetal Hosomi-Sakurai reaction.^[24]

Scheme 10. Scope of the reaction as a function of the substitution of the allylsilane.

[a] **2a**: R = (*E*)-Ph-CH=CH-; **7d**: R = piperonyl; [b] **3b**: R₁ = H, R₂ = CH₂OAc; **3c**: R₁ = Ph, R₂ = H. [c] Typical reaction conditions: **2a** or **7d** (0.5 mmol), **3b-c** (2.0 equiv.), **1a** (1.2 equiv.), solvent (2.5 mL), 45°C in a sealed tube, 1-3h30 for substrate **2a** or 24h for substrate **7d**. Isolated yields.

On the other hand, treating **2a** with methallyltrimethylsilane **3d** under the above reaction conditions gave only methallylTEMPO in 70% yield (with respect to the oxoammonium salt) **1a**, while treating **7d** with **3d** gave the demethoxylated (isohypsic) adduct in 64% yield (with respect to **7d**) as well as methallylTEMPO in 49% yield (with respect to **1a**) (Scheme 11).^[25] These results suggest that this allylsilane-ether C-H coupling is rather sensitive to the nature of both the reaction partners. Indeed, if the allylic silane is much more nucleophilic than simple allylsilane, as is the case of metallylsilane,^[26] it can compete with the ether substrate in the interaction with T⁺BF₄[−], which will behave as an electrophile. On the other hand, the **hydride abstraction** next to the ethereal oxygen atom may be derailed from the allylic/benzylic position toward the alternative α' **methyl** position.

Scheme 11. Deviations from the allylsilane-ether coupling.

Conclusion

In summary, we developed a C-H allylsilane-ether coupling reaction starting from allylic and benzylic methylethers in the presence of oxoammonium salts. The use of the more soluble T⁺BF₄[−] TEMPO-based oxoammonium salt allowed the generation of functionalized homoallyl methylethers in moderate to good yields. The use of cinnamyltrimethylsilane also gave a relatively good diastereoselectivity in favor of the *syn* isomers, which is in accordance with the results reported on the Lewis-acid mediated allylation of acetals with allyltrimethylsilanes. The nature of the O-substitution on the other side of the reactive

allylic moiety is crucial. Indeed, while the methyl group appears ideal to assure enough stability to the transient oxocarbenium ion, a *t*-butyl group opens the way to a rapid **non-hydrolytic** aldehyde formation via C-O cleavage. Future work will be dedicated to the development of catalytic and enantioselective versions as well as to the application of our new procedure to the total synthesis of relevant targets.

Experimental Section

Water-free preparation of the oxoammonium salt 1a: In a round bottom flask under inert atmosphere was dissolved TEMPO (2g, 12.8 mmol, 1.0 equiv.) in 15 mL (C = 1.3M) of dry chloroform. After cooling down the mixture to 0°C (ice/water bath), tetrafluoroboric acid diethylether complex (1.9 mL, 14.1 mmol, 1.1 equiv.) was added dropwise with a syringe. The mixture is warmed up to room temperature and stirred at this temperature for 1h. Diacetoxyiodobenzene (4.12 g, 12.8 mmol, 1.0 equiv.) was then added in one portion and the mixture was stirred at room temperature for 2h. The obtained yellow suspension was then vacuum-filtered with a Büchner or Hirsch funnel and the solid was washed with 2x50 mL of chloroform. The yellow solid was collected in a flask and dried under high vacuum at room temperature for 1h to give the pure oxoammonium salt **1a** (2.7 g, 87% yield). ¹H NMR (CD₃CN, 300 MHz) δ 2.53 – 2.49 (m, 4H), 2.44-2.36 (m, 6H), 1.67 (s, 12H); ¹³C NMR (CD₃CN, 75 MHz) 105.2 (2C), 41.5 (2C), 29.6 (4C), 17.1; ¹⁹F NMR (CD₃CN, 282.3 MHz) δ -151.6 (s). The characterization data are in accordance with the ones reported in the literature.^[27]

General procedure for the allylation of allyl- and benzylic methylethers: A sealed tube equipped with a magnetic stirrer was charged with the allylether or the benzylic ether substrate (1.0 equiv.) and the tube was placed under high vacuum and then backfilled with argon. The vacuum/argon cycles were repeated twice and anhydrous dichloromethane (0.2 M) was introduced. To this solution was added the oxoammonium salt (1.2 equiv.) followed by the allylsilane (2.0 equiv.). The reaction mixture was stirred at 45°C until conversion was complete as checked by TLC (usually around 1h when starting from allylethers and 24h when starting from benzylic ethers). The mixture was then cooled to rt and mixture was filtered over a pad of silica gel with dichloromethane. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography on silica gel to give the desired products.

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Keywords: Oxoammonium, C(sp³)-H functionalization, allylation, cinnamyl ethers, benzyl ethers.

Table of Contents

We disclose an oxoammonium-mediated α -C(sp³) allylation of allyl- and benzyl ethers using allylsilanes as nucleophilic partners. This new C-C bond forming C-H activation process allows to obtain the corresponding coupled products in moderate to good yields.

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Supporting Information

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