EurJOC
European Journal of Organic Chemistry

Research Article
doi.org/10.1002/ejoc.202200051

Chemistry Europe
European Chemical Societies Publishing

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Very Important Paper

Silylium-Catalyzed Alkynylation and Etherification Reactions of Benzylic Acetates

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Dedicated to Prof. Joan Bosch on the occasion of his 75th birthday

Addition of catalytic amounts of bistriflimide triggers useful coupling reactions of benzyl acetates with trimethyl(alkynyl)silanes and trimethyl(alkoxy)silanes to afford propargyl arenes and benzyl alkyl ethers, respectively. The added acid assists the release of reactive trimethylsilylium ion into the reaction media, which were found to act as the ultimate catalytic species responsible for the C–C and the C–O forming steps. The cationic nature of these coupling processes is documented.

Introduction

The development of novel catalytic transformations securing a selective and predictable formation of carbon-carbon and/or carbon-heteroatom bonds from simple precursors is of prime interest for advancing organic synthesis in a sustainable manner. The catalytic transfer of a benzyl substituent to different functional groups comprises a set of valuable transformations.[1] In this regard, Brønsted acid-promoted[2] and Lewis acid-catalyzed[3] processes have gathered much attention. Concerning the related alkynylation process, transition-metal catalyzed coupling reactions involving benzyl halides provide access to propargylic arene frames.[4] Activated benzyl allyl alcohols successfully enter enantioselective iridium-catalyzed coupling-reactions with alkynyltrifluoroborates.[5] Besides, a palladium-catalyzed thermal decarboxylative reaction of benzyl ester derivatives derived from propiolic acid offers an alternative entry to access benzylated alkynes.[6] Furthermore, as for the use of oxygenated benzyl precursors, the alcohol dehydrative substitution process[7] is a source of valuable transformations for cationic-based synthetic approaches.[8] Regarding its merit to promote benzylation reactions of alcohols, terminal alkynes can be coupled with benzhydrol and related bis(benzylic alcohols) using $Fe(OTf)_3$/TfOH as the catalytic system.[9] As the resulting building blocks are synthetically significant, powerful alternative procedures are available for their synthesis relying on other metal-catalyzed approaches.[10–14] Among them, the three-component coupling of an alkyne, an aryl halide and a *N*-tosylhydrazone,[10] or the decarbonylative benzylation of alkynes.[11] Copper(I)–Catalyzed cross-dehydrogenative coupling (CDC) of alkynes and double benzylic, or allyl-benzyl, C–H bonds can be used for this purpose.[12] Also involving further activated benzylic positions, either propargyl benzyl alcohols[13] (1,3-diaryl-2-propyn-1-ols) or allyl benzyl alcohols[14] (1,3-diaryl-2-propen-1-ols), can be used as proper substrates in catalytic alkynylations towards alkynyltrimethylsilanes. However, for the case of simple alkyl-substituted benzylic alcohols, the facts that the ionization step is more demanding and that the resulting cationic species also undergo competitive elimination processes, might compromises is synthetic utility. Therefore, coupling reactions of alkyl-substituted benzyl precursors with alkynyl-silanes have been scantly reported. Using either $InCl_3$[15] or $BiCl_3$[16] as catalysts, broad scope was reported for the reactions of a variety of benzyl alcohols with allyltrimethylsilane. Both processes were useful to accomplish the related alkynylation reaction. However, in both cases, coupling processes involving 1-phenyletanol or the more reactive 1,3-diphenylprop-2-yn-1-ol, were the only examples reported (Scheme 1, reaction 1).

Attempts to accomplish successful substitution chemistry from allyltrimethylsilane and 1-phenylethanol using boron trifluoride as catalyst failed to give the desired allylated product. Instead, polystyrene was formed as major product and only a small amount of the desired coupling product was formed.[17] Further attempts to react allylsilane with 1-phenylethanol using bis(fluorosulfuryl)imide $[HN(SO_2F)_2]$ as Brønsted acid were also unsuccessful, whereas the use of the acid in related alkynylation processes remains unreported.[18] Those result speak in favor of pursuing further developments in this field, in search for establishing useful methodological advance that can be of interest for the synthetic organic community.

Interestingly, organic reactions catalyzed by silylium ions are subject of significant interest and gained much recognition.[19] Commercial Me_3SiOTf,[20] previously prepared Me_3SiNTf_2,[21] or more electrophilic silylium species resulting upon clever design[22] catalyze a variety of interesting organic

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Supporting information for this article is available on the WWW under https://doi.org/10.1002/ejoc.202200051

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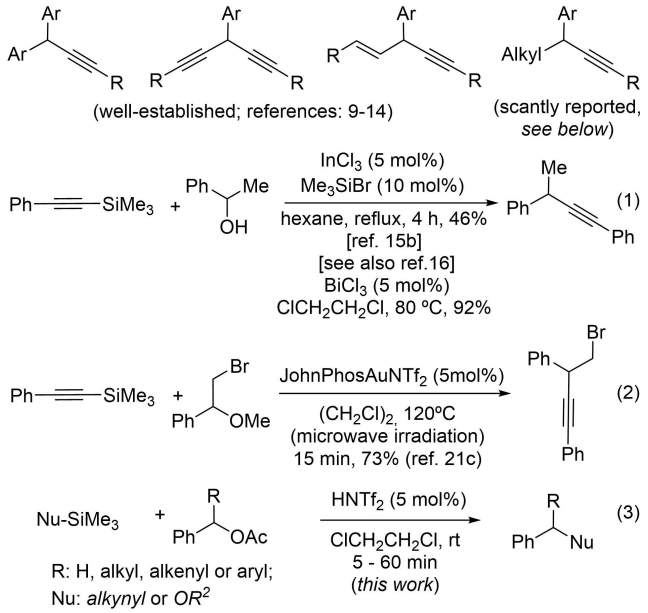
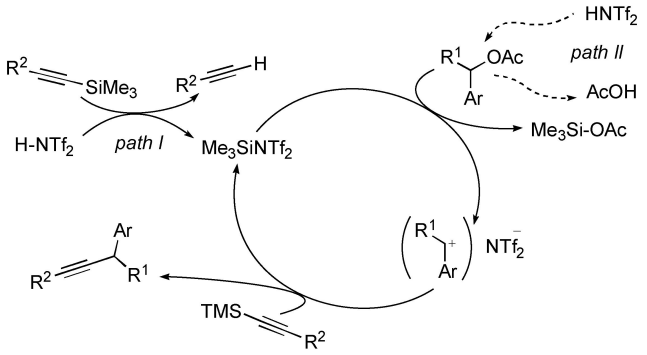


Scheme 1. Benzylation reactions of trimethylsilylalkynes.

transformations. Our search for catalytic reactions associated with the consideration of heteroatom-substituted alkynes[23] as differential starting materials and our experience in using electrophilic gold species to launch silylium-catalyzed transformations[21d,24] (Scheme 1, reaction 2), encouraged us to broach the possibility of attempting mild and selective silylium-catalyzed conversions of benzyl alcohol ester derivatives into useful products, focusing on both, C–C and C–O bond-forming processes, as outlined in Scheme 1, reaction 3.

Results and Discussion

Initial attention was drawn to the C(sp)–C(sp^3) coupling, which eventually might also provide ground for the additionally pursued catalytic O–C bond elaboration. Considering our previous work on *in situ* releasing silylium ions from alkynylsilanes upon the reaction of alkynylsilanes with gold(I),[21d,24] and taking into account the ability of triflimide (bistrifluoromethanesulfonimide, $HNTf_2$)[25] to liberate silylium reactive species in solution from organosilanes,[26] we decided to explore the potential offered by this acid as a convenient Brønsted acid promoter to accomplish the target alkynylation reaction. To undertake this task, we decided to use a better leaving group, switching from OH to OAc. In terms of the associated synthetic requirements this still acceptable, as the acetylation of the parent alcohol is an easy and convenient reaction to perform. At the same time, if successful, the resulting approach would offer a simple and truly practicable metal-free protocol to access this elusive and synthetically valuable cross-coupling reaction. The hypothesis behind this design, and its likely extension using other silyl-masked nucleophiles is outlined in Scheme 2.

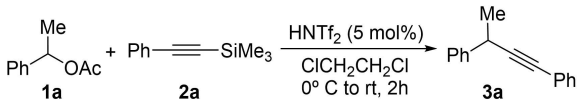


Scheme 2. Target cross-coupling: working hypothesis.

Thus, *in situ* generation of $TMSNTf_2$ from the silyl-containing nucleophile (this time the corresponding alkynylsilane) by reacting it with $HNTf_2$ is a feasible way of launching the catalytic event (see *path I*, Scheme 2).[26] A different initiation mode of the catalytic cycle can be also considered (see *path II*). Thus, an alternative direct activation of the electrophile could play a key role behind triggering the initial sacrificial cycle,[27] which then would also evolve the process for the remaining cycles on silylium basis.

At room temperature, the reaction of 1-phenylethyl acetate **1a** and trimethyl(phenylethynyl)silane **2a** in 1,2-dichloroethane was tested. In keeping with the hypothesis, catalytic addition of $HNTf_2$ gave the desired coupling product **3a**. The efficiency of the reaction as function of the molar ratio between the alkynylsilane and the acetate was investigated (Scheme 3).

For all assayed cases, bistriflimide showed the desired catalytic activity. Nonetheless, the conversion was just in the range of 50% using equimolar amount of alkyne to acetate. Interestingly, adding excess of alkynylsilane resulted in higher conversion, with four equivalents of the alkyne giving rise to virtually full conversion of acetate **1a**, affording synthetically valuable figures for the assembled alkynylated benzyl product **3a**. This result was significant, as the substitution/elimination competition was still largely in favor of the target process under the assayed reaction conditions.



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

1a : **2a** (ratio)	Conversion (%)	**1** (%)	**3a** (%)
1 : 1	50	50	25
1 : 2	54	46	31
1 : 3	80	20	50
1 : 4	>95	<5	78

Conversion and yield determined by NMR spectroscopy using tribromomethane as internal standard for reactions using 0.2 mmol of **1a**.

Scheme 3. Bistriflimide-catalyzed alkyne-benzyl coupling: model studies.

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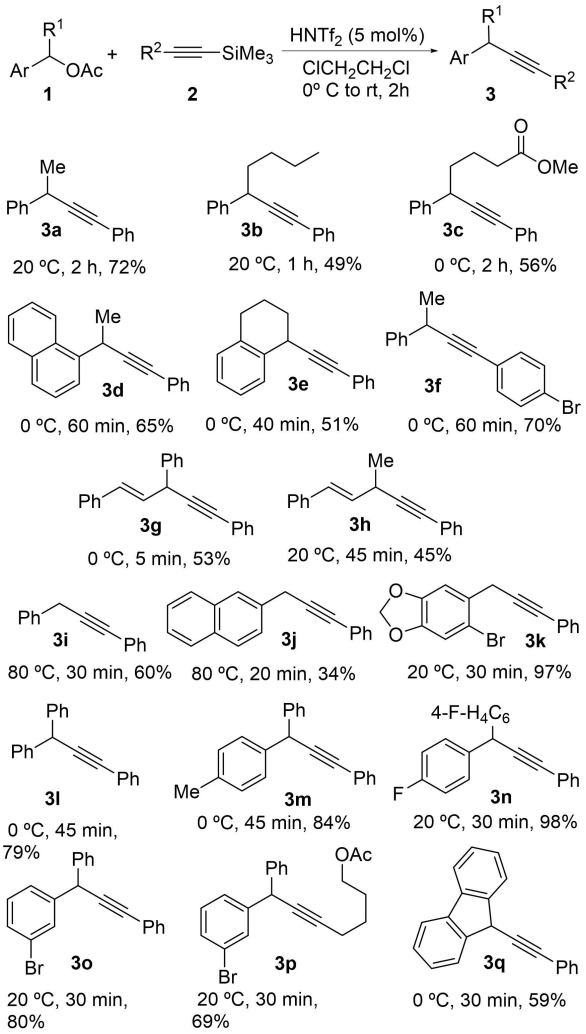
Furthermore, other Brønsted and Lewis acids, as well as some gold(I) catalysts, were tested and resulted in poorer coupling processes or showed lack of the desired reactivity, as shown in Table 1. Both triflic acid and trimethylsilyltriflate failed to produce the target reaction. Remarkably, the addition of freshly prepared $TMSNTf_2$ (entry 2) afforded **3a** in similar 72% yield, nicely supporting the involvement of the proposed active silylium catalytic cycle. Also worth noting, the potential of gold(I) complexes to release silylium species in solution by activation of trimethylsilylalkynes was explored in this context, using gold complex with the 2-(di-*tert*-butylphosphino)biphenyl ligand (JohnPhos ligand). Catalytic alkynylation was noted using the complex with the bistriflimidate anion, though the recorded yield was lower. On the contrary, lack of the desired reactivity was observed for the nitrile stabilized cationic gold complex with the hexafluoroantimoniate anion (Table 1, entries 5 and 6).

Similarly, for the case of triflimide as the added catalytic species, control experiments using phenylacetylene and/or the parent benzyl alcohol were conducted, but they failed to produce synthetically useful results. Besides, the reaction using some representative alternative solvent were assayed but did not result in an efficient process. Relevant additional data are collected within the Supporting Information.

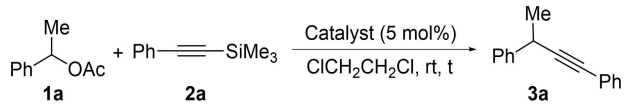
With these promising results in hand, the scope of this new C(sp^3)–C(sp) coupling process was tested. The structures of the obtained compounds **3** are depicted within Scheme 4. As documented in the introduction, previous acid-catalyzed reports mostly addressed the activation of allyltimethylsilanes and that of silyl enolates, just touching marginally the case of alkynylsilanes. So, an added-metal-free alkynylation reaction is essentially missing. Therefore, from a practical viewpoint, this triflimide-catalyzed triggered alkyne benzylation is synthetically relevant and might deserve attention.

As shown in Scheme 4, the synthesis of different propargyl arenes takes place satisfactorily, under mild conditions. Although, as previously mentioned, the bis(fluorosulfuryl)imide-promoted [$HN(SO_2F)_2$] allylation reaction of 1-phenylethanol with allylsilane is not feasible,[18] the role of acetate as the leaving group makes now viable the coupling of regular linear benzyl acetates with alkynylsilanes at room temperature (**3a**–**3k**), in agreement with the results obtained by Gevorgyan for the tris(pentafluorophenyl)borane-catalyzed allylation reactions of benzyl acetates.[27a]



Scheme 4. C(sp^3)–C(sp) catalytic coupling adding $HNTf_2$.

Table 1. Catalyst screening for alkynylation reactions.



Entry[a]	Catalyst	t	**3a** (Yield)[b]
1	TMSOTf	24 h	–
2	$TMSNTf_2$	2 h	72%
3	$HNTf_2$	2 h	71%
4	TfOH	2 h	–
5	JohnPhosAuNTf_2[c]	24 h	50%
6	JohnPhosAu(MeCN)SbF_6[c]	24 h	–

[a] **1** (0.2 mmol), **2a** (0.8 mmol), $ClCH_2CH_2Cl$ (0.4 ml). [b] Isolated yields. [c] JohnPhos stands for (2-biphenyl)di-*tert*-buthylphosphine, also commonly referred as 2-(di-*tert*-butylphosphino)biphenyl.

Thus, for the case of 1-phenylpentyl acetate, far from isolating pure samples of the target coupling product **3b**, the byproduct arising from an alternative elimination process from the likely intermediate cationic species was also isolated in 23% yield. Remarkably, this silylium-based approach tolerates the presence of a remote ester functionality at the side-chain of the electrophilic benzyl-alkyl ester precursor, and still produces the desired coupling, see compound **3c** in Scheme 4.

Naphthyl and 1,2,3,4-tetrahydronaphthalen-1-yl secondary benzylic scaffolds can be satisfactorily coupled with trimethyl(phenylethynyl)silane following this strategy (see compounds **3d** and **3e**). The alkyne partner might also contain halogen-functionality (see **3f**), which eventually can be regarded as a useful handle for a subsequent functionalization. As for the substrates, more reactive acetates, such those featuring allyl-benzyl or dibenzyl scaffolds, can be also selectively transformed into the corresponding alkynyl derivatives (compounds **3g-h** and **3l–q**, respectively), which are more commonly used

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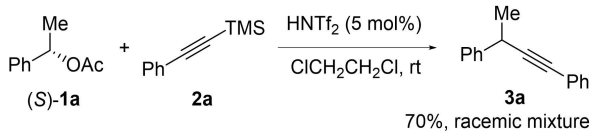
substrates in alternative S_N1 alkynylation processes.[9–16] Again, the selective activation of the benzylic acetate frame enabled the elaboration of small propargylic molecules bearing a remote functionality, this time as the result of the coupling of a benzyl acetate with an silane containing an remote *O*-acyl fragment at the nucleophilic alkyne partner (see **3 p**). For some example, almost quantitative yield was accomplished for the coupling process without adding any transition metal, just mixing the required alkynyl silane and benzyl acetate, at room temperature, in the presence of a catalytic amount of convenient bistriflimide (see **3 k** and **3 n**).

The cationic nature of the alkynylation was further investigated and corroborated. In this regard, the outcome of the coupling reaction using a chiral probe was further tested. In agreement with the initial assumption, when the acetate derived from (*S*)-1-phenylethanol (*S*)-**1 a** was exposed to a catalytic amount of triflimide, the resultant coupling product **3 a** was formed in 70% isolated yield, as a racemic mixture.[28] This result nicely accommodates the mechanistic hypothesis behind the formulated design (Scheme 5).

The resulting alkynylsilane benzylation reaction offers interest in a sustainable context as the required benzyl and alkynyl precursors can be traced from simple hydrocarbon resources using catalytic approaches.[29]

From a mechanistic point of view, taking into account the different features associated with the outcome of this bistriflimide triggered C–C bond making event, it is reasonable to postulate the generation of $TMSNTf_2$ and its key role within the catalytic cycle. The facile protodesilylation of TMS-acetylene derivatives in presence of acids such as bistriflimide supports an efficient *in situ* catalytic releasing of $TMSNTf_2$ by sacrificial activation of a catalytic amount of the parent alkynylsilane. At present, although in the presence of the alkynyl silane it seems unlikely, the possibility of bistriflimide directly activating the benzyl acetate to launch the initial cycle cannot be firmly excluded. In any case, after the initiation step, the cycle would then nicely move forward on silylium bases, as depicted in Scheme 6.



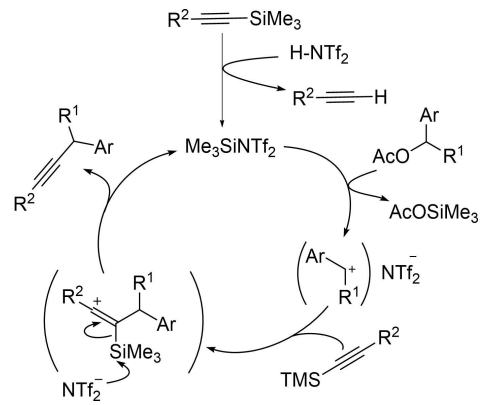
Scheme 5. Coupling of (*S*)-1-phenylethyl acetate with **2 a**.

This proposed evolution mode is in good agreement with the noted ability of trimethylsilyl bistriflimidate to trigger this catalytic reaction, in a comparable manner. The subsequent generation of a benzyl cation prior to the alkynylation step supports the racemization observed when starting from a chiral enantio-enriched substrate, as acetate partner.[30] The formation and isolation of competitive elimination products in some case further support the involvement of cationic intermediates in this process. Next, the trapping of the electrophilic benzyl species by the alkynyl silane would account for the formation of the noticed C–C bond at the time of generating a β-silicon-stabilized vinyl cation, which eventually closes the cycle releasing the target alkynylated product **3** and the required active silicon species to launch a new catalytic cycle operating on silylium basis.

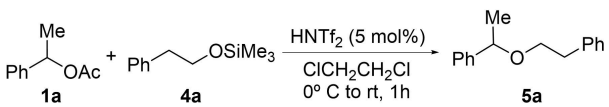
Besides, the development of novel etherification strategies keeps on attracting attention.[31] More specifically, catalytic benzylation processes of alcohols are of synthetic significance.[32] On this ground, we focused our attention in an attempt to apply the potential associated with the above discussed alkyne benzylation strategy to launch another catalytic event, which this time might result in the formation of benzyl ethers upon addition of a catalytic amount of bistriflimide to a mixture of a silylated alcohol and a benzyl acetate, establishing a new silylium-based synthetic transformation involving oxygen as nucleophile.[33] At the onset of this approach is also the intention to expand the reactivity profile of silyl ethers adding new acid-catalyzed transformations.[34]

On this basis, to 0.2 mmol of a solution of the benzyl acetate **1 a** in dichloroetane (0.4 ml) variable amounts of trimethyl(2-phenylethoxy)silane **4 a** were added (from 1 to 4 equiv.). The resulting mixture was then treated with triflimide (5 mol%) and allowed to react for one hour. The obtained results are collected within Scheme 7.

Again, as noted for the previously described alkynylation reaction, the addition of an excess of the trialkyl(alkoxy)silane



Scheme 6. Proposed mechanistic rationale for the catalytic alkynylation.



1a : **4a** (ratio)	Conversion (%)	**1** (%)	**5a** (%)
1 : 1	80	20	30
1 : 2	80	20	50
1 : 3	85	15	65
1 : 4	>95	--	79

Conversion and yield determined by NMR spectroscopy using tribromomethane as internal standard for reactions using 0.2 mmol of **1a.**

Scheme 7. Silylium-catalyzed etherification reaction: model studies.

Research Article
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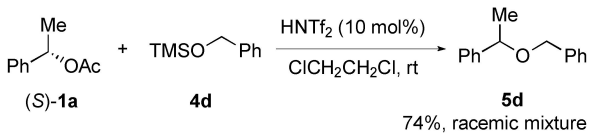
has beneficial effect over the generation of the substitution product, as often encountered for solvolytic reactions involving weak nucleophiles. In any event, though using a 1:1 to molar ratio of acetate to alkoxysilane the yield for **5a** is low (30%), its formation involved the catalytic performance of the added bistriflimide. Interestingly, using four equivalents of **4a**, after reacting for one hour, from 0 °C to room temperature, **5a** was obtained as the resulting product in 73% isolated yield (see Scheme 7). Furthermore, the influence of the solvent over the reaction outcome was tested and the following information was gathered. Thus, full consumption of **1a** occurred in comparable time for the case of reactions conducted in dichloromethane or toluene, but giving **5a** in slightly lower yield for the case of the latter solvent. Conversely, the reaction in acetonitrile was inefficient, and only 26% conversion of **1a** was noticed after 5 hours. Using 1,4-dioxane, the reaction gives **5a** in comparable yield, but requires significantly longer reaction time (5 hours). The effect of the concentration of the substrate was also analyzed. Reducing the initial concentration of **1a** with respect to the solvent to 0.2 M resulted in lower yield for the formation of **5a** (54%). Additional information concerning the impact of the structure of the silylated alcohol over the etherification was gathered using 1-phenylethylacetate **1a**, as model electrophile, see Scheme 8.

Thus, benzyl acetates bearing either a remote bromoalkyl or a challenging terminal alkynyl substituted-chain can be properly etherified using this protocol, as depicted for the synthesis of **5b** and **5c**. At the same time, the benzylic ester present in **1a** can be selectively activated by catalytic reaction with silyl benzyl ethers **4d** and **4**e leading to unsymmetrical dibenzyl ethers **5d** and **5e** in fairly good isolated yields without involving transition-metals or the help of strong bases. The reaction with (cyclohexyloxy)trimethylsilane **4f** is also feasible and gives **5f**, although it is a more sluggish process. Interestingly, the trimethylsilyl ether derived from adamantanol can be also benzylated using this approach, furnishing ether **5g**. However, the etherification did not proceed when **1a** was reacted with a tertiary nucleophile, such as the *O*-silylated derivatives of *t*-butanol or 2,3-dimethylbutan-2-ol. In both cases, unaltered **1a** was recovered upon treating the reagents with 5 mol% of triflimide for two hours (80 and 66%, respectively). On the other hand, the electrophile can be modified, as proved in catalytic reactions of (benzyloxy)trimethylsilane **4d** with esters **1j**, **1p** and **1b**, giving rise to the elaboration of ethers **5h**, **5i** and **5j**, respectively.

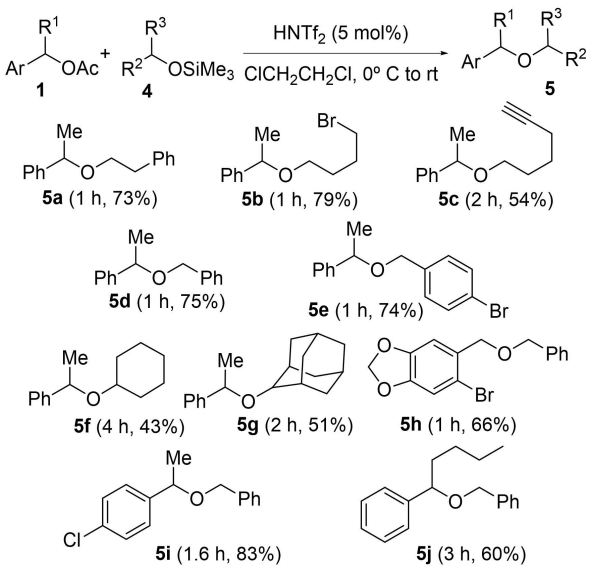
The stereochemical outcome of this this mild catalytic etherification was tested over (*S*)-1-phenylethylacetate as a chiral enantiopure probe (Scheme 9).

Again, as for the case of the previously referred alkynylation, (*S*)-**1a** was fully consumed upon reaction with **4d** in the presence of 10 mol% of $HNTf_2$. It was selectively transformed into **5d**, which was isolated in 74% yield as a racemic mixture. This control experiment provides strong support for a mechanistic connection between the catalytic etherification and alkynylation reactions herein presented.

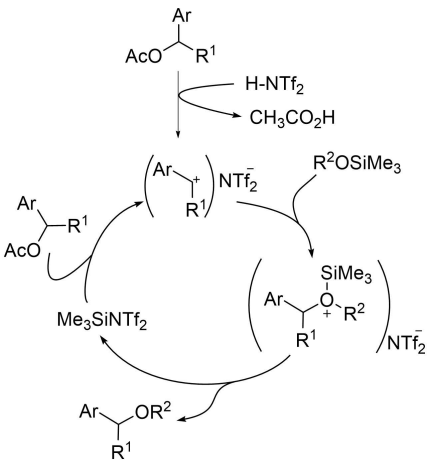
Additionally, the behavior of the starting acetate and alkoxysilane towards a catalytic amount of bistriflimide was also tested. NMR spectroscopy proved that the alkoxysilane remains essentially unaffected upon exposure to $HNTf_2$ of a solution of **4a** in 1,2-dichloroethane, for one hour at room temperature. On the contrary, related treatment of a solution of **1a** showed significant decomposition. Thus, on the basis of the features of the reaction and of the reported control experiments, the mechanism outlined in Scheme 10 is proposed to account for this etherification reaction.



Scheme 9. Stereochemical course of $HNTf_2$-catalyzed ether preparation.



Scheme 8. Mild ether formation from ROTMS and benzyl acetates upon addition of 5 mol% of $HNTf_2$ (10 mol% for **5d**).



Scheme 10. Proposed mechanistic evolution of the etherification reaction.

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On the basis of the quoted reactivity for both substrates towards bistriflimide, the activating step might reasonably invoke a ionization of the ester by interaction with bistriflimide, giving rise to a benzyl cation, which subsequently would be trapped by the alkoxysilane.[35] The release of the product liberates Me_3SiNTf_2 that, afterwards, will account for the formation of the product along the remaining cycles.

Conclusion

In summary, C- and O-silyl masked nucleophiles take advantage of the leaving ability of the acetate function to establish selective protocols to accomplish valuable alkynylation and etherification reactions of benzylic positions. Catalytic addition of bistriflimide launches these transformations, which take place under mild reaction conditions. Testing both processes over an enantiopure substrate provides consistent results supporting a cationic path for their conversion into the products. Furthermore, decent functional group tolerance and fair to good figures for isolated yields of the target products are attributes of this flexible catalytic strategy, both in terms of the nucleophile and the electrophile. The facile elaboration of these building blocks from simple precursors is complementary to others based on transition metal catalysts.

Experimental Section

General Remarks. Alkynylation and etherification reactions were performed in a RR9803012 place Carousel Reaction Station™ from Radleys Discovery Technologies, equipped with gastight threaded caps with a valve, cooling reflux head system, and digital temperature controller. All reactions were carried out using oven dried glassware under an atmosphere of nitrogen (99.99%) or argon (99.999%), unless otherwise noted. Commercial reagents were purchased with the best quality affordable and used without further purification unless otherwise noted. 1,2-Dichloroethane, dichloromethane and methanol were distilled from CaH_2 prior its use. Toluene and acetonitrile were purified through an Innovative Technology System, provided with two one meter length columns, filled with activated alumina. TLC was performed on aluminium-backed plates coated with silica gel 60, with F245 indicator, and developed using phosphomolybdic acid or *p*-anisaldehyde stains. Column chromatography was carried out on silica gel (230–400 mesh). Solvents used in column chromatography (hexane and ethyl acetate) were obtained from commercial suppliers and used without further purification unless otherwise noted. HPLC separations were carried out using a Waters® UHPLC ACQUITY Arc™ System equipment provided with a 2998 PDA detector and an oven for thermal management of the separation conditions. ^{1}H-NMR (300, 400 MHz) and ^{13}C-NMR (75, 100 MHz) spectra were measured in $CDCl_3$, at room temperature, on a Bruker DPX-300 MHz, Bruker AV-300 MHz, and Bruker AV-400 MHz instruments, with $CDCl_3$ (^{1}H-NMR $\delta = 7.26$, ^{13}C-NMR $\delta = 77.2$) as internal standard. Data are reported as follows: chemical shift, multiplicity (s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet, etc.), coupling constants (*J* in Hz) and integration. ^{13}C multiplicities were assigned by DEPT techniques. High resolution mass spectra (HRMS) were determined by the University of Vigo (CACTI) with a Bruker Microflex spectrometer, and the University of Oviedo with a Bruker Impact II spectrometer. For characterization data and copies of the corresponding spectra, see the Supporting Information.

General procedures for preparation of starting materials and catalysts

Preparation of $HNTf_2$. 0.5 mmol of commercially available $LiNTf_2$ were placed in a round bottom flask provided with a stirring bar and 1 mL of concentrated sulfuric acid was added. A distillation system provided with a two-necked collector flask (also with a stirring bar inside) was attached and the mixture was heated at 90 °C under reduced pressure (0.1 mmHg). Solid $HNTf_2$ sublimated under these conditions and was collected in the two-necked flask, which was cooled with an ice bath. After completion of the distillation, the collecting flask was filled with argon. This procedure was found to afford a 60% yield of the product for this amount of starting material (yields were found not reproducible for less than 0.5 mmol of starting $LiNTf_2$).

Preparation of $TMSNTf_2$. 300 μL of allyltrimethylsilane were added to the collector flask with the sublimated $HNTf_2$, and the mixture was stirred at room temperature for 1 hour. The excess of allyltrimethylsilane was eliminated under reduced pressure and $TMSNTf_2$ was obtained as a colorless liquid in quantitative yield. Subsequently, and always under an argon atmosphere, a 0.1 M solution of the $TMSNTf_2$ in the reaction solvent is made and used immediately.

Preparation of acetates 1. All compounds **1** were obtained from acylation of the corresponding benzylic alcohol, using previously reported conditions in the literature[36] Enantiopure compound (*S*)-**1 a** was prepared by acylation of commercially available alcohol (*S*)-1-phenylethanol (> 99%ee) and was obtained as a single enantiomer.[34] The enantiomeric excess was analyzed by HPLC (Chiracel® OD–H, hexane/isopropanol 99:1, 0.5 mL/min); *rac*-**1 a**: 14.840 min (50.17%), 16.052 (49.83%); (*S*)-**1 a**: 14.551 min (> 99.9%).

Preparation of alkynylsilanes 2. Trimethyl(phenylethynyl)silane was obtained from commercial suppliers and distilled prior its use. 6-(trimethylsilyl)hex-5-yn-1-yl acetate was prepared according to a reported procedure in literature.[37]

General procedure for the alkynylation reaction

0.2 mmol (1 equiv) of acetate **1** and 0.8 mmol of alkynylsilane **2** (4 equiv) were dissolved in 0.3 mL of 1,2-dichloroethane, under argon atmosphere. Subsequently, 0.1 mL of a 0.1 M solution of freshly prepared $HNTf_2$ in 1,2-dichloroethane were added at 0 °C. The reaction mixture was stirred at the corresponding temperature during the time indicated in Scheme 4. Then, 0.2 mL of toluene were added to the crude reaction mixture and 1,2-dichloroethane was eliminated under reduced pressure. The product contained in the remaining toluene solution was purified by column chromatography in silica gel (the excess of **2** was separated first with hexane and then the product was eluted using hexane or hexane/ethyl acetate mixtures) to afford the corresponding product **3**.

General procedure for the etherification reaction

0.2 mmol (1 equiv) of acetate **1** and 0.8 mmol of silyl ether **4** (4 equiv) were dissolved in 0.3 mL of 1,2-dichloroethane, under an argon atmosphere. The mixture was cooled to 0 °C. Subsequently, 0.1 mL of a 0.1 M solution of freshly prepared $HNTf_2$ in 1,2-dichloroethane were added at 0 °C. The reaction mixture was stirred at rt during the time indicated in Scheme 8. Upon completion, the solution was filtered through a short path of basic alumina, with

copious rinsing using dichloromethane, in order to remove the catalyst and convert the excess of starting silyl ether into the corresponding alcohol. 0.2 mL of toluene were added to the crude mixture and other solvents were eliminated under reduced pressure. The product contained in the remaining toluene solution was purified by column chromatography in silica gel using hexanes/ethyl acetate mixtures to afford the corresponding product **5**.

Acknowledgements

Agencia Estatal de Investigación (AEI), Fondo Europeo de Desarrollo Regional (FEDER), is acknowledged for financial support, grants CTQ2016-76840-R (AEI/FEDER/UE) and AEI (PID2019-107469RB–I00/AEI/10.13039/501100011033). B. R. is grateful to the Ministerio de Educación, Cultura y Deporte of Spain for a FPU-predoctoral fellowship.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: Alkynes · Bistriflimide · Catalysis · Cations · Ethers

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Manuscript received: January 19, 2022
Revised manuscript received: April 4, 2022
Accepted manuscript online: April 5, 2022