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Gold-catalyzed substitution reaction with *ortho*-alkynylbenzoic acid alkyl ester as an efficient alkylating agent

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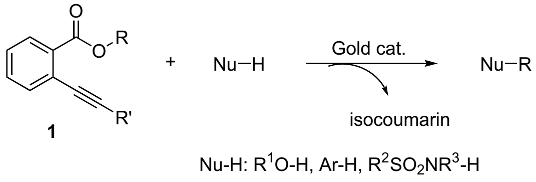
ABSTRACT

ortho-Alkynylbenzoic acid alkyl esters behave as alkylating agents in combination with gold catalysts. The reaction with alcohols occurs smoothly in the presence of catalytic amounts of Ph_3PAuCl and AgOTf under mild conditions to produce the corresponding ether products in high yields. The protocol is also useful for Friedel–Crafts alkylation and N-alkylation of sulfonamides. The reaction likely proceeds through the gold-induced in situ construction of leaving groups and subsequent nucleophilic attack of nucleophiles, such as alcohols, aromatic compounds, and sulfonamides.

1. Introduction

Substitution reactions are of prime importance in organic chemistry. Lewis acid is one of the most frequently used catalysts for this type of reaction and a number of effective reactions have been reported.[1] Generally, Lewis acids activate electrophiles by their strong affinities toward heteroatoms of the leaving groups, such as acetate, acetal, and epoxide. Recently, the direct catalytic substitution of alcohols has received considerable attention since the products are produced with water as the only waste.[2] However, with these methods, the substrate is generally limited to the reactive alcohols, such as allyl, propargyl, and benzyl alcohols, due to the poor leaving group ability of the hydroxyl group. In recent years, gold complexes have emerged as a powerful Lewis acid catalyst due to its unique ability to activate C–C multiple bonds as soft and carbophilic Lewis acids, allowing for the formation of new C–C, C–O, C–N, and C–S bonds by nucleophilic attack to these activated substrates.[3] As part of a program aimed at expanding the synthetic utility of the gold catalyst in the substitution reaction,[4] we have recently reported a gold-catalyzed alkylation of alcohols and aromatic compounds by using *ortho*-alkynylbenzoic acid alkyl ester **1** as novel electrophiles, leading to ether and Friedel–Crafts alkylation products in good to high yields under mild conditions.[5] In this paper, we report an N-alkylation method of sulfonamides inter- and intramolecularly based on this concept along with a detailed study on the etherification and the Friedel–Crafts alkylation (Scheme 1).[6,7]



Scheme 1.

2. Results and discussion

2.1. Etherification

We started this study with the reaction of *ortho*-alkynylbenzoic acid benzyl ester **1a** with phenethyl alcohol **2a** as we previously reported[5] and the results are summarized in Table 1. When we examined the reaction of **1a** (1 equiv) with **2a** (1.5 equiv) in the presence of 10 mol % of $AuCl_3$ at room temperature for 3 h, the desired benzyl phenethyl ether **3a** was obtained in 6% yield together with isocoumarin **5a** and the recovered starting material **1a** in 20 and 55% yields, respectively (entry 1). This result prompted us to optimize the reaction conditions with various kinds of gold

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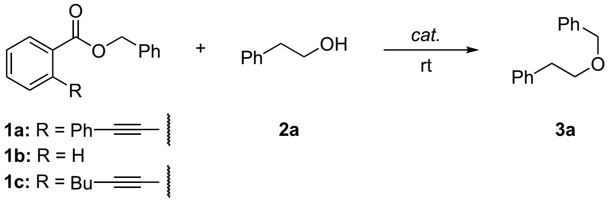
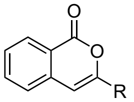
Table 1
The reaction of *ortho*-alkynylbenzoic acid alkyl esters **1** with alcohols **2**[a]



Entry	**1**	Cat.	Solvent	Time	Yield (%)[b]		
					3a	**4**	**1**
1[c]	**1a**	$AuCl_3$	$(ClCH_2)_2$	3 h	6	0	55
2[c]	**1a**	$AuBr_3$	$(ClCH_2)_2$	3 h	21	0	50
3[c]	**1a**	Ph_3PAuCl–AgOTf	$(ClCH_2)_2$	3 h	64	7	0
4[c]	**1b**	Ph_3PAuCl–AgOTf	$(ClCH_2)_2$	3 h	0	0	99
5[c]	**1a**	Ph_3PAuCl–$AgBF_4$	$(ClCH_2)_2$	3 h	45	7	0
6[c]	**1a**	Ph_3PAuCl–$AgSbF_6$	$(ClCH_2)_2$	3 h	34	4	0
7[c]	**1a**	Ph_3PAuCl–$AgPF_6$	$(ClCH_2)_2$	3 h	19	6	7
8[c]	**1a**	Ph_3PAuCl	$(ClCH_2)_2$	3 h	0	0	100
9[c]	**1a**	AgOTf	$(ClCH_2)_2$	3 h	0	0	100
10	**1a**	Ph_3PAuCl–AgOTf	$(ClCH_2)_2$	12 h	86	7	0
11	**1a**	Ph_3PAuCl–AgOTf	C_6H_6	1 h	84	8	0
12	**1a**	Ph_3PAuCl–AgOTf	C_6H_5Cl	1 h	81	9	0
13	**1a**	Ph_3PAuCl–AgOTf	THF	3 h	48	15	0
14	**1a**	Ph_3PAuCl–AgOTf	CH_3CN	3 h	0	0	95
15	**1c**	Ph_3PAuCl–AgOTf	C_6H_5Cl	1 h	87	6	0
16[d]	**1c**	Ph_3PAuCl–AgOTf	C_6H_5Cl	1 h	80	12	—
17	**1c**	TfOH	C_6H_5Cl	1 h	0	0	100

$(PhCH_2)_2O$ **4**



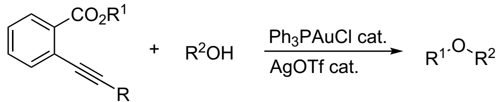
5a: R = Ph
5b: R = Bu

[a] Reactions were carried out using **1** (1 equiv) and **2a** (3 equiv) in the presence of catalyst (5 mol %) at room temperature unless otherwise noted.
[b] Determined by ^1H NMR spectra using *p*-xylene as an internal standard.
[c] Reactions were carried out using **1a** (1 equiv) and **2a** (1.5 equiv) in the presence of catalyst (10 mol %) at room temperature.
[d] Reaction was conducted using **1c** (3 equiv) and **2a** (1 equiv).

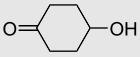
catalysts. Although the chemical yield of **3a** was low with $AuBr_3$ (entry 2), it was improved significantly by the cationic gold catalyst, derived from Ph_3PAuCl and AgOTf, and **3a** was obtained in 64% yield along with a small amount of dibenzyl ether **4** (entry 3). In contrast, any substitution products were not generated in the reaction of benzyl benzoate **1b**, having no alkynyl group at the *ortho*-position, with **2a**, and **1b** was recovered nearly quantitatively (entry 4). Obviously, these results suggest that the alkynyl moiety of **1a** is essential for the current etherification. Other silver additives, such as $AgBF_4$, $AgSbF_6$, and $AgPF_6$, were not effective and **3a** was obtained in lower yields (entries 5–7). Neither Ph_3PAuCl nor AgOTf promoted the reaction (entries 8–9). Interestingly, the use of 3 equiv of **2a** and 5 mol % of catalyst increased the chemical yield of **3a** to 86% although a longer reaction time was needed for completion (entry 10). To our delight, however, we found that the reaction was dramatically accelerated by just changing the solvent from $(ClCH_2)_2$ to benzene or chlorobenzene and **3a** were obtained in high yields within a shortened period (1 h) (entries 11 and 12). THF and CH_3CN were not suitable solvents in the present reaction (entries 13 and 14). The etherification proceeded not only with **1a** but also with *ortho*-hexynylbenzoic acid benzyl ester **1c**, and **3a** was produced in 87% yield (entry 15). In entries 10–12 and 15, isocoumarins **5** were formed nearly quantitatively in each reaction, which would be generated by the gold-catalyzed electrocyclization of **1** (vide infra).[8] The reaction also proceeded smoothly when 3 equiv of **1c** was used over **2a** (entry 16). In the current catalyst system, TfOH might be produced during the reaction. In order to clarify the effect of TfOH, we conducted the reaction with 5 mol % of TfOH instead of the gold catalyst. However, no reaction occurred with TfOH catalyst and this result clearly indicates that the gold complex works as a catalyst in the current transformations (entry 17).

To explore the synthetic utilities of the present etherification method, we examined reactions with various combinations of esters **1** and alcohols **2** and the results are summarized in Table 2. The reaction of primary alkyl ester **1d** with dodecanol **2b** proceeded at 80 °C for 5 h to give didodecyl ether **3b** in 50% yield (entry 1). The chemical yield was increased up to 86% by changing the substituent at the terminus of the alkynyl moiety of **1** from phenyl group to *ortho*-anisyl group although longer reaction times were needed (entries 2 and 3). Probably, the methoxy moiety of the anisyl group would assist the coordination of the alkynyl part of **1** to the gold catalyst, which facilitates the substitution reaction. Other examined reactions proceeded smoothly at room temperature to give the corresponding ether products in good to high yields (entries 4–11). The reactions with *p*-methoxybenzyl (PMB) ester **1g** afforded the corresponding ethers in good to high yields together with a small amount of 4-(4-methoxybenzyl)-3-butyl-1*H*-isochromen-1-one **6a** (entries 5, 8, and 10). This type of rearrangement reaction has been reported by Fürstner and Davies in the reaction of *ortho*-alkynylbenzoic acid ester with $PtCl_2$ catalyst under CO atmosphere.[9,10] It is noteworthy that ester, ketone, and nitrile groups in **2e–h** were inert during the reaction and the corresponding products **3g–j** were obtained in good yields, respectively (entries 8–11). A large number of catalytic etherification methods have been reported on the basis of the substitution reactions.[11] Dehydration of alcohols with metal catalysts is a direct approach for the synthesis of ethers and such protocols have been recently studied well.[12] Transition metal-catalyzed C–O bond formations from allyl and propargyl esters with alcohols are also attractive way.[13] However, there are still limitations on substrates and drawbacks such as the requirement of elevated temperature and long reaction time in the known procedures. In contrast, neither severe reaction conditions

Table 2
The gold-catalyzed etherification of alcohols **2** with *ortho*-alkynylbenzoic acid alkyl esters **1**[a]



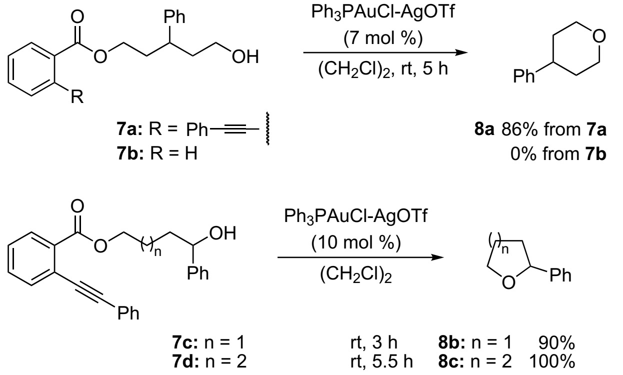
1 **2** **3**

Entry	**1**	R	R^1	**2**	R^2OH	Conditions		Yield (%)[b]
1[c]	**1d**	Ph	$C_{12}H_{25}$	**2b**	$C_{12}H_{25}OH$	80 °C, 5 h	**3b**	50
2[c]	**1e**	*o*-Anisyl	$C_{12}H_{25}$	**2b**	$C_{12}H_{25}OH$	80 °C, 12 h	**3b**	80
3[c,d]	**1e**	*o*-Anisyl	$C_{12}H_{25}$	**2b**	$C_{12}H_{25}OH$	80 °C, 18 h	**3b**	86
4	**1f**	Bu	iPr	**2a**	$PhCH_2CH_2OH$	rt, 12 h	**3c**	73
5	**1g**	Bu	PMB	**2a**	$PhCH_2CH_2OH$	rt, 1 h	**3d**	92[e]
6	**1c**	Bu	$PhCH_2$	**2c**	*c*-$C_6H_{11}OH$	rt, 3 h	**3e**	70[f,g]
7	**1c**	Bu	$PhCH_2$	**2d**	*t*-BuOH	rt, 1 h	**3f**	90
8	**1g**	Bu	PMB	**2e**	$EtOCOCH_2OH$	rt, 1 h	**3g**	70[e]
9	**1c**	Bu	$PhCH_2$	**2f**	$AcO(CH_2)_2OH$	rt, 1 h	**3h**	70[f]
10	**1g**	Bu	PMB	**2g**		rt, 1 h	**3i**	69[e]
11	**1c**	Bu	$PhCH_2$	**2h**	$NC(CH_2)_2OH$	rt, 16 h	**3j**	75[f]

[a] Reactions were carried out using **1** (1 equiv) and **2** (3 equiv) in the presence of Ph_3PAuCl (5 mol %) and AgOTf (5 mol %) in C_6H_5Cl unless otherwise mentioned.
[b] Isolated yields.
[c] Reactions were conducted in C_6H_6.
[d] Reaction was conducted using **1e** (3 equiv) and **2b** (1 equiv).
[e] Compound **6a** was obtained in 8% (entry 5), 9% (entries 8), and 12% (entry 10) yield.
[f] Compound **4** was obtained in 9% (entry 6) and 7% (entries 9 and 11).
[g] Determined by ^1H NMR spectra using *p*-xylene as an internal standard.

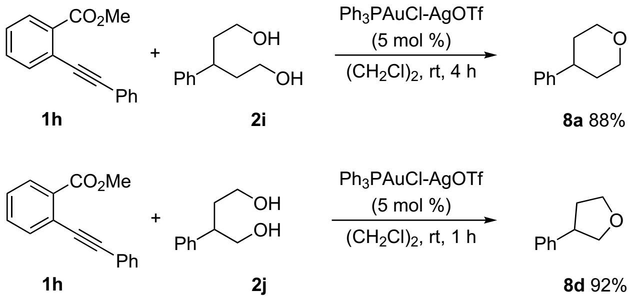
nor highly reactive electrophiles are necessary in the current catalytic system.

The cyclic ether compounds were also prepared with the current etherification method. When we treated **7a** with the gold catalyst, the six-membered cyclic ether product **8a** was formed in 86% yield. In contrast, no reaction occurred with **7b**, which has no alkynyl group at the *ortho*-position. The reactions of **7c** and **7d** also gave **8b** and **8c** in 90 and 100% yields, respectively (Scheme 2).



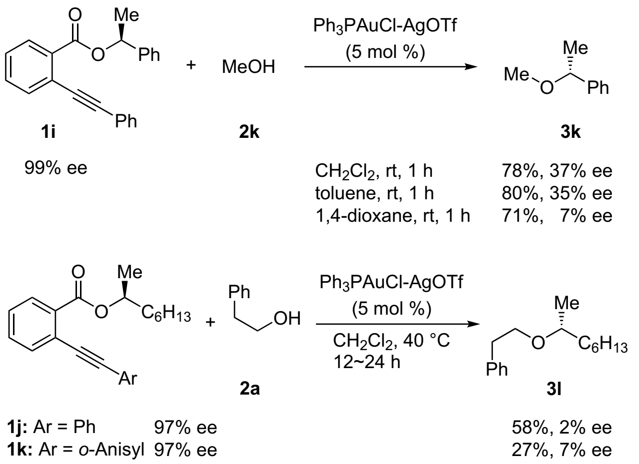
Scheme 2.

It is worth mentioning that the current cyclization can be conducted directly with diol compounds and methyl ester **1h** without preparation of the corresponding esters **7**. Indeed, treatment of 3-phenylpentane-1,5-diol **2i** with 1.5 equiv of **1h** in the presence of the gold catalyst resulted in the formation of **8a** in 88% yield at room temperature for 4 h. Analogously, **8d** was produced from **2j** in high yield (Scheme 3). These direct cyclizations would be explained by the gold-catalyzed transesterification of **1h** with diols **2i**,**j**, allowing in situ construction of the corresponding esters **7** under the reaction conditions.[14]



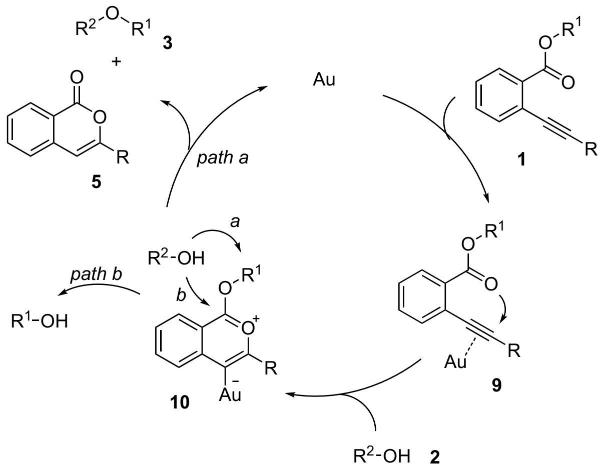
Scheme 3.

We applied this method to the etherification of chiral esters **1i**–**k** (Scheme 4). First, the reaction of secondary benzylic ester (*S*)-**1i** with MeOH **2k** was carried out in CH_2Cl_2. The reaction proceeded smoothly at room temperature for 1 h and the corresponding ether **3k** was obtained in 78% yield. The absolute configuration of **3k** was determined to be *R* by comparison of the observed optical rotation to a literature value for (*R*)-(1-methoxyethyl)benzene.[15] The enantiomeric excess was 37%, which suggests that the reaction between **1i** and **2k** involves S_N1 mechanism having some S_N2 character. Although the reactions were conducted with other solvents, such as toluene and 1,4-dioxane, ee values of **3k** were not improved. We then conducted the reactions of non-benzylic esters (*S*)-**1j**,**k** with **2a**. However, the corresponding ether product **3l** was generated in nearly racemic form in both reactions. We treated (*S*)-**1j** with the gold catalyst in the absence of **2a** to know whether the racemization occurs or not under the reaction conditions. Although the enantio purity of (*S*)-**1j** was slightly decreased from 97 to 96% ee after 12 h at 40 °C, racemization was not observed. These results clearly indicated that the reactions between **1j**,**k** and **2a** proceed via S_N1 mechanism.



Scheme 4.

A plausible mechanism for the gold-catalyzed etherification is shown in Scheme 5.[16] The gold catalyst enhances the electrophilicity of the alkynyl part of **1**, leading to the formation of a zwitterionic intermediate **10** via the intramolecular nucleophilic attack of the carbonyl oxygen to the alkyne as shown in **9**.[17,18] Due to the strong electrophilicity of **10**, the nucleophilic attack of alcohol **2** to R^1 part of **10** would occur to give ether compound **3** together with isocoumarin **5** (path a). In the reactions of benzyl esters **1a**,**c**, a small amount of dibenzyl ether **4** was obtained as a byproduct. Probably, benzyl alcohol was liberated from **1a**,**c** by the attack of alcohol **2** to intermediate **10** as shown by the arrow (path b), and then it works as a nucleophile to give **4**.[14] The reaction of **1h** with diols **2i**,**j** would also proceed through the similar alcohol exchange pathway.

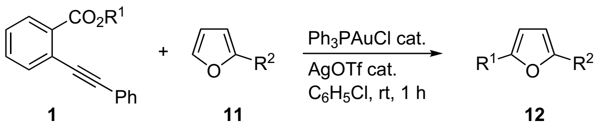


Scheme 5.

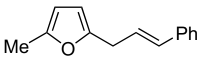
2.2. Friedel–Crafts reaction

To extend the synthetic utilities of the gold-catalyzed alkylation methods, we next turned our attention to the Friedel–Crafts alkylation.[19] It is generally difficult to introduce alkyl substituents on π-rich heteroaromatics under the traditional Friedel–Crafts conditions because of catalyst-promoted polymerization and polyalkylation.[20]

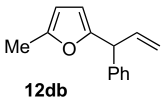
Table 3
The gold-catalyzed Friedel–Crafts alkylation of furan[a]



Entry	1	R^1	11	R^2	12	Yield (%)[b]
1[c]	**1a**	PhCH$_2$	**11a**	H	**12a**	70
2	**1a**	PhCH$_2$	**11b**	Me	**12b**	80
3	**1l**	PMB	**11b**	Me	**12c**	72
4	**1m**	PhCH=CHCH$_2$	**11b**	Me	**12d**	61 (7:3)[d]



12da

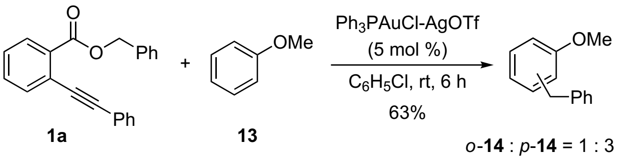


12db

[a] Reactions were carried out using **1** (1 equiv) and **11** (5 equiv) in the presence of Ph$_3$PAuCl (5 mol %) and AgOTf (5 mol %) in C$_6$H$_5$Cl at room temperature within 1 h unless otherwise noted.
[b] Isolated yields.
[c] Reaction was conducted with 10 equiv of **11a**.
[d] The ratio of **12da** and **12db**.

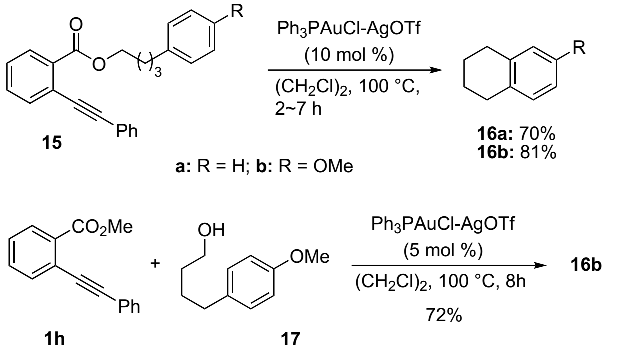
Recently, some effective synthetic methods of poly-substituted heteroaromatics based on the substitution reactions with lanthanide triflates[21] and transition metal catalysts[22] have been reported. However, there are still drawbacks such as the necessity of high temperature and long reaction time. In this context, we conducted the gold-catalyzed Friedel–Crafts alkylation of furan and the results are summarized in Table 3.[23] The benzylation reactions proceeded smoothly at room temperature for 1 h, and the corresponding products **12** were obtained in good yields, respectively (entries 1–3). When we examined the reaction of cinnamyl ester **1m**, a mixture of **12da** and **12db** was obtained in 61% yield with a 7:3 ratio (entry 4).

The reaction of **1a** with anisole **13** also proceeded smoothly to give a benzylation product **14** in 63% yield as a mixture of *ortho*- and *para*-isomers in a 1:3 ratio (Scheme 6).



Scheme 6.

Intramolecular Friedel–Crafts alkylation reaction has been used as an effective synthetic method of cyclic compounds.[24] However, only a few examples have been known for synthesis of simple tetralines from primary alkyl halides, alcohols, and their derivatives.[25] When the reaction of **15a** was carried out with the gold catalyst at 100 °C for 7 h, the cyclized product **16a** was obtained in 70% yield. The reaction proceeded much smoothly with **15b**, having methoxy group on the benzene ring, and **16b** was obtained in 81% yield under 100 °C for 2 h. In Scheme 3, we showed that the intramolecular etherification proceeded with diols. We wondered if it is possible to extend such protocol to the Friedel–Crafts alkylation. To our delight, cyclization of **17** also proceeded in the presence of **1h**, and **16b** was constructed in 72% yield (Scheme 7).

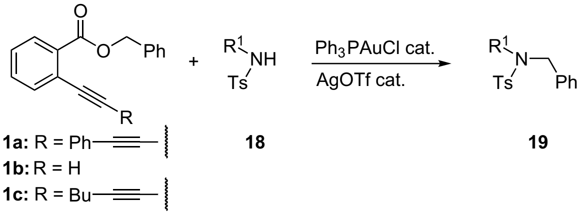


Scheme 7.

2.3. N-Alkylation of sulfonamides

Catalytic C–N bond formations have received significant interest in organic synthesis,[26] since substituted amines are of considerable importance in the pharmaceutical, agrochemical, and fine chemical industries.[27] A number of effective methods have been reported, such as transition metal-catalyzed amination of aryl halides,[28] hydroamination,[29] hydroaminomethylation,[30] and reductive amination.[31] Although direct aminations of reactive alcohols, such as allyl alcohols and propargyl alcohols, have been reported,[2,32] an efficient and convenient method with wide applicability is still needed. We applied our alkylation method for the substitution reaction of sulfonamides **18** and the results are summarized in Table 4. The reaction of **1a** with 2 equiv of *N*-methyl-*p*-toluene sulfonamide **18a** (R^1=Me) proceeded smoothly at room temperature for 1 h in the presence of 10 mol % of Ph$_3$PAuCl and AgOTf in benzene and N-benzylation product **19a** was obtained in 75% (entry 1). The chemical yield of **19a** was increased to 99% yield when the reaction was carried out in 1,4-dioxane (entry 3). The reaction proceeded even in the presence of 3 mol % catalyst, affording **19a** in 91% yield (entry 4). On the other hand, no reaction took place with either Ph$_3$PAuCl or AgOTf only. The reaction was not catalyzed by TfOH (10 mol %) and any products were not obtained even after 1 day at room temperature. The reaction of benzyl benzoate **1b**, having no alkynyl group at the *ortho*-position, with **18a** did not take place at all even under 100 °C for 2 h and the starting material was recovered nearly quantitatively. The reaction of **1c**, bearing a hexynyl group at the *ortho*-position, with **18a** also proceeded well, and **19a** was produced in 98% yield (entry 5). We also conducted the reaction with other sulfonamides **18b–d**. In the reaction of **1a** with *N*-benzyl-*p*-toluene sulfonamide **18b** (R^1=Bn), the chemical yield of the desired N-alkylation product **19b** was

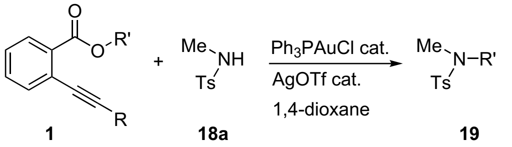
Table 4
The reaction of sulfonamides **18** with **1**[a]



Entry	1	R	18	R^1	Cat.	Solvent	19	Yield (%)[b]
1	**1a**	Ph	**18a**	Me	10 mol %	C$_6$H$_6$	**19a**	75
2	**1a**	Ph	**18a**	Me	10 mol %	(CH$_2$Cl)$_2$	**19a**	77
3	**1a**	Ph	**18a**	Me	10 mol %	1,4-Dioxane	**19a**	99
4	**1a**	Ph	**18a**	Me	3 mol %	1,4-Dioxane	**19a**	91
5	**1c**	Bu	**18a**	Me	3 mol %	1,4-Dioxane	**19a**	98
6	**1a**	Ph	**18b**	Bn	3 mol %	1,4-Dioxane	**19b**	50[d]
7	**1a**	Ph	**18c**	Ph	3 mol %	1,4-Dioxane	**19c**	82
8[c]	**1a**	Ph	**18d**	H	3 mol %	1,4-Dioxane	**19d** (**18b**)	70[d]

[a] Reactions were conducted at room temperature for 1 h unless otherwise noted.
[b] Isolated yields.
[c] Reaction was conducted at 100 °C for 0.3 h.
[d] 4-Benzyl-3-phenyl-1*H*-isochromen-1-one (**6b**) was obtained in 29% (entry 6) and 12% (entry 8) yield.

Table 5
The gold-catalyzed N-alkylation of sulfonamides **18a** with **1**



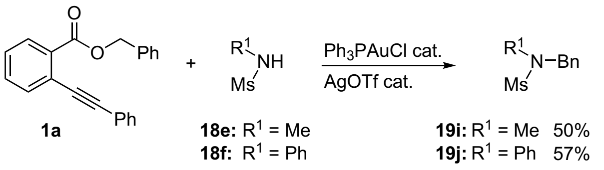
Entry	**1**	R	R′	Cat.	Conditions	**19**	Yield (%)[a]
1	**1n**	Ph	Allyl	3 mol %	rt, 13 h	**19e**	98
2	**1o**	Bu	Allyl	3 mol %	rt, 13 h	**19e**	90
3	**1p**	Ph	$PhC{\equiv}CCH_2$	10 mol %	100 °C, 1 h	**19f**	87
4	**1q**	Bu	$PhC{\equiv}CCH_2$	10 mol %	100 °C, 1 h	**19f**	81
5	**1r**	Ph	$PhCH_2CH_2$	10 mol %	100 °C, 2 days	**19g**	81
6	**1s**	Bu	Me	3 mol %	100 °C, 6 h	**19h**	57

[a] Isolated yields.

decreased to 50% yield probably due to the steric hindrance of **18b**. Besides **19b**, the rearranged product, 4-benzyl-3-phenyl-1*H*-isochromen-1-one (**6b**), was produced in 29% yield (entry 6).[9] Not only alkyl-substituted sulfonamides but also aryl-substituted **18c** (R^1=Ph) and non-substituted **18d** (R^1=H) worked well and the corresponding products **19c** and **19d** (=**18b**) were obtained in 82% and 70% yields, respectively (entries 7 and 8). In the reaction of **18d**, heating was necessary due to the low solubility of **18d** to the solvent.

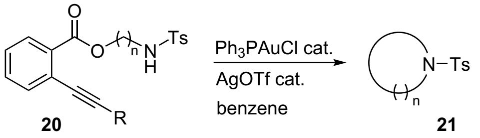
Because N-benzylations of sulfonamides occurred unexpectedly easily, we next examined the reaction of other benzoate esters **1n–s** with **18a** and the results are summarized in Table 5. N-Allylation of **18a** proceeded with allyl benzoates **1n**,**o** at room temperature for 13 h and the corresponding product **19e** was obtained in high yields in both reactions (entries 1 and 2). Phenylpropargyl esters **1p**,**q** also worked well as effective alkylating agents and the corresponding product **19f** was obtained under 100 °C in high yields (entries 3 and 4). We also conducted the reaction of esters consisting of simple primary alkyl groups. Generally, it is difficult to conduct the substitution reaction with simple primary alcohols or their derivatives under acidic conditions since the corresponding primary carbocation intermediates are highly unstable. However, the reaction of phenylethyl ester **1r** with **18a** proceeded to give **19g** in 81% yield although the longer reaction time was needed (entry 5). The methylation product **19h** was also obtained in 57% yield when the reaction was conducted with methyl ester **1s** (entry 6).

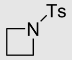
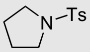
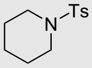
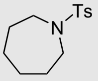
Besides *p*-toluene sulfonamides, methane sulfonamides are suitable nucleophiles in the present transformations as shown in Scheme 8. Benzylations of methyl- and phenyl-substituted amides **18e**,**f** proceeded smoothly with **1a** and the corresponding products **19i**,**j** were obtained in 50 and 57% yields, respectively.



Scheme 8.

Table 6
The gold-catalyzed intramolecular N-alkylation of sulfonamides **20**



Entry	**20**	*n*	R	Cat.	Conditions	**21**		Yield (%)[a]
1	**20a**	3	Ph	10 mol %	80 °C, 20 h	**21a**		61
2	**20b**	4	Ph	5 mol %	rt, 1 h	**21b**		91
3	**20c**	5	Bu	5 mol %	rt, 1 d	**21c**		85
4	**20d**	6	Bu	10 mol %	80 °C, 1.5 d	**21d**		22

[a] Isolated yields.

Since nitrogen heterocycles are quite often seen in a wide range of biologically active natural products, a lot of preparation methods have been developed.[33,34] We examined the cyclization reaction by the intramolecular N-alkylation and the results are summarized in Table 6. The requisite ω-sulfonamido-alkyl esters **20** were prepared from the corresponding aminoalcohols easily. The reaction of 3-sulfonamido-propyl ester **20a** proceeded at 80 °C for 20 h and the corresponding four-membered tosylazetidine **21a** was obtained in 61% yield (entry 1). Five- and six-membered products **21b**,**c** were produced from **20b**,**c** at room temperature in high yields (entries 2 and 3). The protocol can be used for the formation of seven-membered 1-tosylazepane **21d** although the chemical yield was low (entry 4).

We also constructed the cyclic sulfonamides from the reaction of ω-hydroxyalkyl-sulfonamides with methyl ester **1h**,**s** and results are summarized in Table 7. Treatment of *N*-(4-hydroxybutyl)-4-methylbenzenesulfonamide **22a** with 2.2 equiv of **1h** in the presence of the gold catalyst resulted in the formation of 1-tosylpyrrolidine **21b** in 98% yield at room temperature for 0.7 h (entry 1). Not only five-membered ring but also six-membered product **21c** was obtained via the direct cyclization in 80% yield (entry 2). The protocol was also useful for the synthesis of benzo-fused cyclic sulfonamides, 1-tosylindoline **21e** and 1-tosyl-1,2,3,4-tetrahydroquinoline **21f**, which were obtained in 78 and 75% yields, respectively (entries 3 and 4).

3. Conclusion

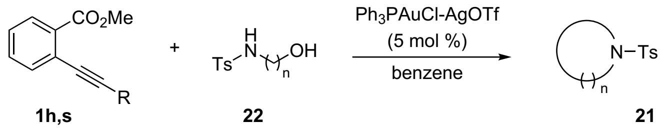
In summary, we have developed a new catalytic, practical etherification method of alcohols with a designed *ortho*-alkynylbenzoic acid alkyl ester **1** as an effective alkylating agent. The reaction likely proceeds through the gold-induced in situ construction of leaving groups and subsequent nucleophilic attack of alcohols. The synthetic utility of the current protocol is further enhanced by its ability to promote the Friedel–Crafts alkylation and N-alkylation of sulfonamides under relatively mild conditions. Moreover, intramolecular versions of these three kinds of reactions can be conducted with methyl esters **1h**,**s** without preparation of the corresponding esters **7**, **15**, **20**. Further studies to extend the scope of synthetic utility are in progress in our laboratory.

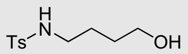
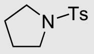
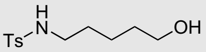
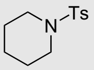
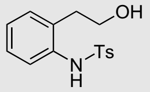
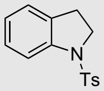
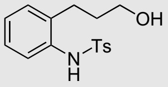
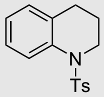
4. Experimental

4.1. General

NMR spectra were measured at 400 MHz for ^1H and 100 MHz for ^{13}C by JEOL JNM-AL 400 spectrometer. Chemical shifts of ^1H NMR were expressed in parts per million downfield from tetramethylsilane with reference to internal residual $CHCl_3$ (δ=7.26) in $CDCl_3$. Chemical shifts of ^{13}C NMR were expressed in parts per million downfield from $CDCl_3$ as an internal standard (δ=77.0) in $CDCl_3$. High performance liquid chromatography (HPLC) was performed on JASCO LC-2000 plus series system with Daicel Chiralcel$^{®}$

Table 7
The gold-catalyzed cyclization of ω-hydroxyalkyl-sulfonamides **22** with **1**



Entry	1	R	22	*n*		Conditions	21		Yield (%)[a]
1	**1h**	Ph	**22a**	4		rt, 0.7 h	**21b**		98
2	**1s**	Bu	**22b**	5		rt, 6 h	**21c**		80
3	**1s**	Bu	**22c**	4		rt, 5 h	**21e**		78
4	**1s**	Bu	**22d**	5		rt, 10 h	**21f**		75

[a] Isolated yields.

and Chiralpak® columns in hexane/isopropanol mixtures. High-resolution mass spectra (HRMS) were performed on BRUKER DALTONICS APEX III spectrometer. Optical rotations were measured on a JASCO P-2205 digital polarimeter. For thin layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (Kieselgel 60 F_{254}, 0.2 mm) were used. The products were purified by flash column chromatography on silica gel 60N (KANTO, 40–50 μm). All manipulations were carried out under argon atmosphere using standard Schlenk techniques.

4.2. General procedure of the intermolecular gold-catalyzed etherification

To a mixture of Ph_3PAuCl (12.4 mg, 5 mol %) and AgOTf (6.4 mg, 5 mol %) in chlorobenzene (2 mL) were added *ortho*-alkynylbenzoic acid alkyl ester **1** (0.5 mmol) and alcohol **2** (1.5 mmol) successively at room temperature under Ar atmosphere. The mixture was stirred until the total consumption of **1**. Then, a saturated aqueous solution of $NaHCO_3$ was added, and the mixture was extracted with ether three times. The combined extracts were washed with brine, dried ($MgSO_4$), and evaporated to leave the crude product, which was purified by silica gel column chromatography using a mixture of hexane and ether as an eluent to give the ether product **3**.

4.2.1. Benzyl 2-(phenylethynyl)benzoate (1a)

Light yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.03 (dd, *J*=7.9, 1.2 Hz, 1H), 7.66 (dd, *J*=7.6, 1.2 Hz, 1H), 7.50–7.30 (m, 12H), 5.43 (s, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.0, 135.7, 134.1, 131.7, 131.6, 131.6, 130.6, 128.5, 128.4, 128.3, 128.2, 128.1, 127.8, 123.7, 123.1, 94.4, 88.2, 67.1. IR (neat) 3063, 2953, 2218, 1726, 1495, 1288, 1246, 1126, 1070, 756, 692 cm^{-1}. GC–MS (EI) *m*/*z* 312 (M^+, 16), 91 (100). Anal. Calcd for $C_{22}H_{16}O_2$: C, 84.59; H, 5.16. Found: C, 84.43; H, 5.20.

4.2.2. Benzyl 2-(hex-1-ynyl)benzoate (1c)

Light yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.92 (dd, *J*=7.8, 1.5 Hz, 1H), 7.52–7.25 (m, 8H), 5.37 (s, 2H), 2.36 (t, *J*=7.1 Hz, 2H), 1.58–1.41 (m, 4H), 0.93 (t, *J*=7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.3, 135.9, 134.2, 131.6, 131.5, 130.2, 128.4, 128.2, 128.1, 127.0, 124.5, 96.2, 79.2, 66.8, 30.7, 22.1, 19.5, 13.7. IR (neat) 3065, 2957, 2872, 2230, 1738, 1456, 1286, 1244, 1126, 1074, 756, 698 cm^{-1}. GC–MS (EI) *m*/*z* 105 (M^+-187, 100). Anal. Calcd for $C_{20}H_{20}O_2$: C, 82.16; H, 6.89. Found: C, 82.27; H, 6.96.

4.2.3. Dodecyl 2-(phenylethynyl)benzoate (1d)

Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.97 (dd, *J*=8.1, 1.2 Hz, 1H), 7.65 (dd, *J*=7.8, 1.2 Hz, 1H), 7.58–7.56 (m, 2H), 7.49 (td, *J*=7.6, 1.2 Hz, 1H), 7.39 (dd, *J*=7.8, 1.5 Hz, 1H), 7.37–7.33 (m, 3H), 4.35 (t, *J*=6.6 Hz, 2H), 1.80–1.73 (m, 2H), 1.46–1.38 (m, 2H), 1.32–1.21 (m, 16H), 0.89 (t, *J*=7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.3, 134.0, 132.2, 131.6, 131.5, 131.4, 130.3, 128.4, 128.2, 127.7, 123.5, 123.3, 88.3, 65.5, 32.0, 29.7, 29.7, 29.6, 29.5, 29.4, 29.3, 28.8, 26.2, 22.7, 14.2. IR (neat) 2926, 2855, 1728, 1712, 1599, 1495, 1290, 1248, 1128, 1076, 756, 691 cm^{-1}. MS (EI) *m*/*z* 390 (M^+, 5), 222 (100). Anal. Calcd for $C_{27}H_{34}O_2$: C, 83.03; H, 8.77. Found: C, 83.14; H, 8.62.

4.2.4. Dodecyl 2-((2-methoxyphenyl)ethynyl)benzoate (1e)

Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.96 (dd, *J*=7.8, 1.2 Hz, 1H), 7.68 (dd, *J*=7.6, 1.2 Hz, 1H), 7.54 (dd, *J*=7.6, 1.7 Hz, 1H), 7.47 (td, *J*=7.6, 1.5 Hz, 1H), 7.36 (td, *J*=7.6, 1.2 Hz, 1H), 7.33–7.29 (m, 1H), 6.94 (td, *J*=7.6, 1.0 Hz, 1H), 6.91–6.89 (m, 1H), 4.35 (t, *J*=6.8 Hz, 2H), 3.92 (s, 3H), 1.79–1.72 (m, 2H), 1.44–1.37 (m, 2H), 1.32–1.21 (m, 16H), 0.89 (t, *J*=6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.4, 159.9, 134.1, 133.6, 132.0, 131.3, 130.2, 129.8, 127.6, 123.8, 120.3, 112.6, 110.6, 92.2, 90.8, 65.4, 55.8, 31.9, 29.7, 29.6, 29.6, 29.5, 29.4, 29.3, 28.7, 26.1, 22.7, 14.2. IR (neat) 2924, 2855, 1728, 1712, 1595, 1496, 1290, 1246, 1163, 1109, 754, 698 cm^{-1}. MS (EI) *m*/*z* 420 (M^+, 5), 234 (100). Anal. Calcd for $C_{28}H_{36}O_3$: C, 76.18; H, 4.79. Found: C, 76.10; H, 4.97.

4.2.5. Isopropyl 2-(hex-1-ynyl)benzoate (1f)

Light yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.84 (dd, *J*=7.8, 1.5 Hz, 1H), 7.49 (dd, *J*=7.6, 1.2 Hz, 1H), 7.39 (td, *J*=7.6, 1.4 Hz, 1H), 7.29 (td, *J*=7.6, 1.2 Hz, 1H), 5.27 (sept, *J*=6.3 Hz, 1H), 2.47 (t, *J*=7.1 Hz, 2H), 1.66–1.59 (m, 2H), 1.57–1.45 (m, 2H), 1.38 (d, *J*=6.3 Hz, 6H), 0.95 (t, *J*=7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.1, 134.1, 132.7, 131.0, 129.8, 127.0, 124.1, 95.6, 79.2, 68.5, 30.8, 22.2, 22.0, 19.6, 13.7. IR (neat) 3064, 2933, 2873, 2230, 1726, 1597, 1483, 1290, 1252, 1109, 1078, 918, 758, 702 cm^{-1}. GC–MS (EI) *m*/*z* 160 (M^+-84, 100). Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.69; H, 8.27.

4.2.6. 4-Methoxybenzyl 2-(hex-1-ynyl)benzoate (1g)

Light yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.89 (dd, *J*=7.9, 1.4 Hz, 1H), 7.50 (dd, *J*=7.8, 1.2 Hz, 1H), 7.42–7.38 (m, 3H), 7.28 (td, *J*=7.7, 1.5 Hz, 1H), 6.91 (m, 2H), 5.31 (s, 2H), 3.82 (s, 3H), 2.37 (t, *J*=7.0 Hz, 2H), 1.59–1.41 (m, 4H), 0.94 (t, *J*=7.2 Hz, 3H). ^{13}C NMR

($CDCl_3$, 100 MHz) δ 166.3, 159.4, 134.2, 131.8, 131.4, 130.2, 130.0, 128.0, 127.0, 124.5, 113.8, 96.1, 79.2, 66.7, 55.3, 30.7, 22.1, 19.5, 13.7. IR (neat) 3065, 2957, 2230, 1728, 1614, 1516, 1286, 1244, 1177, 1126, 1076, 1038, 827, 758, 700 cm^{-1}. GC–MS (EI) m/z 322 (M^+, 3), 121 (100). Anal. Calcd for $C_{21}H_{22}O_3$: C, 78.23; H, 6.88. Found: C, 78.17; H, 6.83.

4.2.7. *(S)-1-Phenylethyl 2-(phenylethynyl)benzoate (**1i**)*

The ee was determined on an AD-H column (hexanes/isopropanol 97:3, flow 0.4 mL/min) with t_R (minor) 23.1 min, t_R (major) 30.2 min: 99% ee. $[\alpha]_D^{19}$ −16.5 (c 0.11, cyclohexane). Brown oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.11 (m, 1H), 7.66 (m, 1H), 7.49 (m, 5H), 7.39 (m, 1H), 7.33 (m, 6H), 6.20 (q, J=6.4 Hz, 1H), 1.69 (d, J=9.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.5, 141.5, 134.1, 132.0, 131.6, 131.5, 130.4, 128.4, 128.3, 128.2, 127.8, 127.7, 126.1, 123.5, 123.2, 94.3, 88.3, 73.4, 22.6. IR (neat) 3062, 2981, 2218, 1722, 1598, 1494, 1442, 1288, 1247, 1130, 1070, 756, 696 cm^{-1}. GC–MS (EI) m/z 326 (M^+, 12), 105 (100). Anal. Calcd for $C_{23}H_{18}O_2$: C, 84.64; H, 5.56. Found: C, 84.57; H, 5.65.

4.2.8. *(S)-Octan-2-yl 2-(phenylethynyl)benzoate (**1j**)*

The ee was determined on an OJ-H column (hexane/isopropanol 99:1, flow 0.5 mL/min) with t_R (minor) 13.7, t_R (major) 15.0 min: 97% ee. $[\alpha]_D^{23}$ +12.2 (c 0.672, $CHCl_3$). Colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.96 (ddd, J=7.8, 1.5, 0.5 Hz, 1H), 7.64 (ddd, J=7.8, 1.5, 0.5 Hz, 1H), 7.59–7.55 (m, 2H), 7.48 (td, J=7.8, 1.5 Hz, 1H), 7.40–7.33 (m, 4H), 5.20 (qt, J=6.3, 6.3 Hz, 1H), 1.80–1.71 (m, 1H), 1.64–1.55 (m, 1H), 1.44–1.34 (m, 2H), 1.36 (d, J=6.3 Hz, 3H), 1.31–1.19 (m, 6H), 0.86 (t, J=6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.9, 134.0, 132.6, 131.5, 131.2, 130.2, 128.3, 128.2, 127.8, 123.4, 123.3, 94.0, 88.3, 72.2, 36.1, 31.7, 29.2, 25.5, 22.6, 20.2, 14.1. IR (neat) 2929, 2857, 2217, 1721, 1705, 1493, 1289, 1246, 1117, 1072, 754, 689 cm^{-1}. GC–MS (EI) m/z 334 (M^+, 50), 222 (100). Anal. Calcd for $C_{23}H_{26}O_2$: C, 82.60; H, 7.84. Found: C, 82.50; H, 7.68.

4.2.9. *(S)-Octan-2-yl 2-((2-methoxyphenyl)ethynyl)benzoate (**1k**)*

The ee was determined on an OJ-H column (hexane/isopropanol 99:1, flow 0.5 mL/min) with t_R (minor) 23.9, t_R (major) 25.9 min: 97% ee. $[\alpha]_D^{23}$ +11.7 (c 0.510, $CHCl_3$). Colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.94 (ddd, J=7.8, 1.5, 0.5 Hz, 1H), 7.67 (ddd, J=7.8, 1.5, 0.5 Hz, 1H), 7.53 (dd, J=7.6, 1.7 Hz, 1H), 7.46 (td, J=7.6, 1.5 Hz, 1H), 7.36 (td, J=7.8, 1.5 Hz, 1H), 7.31 (ddd, J=8.3, 7.6, 1.7 Hz, 1H), 6.94 (td, J=7.6, 1.0 Hz, 1H), 6.91–6.88 (m, 1H), 5.19 (qt, J=6.3, 6.3 Hz, 1H), 3.92 (s, 3H), 1.79–1.70 (m, 1H), 1.62–1.53 (m, 1H), 1.41–1.31 (m, 2H), 1.35 (d, J=6.3 Hz, 3H), 1.28–1.17 (m, 6H), 0.85 (t, J=6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.9, 159.9, 134.2, 133.5, 132.4, 131.1, 130.1, 129.8, 127.6, 123.7, 120.3, 112.6, 110.6, 92.3, 90.7, 72.1, 55.8, 36.0, 31.7, 29.2, 25.5, 22.6, 20.1, 14.1. IR (neat) 2929, 2857, 2216, 1720, 1703, 1462, 1288, 1273, 1243, 1106, 1072, 750 cm^{-1}. GC–MS (EI) m/z 364 (M^+, 10), 252 (100). Anal. Calcd for $C_{24}H_{28}O_3$: C, 79.09; H, 7.74. Found: C, 78.93; H, 7.61.

4.2.10. *1-(Dodecyloxy)dodecane (**3b**)*

White solid. ^{1}H NMR ($CDCl_3$, 400 MHz) 3.39 (t, J=6.8 Hz, 4H), 1.56 (tt, J=7.1, 6.8 Hz, 4H), 1.33–1.25 (m, 36H), 0.88 (t, J=6.8 Hz, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 71.0, 32.0, 29.8, 29.7, 29.7, 29.7, 29.6, 29.5, 29.4, 29.3, 22.8, 14.2. IR (KBr) 2955, 2925, 2850, 1472, 1377, 1130, 962, 717, 461 cm^{-1}. GC–MS (EI) m/z 354 (M^+, 10), 57 (100). Anal. Calcd for $C_{24}H_{50}O$: C, 81.28; H, 14.21. Found: C, 81.19; H, 14.17. Mp=35 °C.

4.2.11. *(2-Isopropoxyethyl)benzene (**3c**)*

Colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.32–7.19 (m, 5H), 3.65–3.55 (m, 3H), 2.89 (t, J=7.6 Hz, 2H), 1.17 (d, J=6.1 Hz, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.0, 128.8, 128.2, 126.0, 71.5, 69.2, 36.9, 22.2. IR (neat) 3028, 2972, 2866, 1605, 1497, 1454, 1379, 1337, 1128, 1080, 748, 698 cm^{-1}. GC–MS (EI) m/z 164 (M^+, 2), 91 (100). HRMS (ESI) calcd for $C_{11}H_{16}ONa$ (M^++Na) 187.1093, found: 187.1092. Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.48; H, 9.91.

4.2.12. *2-(Benzyloxy)ethyl acetate (**3h**)*

Light yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.38–7.27 (m, 5H), 4.58 (s, 2H), 4.25 (m, 2H), 3.67 (m, 2H), 2.09 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.9, 137.7, 128.4, 127.7, 127.7, 73.1, 67.8, 63.6, 21.0. IR (neat) 3032, 2864, 1740, 1456, 1379, 1246, 1107, 1047, 739, 698 cm^{-1}. GC–MS (EI) m/z 194 (M^+, 1), 91 (100). Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 68.30; H, 7.39.

4.2.13. *(R)-(1-Methoxyethyl)benzene (**3k**)*

The ee was determined on an OJ-H column (hexanes, flow 1.0 mL/min) with t_R (minor) 7.0 min, t_R (major) 7.6 min. Compound **3k** was prepared in CH_2Cl_2: spectral data are consistent with the previously published literature values.[15]

4.2.14. *(R)-(2-(Octan-2-yloxy)ethyl)benzene (**3l**)*

Authentic (R)-**3l** was prepared from (R)-octan-2-ol with phenethyl bromide under Williamson's conditions. Colorless oil, 97% ee. The ee was determined on an OJ-H column (hexane, flow 0.2 mL/min) with t_R (major) 25.2, t_R (minor) 26.4 min. $[\alpha]_D^{23}$ −8.7 (c 0.150, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.31–7.18 (m, 5H), 3.73–3.67 (m, 1H), 3.59–3.52 (m, 1H), 3.39 (qt, J=6.1, 6.1 Hz, 1H), 2.88 (t, J=7.3 Hz, 2H), 1.57–1.48 (m, 1H), 1.41–1.22 (m, 9H), 1.13 (d, J=6.1 Hz, 3H), 0.90 (t, J=6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.1, 128.8, 128.2, 126.0, 75.6, 69.5, 36.9, 36.7, 31.9, 29.4, 25.6, 22.7, 19.8, 14.2. IR (neat) 2956, 2927, 2856, 1454, 1373, 1137, 1120, 1090, 747, 697 cm^{-1}. GC–MS (EI) m/z 234 (M^+, 50), 105 (100). Anal. Calcd for $C_{16}H_{26}O$: C, 81.99; H, 11.18. Found: C, 81.89; H, 11.24.

4.2.15. *3-(2-Methoxyphenyl)-1H-isochromen-1-one (**5c**)*

White solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.31–8.27 (m, 1H), 7.96 (dd, J=8.1, 1.7 Hz, 1H), 7.70 (ddd, J=7.8, 7.3, 1.2 Hz, 1H), 7.50–7.45 (m, 2H), 7.38 (ddd, J=8.3, 7.3, 1.7 Hz, 1H), 7.37 (s, 1H), 7.07 (ddd, J=7.8, 7.3, 1.2 Hz, 1H), 7.00 (dd, J=8.3, 1.0 Hz, 1H), 3.96 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.5, 157.1, 150.3, 137.9, 134.5, 130.7, 129.3, 128.7, 127.9, 126.2, 120.8, 120.7, 120.5, 111.3, 106.9, 55.6. IR (KBr) 1720, 1622, 1595, 1461, 1254, 1225, 1072, 1016, 758, 691 cm^{-1}. GC–MS (EI) m/z 252 (M^+, 100). Anal. Calcd for $C_{16}H_{12}O_3$: C, 76.18; H, 4.79. Found: C, 76.10; H, 4.97. Mp=116 °C.

4.2.16. *3-Butyl-4-(4-methoxybenzyl)-1H-isochromen-1-one (**6a**)*

Light yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.31 (ddd, J=7.8, 1.5, 0.5 Hz, 1H), 7.59 (ddd, J=8.1, 7.3, 1.5 Hz, 1H), 7.42 (ddd, J=8.1, 7.2, 1.0 Hz, 1H), 7.37 (d, J=8.1 Hz, 1H), 7.08 (m, 2H), 6.82 (m, 2H), 3.98 (s, 2H), 3.77 (s, 3H), 2.64 (t, J=7.8 Hz, 2H), 1.70 (m, 2H), 1.39 (sext, J=7.3 Hz, 2H), 0.92 (t, J=7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.7, 158.1, 155.8, 138.0, 134.5, 130.4, 129.6, 128.5, 127.1, 123.4, 120.7, 114.0, 110.2, 55.3, 31.1, 30.9, 30.0, 22.5, 13.9. IR (neat) 2957, 1732, 1643, 1609, 1512, 1248, 1178, 1086, 1032, 777, 746, 691 cm^{-1}. GC–MS (EI) m/z 322 (M^+, 57), 237 (100). Anal. Calcd for $C_{21}H_{22}O_3$: C, 78.23; H, 6.88. Found: C, 78.19; H, 6.84.

4.3. General procedure of the intramolecular gold-catalyzed etherification

To a mixture of Ph_3PAuCl (12.4 mg, 5 mol %) and AgOTf (6.4 mg, 5 mol %) in chlorobenzene (2 mL) was added ω-hydroxyalkyl *ortho*-alkynylbenzoate **7** (0.5 mmol) at room temperature under Ar atmosphere. The mixture was stirred until the total consumption of **7**. Then, a saturated aqueous solution of $NaHCO_3$ was added, and the mixture was extracted with ether three times. The combined extracts were washed with brine, dried ($MgSO_4$), and evaporated to leave the crude product, which was purified by silica gel column chromatography using a mixture of hexane and ether as an eluent to give the ether product **8**.

4.3.1. *5-Hydroxy-3-phenylpentyl 2-(phenylethynyl)benzoate (**7a**)*

Light yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.85 (m, 1H), 7.64 (m, 1H), 7.55 (m, 2H), 7.49 (m, 1H), 7.37 (m, 1H), 7.35 (m, 3H), 7.27 (m, 2H), 7.19 (m, 1H), 7.17 (m, 2H), 4.20 (m, 2H), 3.45 (m, 2H), 2.93 (dddd, J=4.0, 4.0, 4.0, 12.0 Hz, 1H), 2.17 (m, 1H), 2.06 (m, 1H), 1.88 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.0, 143.4, 133.9, 131.8, 131.6, 131.5, 130.3, 128.6, 128.4, 128.2, 127.8, 127.4, 126.5, 123.5, 123.2, 94.1, 88.3, 63.5, 60.7, 39.4, 39.2, 35.6. IR (neat) 3400, 3060, 3028, 2933, 2390, 2218, 1716, 1598, 1494, 1442, 1292, 1251, 1134, 1076, 758, 700 cm^{-1}. GC–MS (EI) m/z 105 (M$-$279, 100). Anal. Calcd for $C_{26}H_{24}O_3$: C, 81.22; H, 6.29. Found: C, 81.02; H, 6.36.

4.3.2. *5-Hydroxy-3-phenylpentyl benzoate (**7b**)*

Light yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.97 (m, 2H), 7.55 (m, 1H), 7.43 (m, 2H), 7.31 (m, 2H), 7.21 (m, 3H), 4.22 (ddd, J=6.0, 7.6, 12.0 Hz, 1H), 4.13 (ddd, J=7.0, 8.0, 12.1 Hz, 1H), 3.56 (ddd, J=5.6, 7.9, 11.0 Hz, 1H), 3.49 (ddd, J=5.6, 7.6, 11.0 Hz, 1H), 2.97 (dddd, J=4.0, 4.0, 4.0, 12.0 Hz, 1H), 2.16 (m, 1H), 2.07 (m, 1H), 2.02 (m, 1H), 1.91 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.4, 143.4, 132.8, 130.2, 129.4, 128.6, 128.2, 127.5, 126.5, 63.3, 60.8, 39.5, 39.3, 35.7. IR (neat) 3420, 3028, 2935, 1717, 1602, 1452, 1315, 1279, 1120, 702 cm^{-1}. GC–MS (EI) m/z 162 (M$^+-$122, 100). Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 76.16; H, 7.20.

4.3.3. *4-Hydroxy-4-phenylbutyl 2-(phenylethynyl)benzoate (**7c**)*

Light yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.96 (ddd, J=7.8, 1.5, 0.5 Hz, 1H), 7.65 (ddd, J=7.8, 1.4, 0.5 Hz, 1H), 7.58–7.53 (m, 2H), 7.49 (td, J=7.8, 1.5 Hz, 1H), 7.40–7.24 (m, 9H), 4.66 (m, 1H), 4.43–4.34 (m, 2H), 1.97–1.64 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.2, 144.2, 134.0, 131.9, 131.6, 131.5, 130.3, 128.4, 128.3, 127.8, 127.6, 125.7, 123.5, 123.2, 94.2, 88.3, 74.1, 65.1, 35.4, 25.2. IR (neat) 3433, 3060, 2954, 2218, 1709, 1599, 1495, 1442, 1292, 1252, 1132, 1076, 756, 700 cm^{-1}. GC–MS (EI) m/z 222 (M$^+-$148, 100). Anal. Calcd for $C_{25}H_{22}O_3$: C, 81.06; H, 5.99. Found: C, 80.87; H, 6.01.

4.3.4. *5-Hydroxy-5-phenylpentyl 2-(phenylethynyl)benzoate (**7d**)*

Light yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.93 (m, 1H), 7.64 (m, 1H), 7.56 (m, 2H), 7.49 (m, 1H), 7.24–7.40 (m, 9H), 4.60 (t, J=7.0 Hz, 1H), 4.35 (t, J=8.0 Hz, 2H), 1.80 (m, 5H), 1.71 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.8, 144.4, 133.6, 131.5, 131.2, 131.2, 130.0, 128.1, 128.0, 127.8, 127.5, 126.8, 125.4, 123.1, 122.9, 94.0, 88.1, 73.6, 64.8, 38.3, 28.2, 22.0. IR (neat) 3480, 3060, 2941, 2350, 2218, 1724, 1598, 1494, 1292, 1249, 1132, 1076, 758, 700 cm^{-1}. GC–MS (EI) m/z 384 (M$^+$, 1), 222 (100). Anal. Calcd for $C_{26}H_{24}O_3$: C, 81.22; H, 6.29. Found: C, 81.20; H, 6.48.

4.3.5. *4-Phenyltetrahydro-2H-pyran (**8a**)*

White solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.32 (m, 2H), 7.24 (m, 3H), 4.09 (m, 2H), 3.54 (ddd, J=1.7, 6.6, 6.6 Hz, 2H), 2.76 (tt, J=4.0, 12.0 Hz, 1H), 1.79 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 145.7, 128.4, 126.6, 126.2, 68.4, 41.6, 33.9. IR (KBr) 2920, 2840, 2320, 1558, 1126, 756, 698 cm^{-1}. GC–MS (EI) m/z 162 (M$^+$, 70), 117 (100). Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.28; H, 8.78. Mp=43–46 °C.

4.4. General procedure of the gold-catalyzed cyclization of diols

To a mixture of Ph_3PAuCl (12.4 mg, 5 mol %) and AgOTf (6.4 mg, 5 mol %) in $(ClCH_2)_2$ (2 mL) were added **1h** (0.75 mmol) and diol **2** (0.5 mmol) successively at room temperature under Ar atmosphere. The mixture was stirred for 1 h. Then, a saturated aqueous solution of $NaHCO_3$ was added, and the mixture was extracted with ether three times. The combined extracts were washed with brine, dried ($MgSO_4$), and evaporated to leave the crude product, which was purified by silica gel column chromatography using a mixture of hexane and CH_2Cl_2 as an eluent to give the cyclization product **8**.

4.4.1. *3-Phenyltetrahydrofuran (**8d**)*

Colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.34–7.20 (m, 5H), 4.15 (dd, J=8.2, 7.8 Hz, 1H), 4.08 (ddd, J=8.3, 8.1, 4.2 Hz, 1H), 3.93 (ddd, J=8.3, 8.1, 7.3 Hz, 1H), 3.74 (dd, J=8.2, 7.8 Hz, 1H), 3.41 (quint, J=7.8 Hz, 1H), 2.37 (dddd, J=12.4, 8.0, 7.7, 4.6 Hz, 1H), 2.02 (dddd, J=12.4, 8.1, 8.1, 8.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 142.5, 128.5, 127.2, 126.4, 74.6, 68.5, 45.0, 34.7. IR (neat) 3028, 2931, 2861, 1732, 1603, 1493, 1454, 1293, 1252, 1054, 903, 756, 698 cm^{-1}. GC–MS (EI) m/z 148 (M$^+$, 28), 117 (100). Anal. Calcd for $C_{10}H_{12}O$: C, 81.04; H, 8.16. Found: C, 80.81; H, 8.04.

4.5. General procedure of the gold-catalyzed Friedel–Crafts reaction

To a mixture of Ph_3PAuCl (12.4 mg, 5 mol %) and AgOTf (6.4 mg, 5 mol %) in chlorobenzene (2 mL) were added **1** (0.5 mmol) and furan **11** (2.5 mmol) successively at room temperature under Ar atmosphere. The mixture was stirred until the total consumption of **1**. Then, a saturated aqueous solution of $NaHCO_3$ was added, and the mixture was extracted with ether three times. The combined extracts were washed with brine, dried ($MgSO_4$), and evaporated to leave the crude product, which was purified by silica gel column chromatography using a mixture of hexane and ether as an eluent to give the alkylation product **12**.

4.5.1. *4-Methoxybenzyl 2-(phenylethynyl)benzoate (**1l**)*

White solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.00–7.98 (m, 1H), 7.65–7.63 (m, 1H), 7.48 (td, J=7.6, 1.5 Hz, 1H), 7.43–7.29 (m, 8H), 6.86–6.82 (m, 2H), 5.34 (s, 2H), 3.79 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.2, 159.5, 134.0, 131.7, 131.6, 131.6, 130.6, 130.1, 128.3, 128.1, 127.8, 127.8, 123.6, 123.1, 113.9, 94.3, 88.2, 66.9, 55.3. IR (KBr) 3051, 2955, 2835, 2216, 1709, 1611, 1514, 1441, 1377, 1244, 1069, 924, 756, 691 cm^{-1}. MS (EI) m/z (%) 342 (M$^+$, 13), 121 (100). Anal. Calcd for $C_{23}H_{18}O_3$: C, 80.68; H, 5.30. Found: C, 80.80; H, 5.36. Mp=41.4 °C.

4.5.2. *Cinnamyl 2-(phenylethynyl)benzoate (**1m**)*

Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.03 (dd, J=7.9, 1.3 Hz, 1H), 7.66 (dd, J=7.8, 1.2 Hz, 1H), 7.55–7.49 (m, 3H), 7.40 (td, J=7.7, 1.2 Hz, 1H), 7.35–7.22 (m, 8H), 6.76 (d, J=15.9 Hz, 1H), 6.43 (dt, J=15.9, 6.5 Hz, 1H), 5.04 (dd, J=6.5, 1.3 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.0, 136.0, 134.3, 134.0, 131.7, 131.6, 131.6, 130.5, 128.4, 128.3, 128.2, 127.9, 127.8, 126.5, 123.5, 123.1, 123.1, 94.3, 88.2, 65.9. IR (KBr); 3047, 2949, 2216, 1699, 1491, 1439, 1286, 1238, 1121, 951, 750, 691 cm^{-1}. MS (EI) m/z 338 (M$^+$, 10), 117 (100). Anal. Calcd for $C_{24}H_{18}O_2$: C, 85.18; H, 5.36. Found: C, 85.13; H, 5.45. Mp=73.9 °C.

4.6. General procedure of the intramolecular gold-catalyzed Friedel–Crafts reaction

To a mixture of Ph_3PAuCl (24.8 mg, 10 mol %) and AgOTf (12.8 mg, 10 mol %) in 1,2-dichloroethane (2 mL) was added **15** (0.5 mmol) at room temperature under Ar atmosphere. The mixture was stirred until the total consumption of **15**. Then, a saturated aqueous solution of $NaHCO_3$ was added, and the mixture was extracted with ether three times. The combined extracts were washed with brine, dried ($MgSO_4$), and evaporated to leave the crude product, which was purified by silica gel column chromatography using a mixture of hexane and ether as an eluent to give product **16**.

4.6.1. *4-Phenylbutyl 2-(phenylethynyl)benzoate* (***15a***)

Light yellow oil. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.97 (m, 1H), 7.64 (m, 1H), 7.58–7.53 (m, 2H), 7.49 (m, 1H), 7.41–7.32 (m, 4H), 7.28–7.16 (m, 5H), 4.38 (t, J=6.9 Hz, 2H), 2.62 (t, J=7.3 Hz, 2H), 1.87–1.72 (m, 4H). ^{13}C NMR (CDCl$_3$, 100 MHz) δ 166.1, 141.8, 133.9, 131.9, 131.5, 131.4, 130.3, 128.3, 128.2, 128.2, 128.2, 127.8, 125.6, 123.5, 123.2, 94.2, 88.2, 65.1, 35.4, 28.3, 27.8. IR (neat) 2941, 2860, 2359, 2230, 1724, 1599, 1566, 1495, 1443, 1290, 1250, 1130, 1074, 756, 692 cm^{-1}. GC–MS (EI) m/z 354 (M^{+}, 4), 222 (100). Anal. Calcd for C$_{25}$H$_{22}$O$_2$: C, 84.72; H, 6.26. Found: C, 84.55; H, 6.46.

4.6.2. *4-(4-Methoxyphenyl)butyl 2-(phenylethynyl)benzoate* (***15b***)

Light yellow oil. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.76 (m, 1H), 7.65 (m, 1H), 7.58–7.53 (m, 2H), 7.49 (m, 1H), 7.41–7.32 (m, 4H), 7.05 (m, 2H), 6.80 (m, 2H), 4.38 (t, J=5.8 Hz, 2H), 3.78 (s, 3H), 2.56 (t, J=7.3 Hz, 2H), 1.85–1.68 (m, 4H). ^{13}C NMR (CDCl$_3$, 100 MHz) δ 166.0, 157.5, 133.9, 133.8, 131.9, 131.5, 131.4, 130.2, 129.0, 128.3, 128.1, 127.7, 123.4, 123.1, 113.5, 94.1, 88.2, 65.1, 55.1, 34.4, 28.2, 27.9. IR (neat) 2936, 2210, 1724, 1612, 1512, 1495, 1442, 1290, 1247, 1177, 1130, 1074, 1038, 829, 758, 692 cm^{-1}. GC–MS (EI) m/z 384 (M^{+}, 8), 134 (100). Anal. Calcd for C$_{26}$H$_{24}$O$_3$: C, 81.22; H, 6.29. Found: C, 81.08; H, 6.27.

4.7. Procedure of the gold-catalyzed cyclization of 17

To a mixture of Ph$_3$PAuCl (12.4 mg, 5 mol %) and AgOTf (6.4 mg, 5 mol %) in (ClCH$_2$)$_2$ (1 mL) were added **17** (0.5 mmol) and **1h** (1.0 mmol) successively at room temperature under Ar atmosphere. The mixture was stirred at 100 °C for 8 h. After cooling the mixture, a saturated aqueous solution of NaHCO$_3$ was added, and the mixture was extracted with CH$_2$Cl$_2$ twice. The combined extracts were washed with brine, dried (Na$_2$SO$_4$), and evaporated to leave the crude product, which was purified by silica gel column chromatography using a mixture of hexane and EtOAc as an eluent to give the cyclization product **16b** in 72% yield.

4.8. General procedure of the gold-catalyzed N-alkylation of sulfonamide

To a mixture of Ph$_3$PAuCl (7.4 mg, 3 mol %) and AgOTf (3.9 mg, 3 mol %) in 1,4-dioxane (2 mL) were added sulfonamide **18** (1 mmol) and *ortho*-alkynyl benzoates **1** (0.5 mmol) at room temperature. After the completion of the reaction, a saturated aqueous solution of NaHCO$_3$ was added, and the mixture was extracted with CH$_2$Cl$_2$ two times. The combined extracts were washed with brine, dried (MgSO$_4$), and evaporated to leave the crude product, which was purified by silica gel column chromatography using a mixture of hexane and Et$_2$O as eluent to give the N-alkylation product **19**.

4.8.1. *Allyl 2-(phenylethynyl)benzoate* (***1n***)

Colorless oil. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 8.02 (dd, J=8.0, 1.4 Hz, 1H), 7.67 (dd, J=8.0, 1.4 Hz, 1H), 7.64–7.57 (m, 2H), 7.48 (dt, J=15.1, 1.4 Hz, 1H), 7.42–7.32 (m, 4H), 6.13–6.02 (m, 1H), 5.46 (ddd, J=17.2, 2.9, 1.5 Hz, 1H), 5.28 (ddd, J=10.6, 2.6, 1.2 Hz, 1H), 4.90 (dt, J=6.8, 1.2 Hz, 2H). ^{13}C NMR (CDCl$_3$, 100 MHz) δ 165.2, 133.6, 131.8, 131.3, 131.3, 130.1, 128.2, 128.1, 127.9, 127.5, 123.3, 122.9, 117.9, 94.1, 88.1, 65.4. IR (neat) 3062, 2942, 2216, 1725, 1493, 1243, 1127, 1069, 753, 689 cm^{-1}. GC–MS (EI) m/z 262 (M^{+}, 26), 165 (M^{+}−97, 100). Anal. Calcd for C$_{18}$H$_{14}$O$_2$: C, 82.42; H, 5.38. Found: C, 82.56; H, 5.27.

4.8.2. *Allyl 2-(hex-1-ynyl)benzoate* (***1o***)

Colorless oil. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.90 (dd, J=7.9, 1.5 Hz, 1H), 7.51 (dd, J=7.9, 1.5 Hz, 1H), 7.42 (dt, J=15.2, 1.5 Hz, 1H), 7.31 (dt, J=15.2, 1.5 Hz, 1H), 6.11–5.99 (m, 1H), 5.44 (ddd, J=17.2, 3.2, 1.6 Hz, 1H), 5.29 (ddd, J=10.4, 2.8, 1.2 Hz, 1H), 4.83 (dt, J=6.6, 1.8 Hz, 2H), 2.45 (t, J=7.2 Hz, 2H), 1.67–1.44 (m, 4H), 0.95 (t, J=7.2 Hz, 3H). ^{13}C NMR (CDCl$_3$, 100 MHz) δ 166.0, 134.1, 132.1, 131.8, 131.3, 130.0, 127.0, 124.4, 118.1, 95.9, 79.1, 65.6, 30.7, 22.0, 19.5, 13.7. IR (neat) 2957, 2932, 2872, 2229, 1731, 1483, 1283, 1242, 1128, 1075, 930, 755, 701 cm^{-1}. GC–MS (EI) m/z 159 (M^{+}−83, 100). Anal. Calcd for C$_{16}$H$_{18}$O$_2$: C, 79.31; H, 7.49. Found: C, 79.28; H, 7.42.

4.8.3. *3-Phenylprop-2-ynyl 2-(phenylethynyl)benzoate* (***1p***)

White crystal. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 8.06 (dd, J=4.1, 1.1 Hz, 1H), 7.67 (dd, J=4.1, 1.1 Hz, 1H), 7.64–7.58 (m, 2H), 7.52 (dt, J=15.2, 1.1 Hz, 1H), 7.47–7.38 (m, 3H), 7.37–7.23 (m, 6H), 5.21 (s, 2H). ^{13}C NMR (CDCl$_3$, 100 MHz) δ 165.4, 134.0, 131.9, 131.8, 131.7, 131.0, 130.7, 128.6, 128.4, 128.2, 128.1, 127.8, 123.8, 123.1, 122.1, 94.6, 88.0, 86.6, 83.0, 53.6. IR (neat) 3062, 2924, 2360, 2217, 1703, 1288, 1245, 1123, 941, 757, 689 cm^{-1}. GC–MS (EI) m/z 336 (M^{+}, 5), 115 (M^{+}−221, 100). Anal. Calcd for C$_{24}$H$_{16}$O$_2$: C, 85.69; H, 4.79. Found: C, 85.59; H, 4.83. Mp=95–96 °C.

4.8.4. *3-Phenylprop-2-ynyl 2-(hex-1-ynyl)benzoate* (***1q***)

Colorless oil. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.96 (dd, J=6.0, 1.1 Hz, 1H), 7.57–7.42 (m, 4H), 7.38–7.28 (m, 4H), 5.16 (s, 2H), 2.47 (t, J=6.9 Hz, 2H), 1.67–1.57 (m, 2H), 1.52–1.41 (m, 2H), 0.92 (t, J=6.9 Hz, 3H). ^{13}C NMR (CDCl$_3$, 100 MHz) δ 165.6, 134.2, 131.8, 131.7, 131.1, 130.3, 128.6, 128.2, 127.0, 124.7, 122.2, 96.5, 86.5, 83.0, 79.0, 53.4, 30.7, 22.1, 19.6, 13.7. IR (neat) 2931, 2871, 2229, 1734, 1443, 1367, 1282, 1238, 1069, 753, 690 cm^{-1}. GC–MS (EI) m/z 115 (M^{+}−201, 100). Anal. Calcd for C$_{22}$H$_{20}$O$_2$: C, 83.51; H, 6.37. Found: C, 83.73; H, 6.21.

4.8.5. *Phenethyl 2-(phenylethynyl)benzoate* (***1r***)

Brown oil. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.92 (dd, J=7.6, 1.1 Hz, 1H), 7.65 (dd, J=7.6, 1.1 Hz, 1H), 7.60–7.55 (m, 2H), 7.49 (dt, J=14.9, 1.6 Hz, 1H), 7.43–7.19 (m, 9H), 4.58 (t, J=6.9 Hz, 2H), 3.10 (t, J=6.9 Hz, 2H). ^{13}C NMR (CDCl$_3$, 100 MHz) δ 165.9, 137.6, 133.9, 131.8, 131.6, 131.5, 130.3, 128.8, 128.4, 128.4, 128.2, 127.8, 126.5, 123.6, 123.2, 94.3, 88.2, 65.6, 35.2. IR (neat) 3061, 3029, 2954, 2216, 1724, 1597, 1494, 1288, 1245, 1128, 1037, 752, 689 cm^{-1}. GC–MS (EI) m/z 91 (M^{+}−235, 100). Anal. Calcd for C$_{23}$H$_{18}$O$_2$: C, 84.64; H, 5.56. Found: C, 84.84; H, 5.47.

4.8.6. *N,N-Dibenzyl-4-methylbenzenesulfonamide* (***19b***)

Colorless crystal. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.57–7.52 (m, 2H), 7.34–7.27 (m, 2H), 7.24–7.18 (m, 6H), 7.08–7.03 (m, 4H), 4.32 (s, 4H), 2.46 (s, 3H). ^{13}C NMR (CDCl$_3$, 100 MHz) δ 143.2, 137.6, 135.6, 129.6, 128.5, 128.3, 127.5, 127.2, 50.5, 21.6. IR (neat) 3033, 2921, 2851, 1493, 1455, 1315, 1149, 1095, 1058, 811, 727, 656 cm^{-1}. GC–MS (EI) m/z 351 (M^{+}, 1), 91 (100). Anal. Calcd for C$_{21}$H$_{21}$NO$_2$S: C, 71.77; H, 6.02; N, 4.00. Found: C, 71.95; H, 6.14; N, 3.82. Mp=75–77 °C.

4.8.7. *N-Allyl-N,4-dimethylbenzenesulfonamide* (***19e***)

Colorless liquid. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.68 (d, J=8.0 Hz, 2H), 7.32 (d, J=8.0 Hz, 2H), 5.78–5.66 (m, 1H), 5.19 (m, 2H), 3.62 (d, J=6.2 Hz, 2H), 2.66 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (CDCl$_3$, 100 MHz) δ 143.3, 134.2, 132.4, 129.5, 127.3, 119.0, 53.0, 34.2, 21.5. IR (neat) 2923, 2363, 1644, 1598, 1454, 1335, 1157, 1089, 984, 913, 753, 661, 619 cm^{-1}. GC–MS (EI) m/z 225 (M^{+}, 8), 91 (M^{+}-134, 100). Anal. Calcd for C$_{11}$H$_{15}$NO$_2$S: C, 58.64; H, 6.71; N, 6.22. Found: C, 58.67; H, 6.77; N, 6.19.

4.8.8. *N,4-Dimethyl-N-(3-phenylprop-2-ynyl)benzenesulfonamide* (***19f***)

White solid. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.75 (d, J=7.6 Hz, 2H), 7.34–7.20 (m, 5H), 7.13–7.07 (m, 2H), 4.26 (s, 2H), 2.90 (s, 3H), 2.96 (s, 3H). ^{13}C NMR (CDCl$_3$, 100 MHz) δ 143.5, 134.1, 131.3, 129.4, 128.3, 128.0, 127.8, 122.0, 85.8, 81.3, 40.7, 34.6, 21.4. IR (neat) 2924, 2360, 1488, 1348, 1325, 1159, 917, 815, 734, 710, 693, 660 cm^{-1}. GC–MS (EI) m/z 144 (M^{+}−155, 100). Anal. Calcd for C$_{17}$H$_{17}$NO$_2$S: C, 68.20; H, 5.72; N, 4.68. Found: C, 68.17; H, 5.67; N, 4.65. Mp=88–89 °C.

*4.8.9. N,4-Dimethyl-N-phenethylbenzenesulfonamide (**19g**)*

Colorless liquid. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.64 (d, *J*=8.0 Hz, 2H), 7.33–7.16 (m, 7H), 3.27–3.22 (m, 2H), 2.89–2.83 (m, 2H), 2.75 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (CDCl$_3$, 100 MHz) δ 143.2, 138.2, 134.6, 129.5, 128.7, 128.5, 127.3, 126.4, 51.8, 35.2, 34.8, 21.5. IR (neat) 3028, 2924, 2865, 1598, 1454, 1336, 1156, 951, 815, 697, 652 cm^{-1}. GC–MS (EI) *m*/*z* 289 (M$^+$, 15), 94 (100). Anal. Calcd for $C_{16}H_{19}NO_2S$: C, 66.40; H, 6.62; N, 4.84. Found: C, 66.31; H, 6.49; N, 4.85.

*4.8.10. N-Benzyl-N-phenylmethanesulfonamide (**19j**)*

White solid. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.36–7.17 (m, 10H), 4.85 (s, 2H), 2.96 (s, 3H). ^{13}C NMR (CDCl$_3$, 100 MHz) δ 139.0, 136.0, 129.3, 128.7, 128.5, 128.4, 128.0, 127.7, 54.9, 38.2. IR (neat) 3064, 2823, 2360, 1493, 1278, 1325, 1150, 1063, 968, 870, 779, 698 cm^{-1}. GC–MS (EI) *m*/*z* 79 (M$^+$−182). Anal. Calcd for $C_{14}H_{15}NO_2S$: C, 64.34; H, 5.78; N, 5.36. Found: C, 64.55; H, 5.69; N, 5.09. Mp=138–140 °C.

*4.8.11. 4-Benzyl-3-phenyl-1H-isochromen-1-one (**6b**)*

White solid. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 8.40 (m, 1H), 7.65–7.20 (m, 13H), 4.15 (s, 2H). ^{13}C NMR (CDCl$_3$, 100 MHz) δ 162.2, 153.0, 139.1, 137.9, 134.6, 132.8, 129.7, 129.6, 128.8, 128.6, 128.3, 127.9, 127.7, 126.4, 124.4, 121.1, 110.9, 33.3. IR (neat) 3024, 1735, 1629, 1603, 1484, 1249, 1099, 764, 692 cm^{-1}. GC–MS (EI) *m*/*z* 312 (M$^+$, 60), 105 (M$^+$−207, 100). Anal. Calcd for $C_{22}H_{16}O_2$: C, 84.59; H, 5.16. Found: C, 84.53; H, 5.22. Mp=160–161 °C.

4.9. General procedure of the gold-catalyzed intramolecular N-alkylation of sulfonamide

To a mixture of Ph_3PAuCl (12.4 mg, 5 mol %) and AgOTf (6.4 mg, 5 mol %) in benzene (0.5 mL) was added a solution of sulfonamide **20** (1 mmol) in benzene (1.5 mL) at room temperature. After completion of the reaction, a saturated aqueous solution of $NaHCO_3$ was added, and the mixture was extracted with AcOEt two times. The combined extracts were washed with brine, dried ($MgSO_4$), and evaporated to leave the crude product, which was purified by silica gel column chromatography using a mixture of hexane and Et_2O as eluent to give the N-alkylation product **21**.

*4.9.1. 3-(4-Methylphenylsulfonamido)propyl 2-(phenylethynyl)-benzoate (**20a**)*

White solid. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.91 (d, *J*=8.0 Hz, 1H), 7.70–7.60 (m, 3H), 7.59–7.46 (m, 3H), 7.44–7.31 (m, 4H), 7.21 (d, *J*=8.0 Hz, 2H), 4.65 (t, *J*=6.0 Hz, 1H), 4.39 (t, *J*=6.0 Hz, 2H), 3.07 (dt, *J*=6.4, 6.4 Hz, 2H), 2.37 (s, 3H), 1.93 (tt, *J*=6.4, 6.0 Hz, 2H). ^{13}C NMR (CDCl$_3$, 100 MHz) δ 166.2, 143.3, 136.7, 134.1, 131.8, 131.5, 131.3, 130.4, 129.6, 128.6, 128.4, 127.9, 126.9, 123.6, 123.0, 94.3, 88.2, 62.1, 40.1, 29.1, 21.5. IR (neat) 3301, 3249, 3049, 2929, 2884, 1726, 1704, 1327, 1290, 1267, 1242, 1157, 1128, 1077, 997, 815, 754, 687 cm^{-1}. GC–MS (EI) *m*/*z* 91 (100), 222 (M$^+$−211, 16). HRMS (ESI) calcd for $C_{25}H_{23}NO_4SNa$ ([M+Na]$^+$): 456.1240, found: 456.1237. Mp=63–65 °C.

*4.9.2. 4-(4-Methylphenylsulfonamido)butyl 2-(phenylethynyl)-benzoate (**20b**)*

White solid. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.94 (dd, *J*=8.0, 1.6 Hz, 1H), 7.72–7.61 (m, 3H), 7.58–7.46 (m, 3H), 7.43–7.32 (m, 4H), 7.30–7.23 (m, 2H), 4.34 (br, 1H), 4.30(t, *J*=6.4 Hz, 2H), 2.90 (dt, *J*=6.8, 6.8 Hz, 2H), 2.40 (s, 3H), 1.80–1.69 (m, 2H), 1.65–1.54 (m, 2H). ^{13}C NMR (CDCl$_3$, 100 MHz) δ 166.2, 143.3, 136.8, 134.0, 131.7, 131.6, 131.5, 130.4, 129.6, 128.5, 128.4, 127.9, 127.0, 123.5, 123.2, 94.1, 88.3, 64.6, 42.8, 26.5, 25.9, 21.6. IR (neat) 3297, 2952, 1716, 1684, 1325, 1297, 1154, 1136, 1080, 886, 810, 760, 696, 659 cm^{-1}. GC–MS (EI) *m*/*z* 225 (M$^+$−222, 9), 70 (100). Anal. Calcd for $C_{26}H_{25}NO_4S$: C, 69.78; H, 5.63; N, 3.13. Found: C, 69.41; H, 5.79; N, 3.10. Mp=72–74 °C.

*4.9.3. 5-(4-Methylphenylsulfonamido)pentyl 2-(hex-1-ynyl)-benzoate (**20c**)*

Colorless oil. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.85 (d, *J*=7.6 Hz, 1H), 7.73 (d, *J*=8.4 Hz, 2H), 7.51 (d, *J*=7.6 Hz, 1H), 7.42 (dd, *J*=7.6, 7.6 Hz, 1H), 7.35–7.27 (m, 3H), 4.30 (t, *J*=6.8 Hz, 1H), 4.27(t, *J*=6.8 Hz, 2H), 2.96 (dt, *J*=6.8, 6.8 Hz, 2H), 2.46 (t, *J*=7.2 Hz, 2H), 2.42 (s, 3H), 1.80–1.42 (m, 10H), 0.95 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (CDCl$_3$, 100 MHz) δ 166.4, 143.3, 136.8, 134.2, 131.8, 131.3, 129.9, 129.6, 127.0, 127.0, 124.3, 95.9, 79.2, 64.6, 43.0, 30.8, 29.3, 28.2, 23.1, 22.1, 21.5, 19.5, 13.7. IR (neat) 3278, 2954, 2933, 2870, 1725, 1709, 1326, 1289, 1247, 1157, 1135, 1080, 815, 758, 701, 661 cm^{-1}. GC–MS (EI) *m*/*z* 91 (100), 239 (M$^+$−202, 49). HRMS (ESI) calcd for $C_{25}H_{31}NO_4SNa$ ([M+Na]$^+$): 464.1866, found: 464.1863.

*4.9.4. 6-(4-Methylphenylsulfonamido)hexyl 2-(hex-1-ynyl)-benzoate (**20d**)*

Colorless oil. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.85 (d, *J*=7.6 Hz, 1H), 7.73 (d, *J*=8.4 Hz, 2H), 7.50 (d, *J*=7.6 Hz, 1H), 7.41 (dd, *J*=7.6, 7.6 Hz, 1H), 7.34–7.27 (m, 3H), 4.42 (t, *J*=6.8 Hz, 1H), 4.27(t, *J*=6.8 Hz, 2H), 2.93 (dt, *J*=6.8, 6.8 Hz, 2H), 2.46 (t, *J*=7.2 Hz, 2H), 2.42 (s, 3H), 1.77–1.26 (m, 12H), 0.95 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (CDCl$_3$, 100 MHz) δ 166.4, 143.3, 136.8, 134.3, 132.0, 131.3, 129.9, 129.6, 127.0, 127.0, 124.3, 95.9, 79.2, 64.8, 43.1, 30.8, 29.5, 28.6, 26.2, 25.6, 22.1, 21.6, 19.6, 13.7. IR (neat) 3282, 3064, 3033, 2932, 2861, 2229, 1725, 1709, 1326, 1289, 1247, 1157, 1081, 815, 758, 700, 660 cm^{-1}. GC–MS (EI) *m*/*z* 254 (M$^+$−201, 26), 91 (100). HRMS (ESI) calcd for $C_{26}H_{33}NO_4SNa$ ([M+Na]$^+$): 478.2023, found: 478.2019.

*4.9.5. 1-Tosylazepane (**21d**)*

White solid. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.67 (d, *J*=8.4 Hz, 2H), 7.29 (d, *J*=8.4 Hz, 2H), 3.25 (t, *J*=6.0 Hz, 4H), 2.42 (s, 3H), 1.78–1.66 (m, 4H), 1.64–1.54 (m, 4H). ^{13}C NMR (CDCl$_3$, 100 MHz) δ 142.7, 136.5, 129.4, 126.9, 48.2, 29.2, 27.0, 21.5. IR (neat) 3054, 2925, 2858, 1596, 1495, 1453, 1329, 1306, 1156, 1092, 1045, 998, 927, 879, 817, 713, 695, 649 cm^{-1}. GC–MS (EI) *m*/*z* 253 (M$^+$, 16), 91 (100). HRMS (ESI) calcd for $C_{13}H_{19}NO_2SNa$ ([M+Na]$^+$): 276.1029, found: 276.1026. Mp=68–72 °C.

4.10. General procedure of the gold-catalyzed cyclization of ω-hydroxyalkyl sulfonamide

To a mixture of Ph_3PAuCl (12.4 mg, 5 mol %) and AgOTf (6.4 mg, 5 mol %) in benzene (0.5 mL) were added ω-hydroxyalkyl sulfonamide **22** (0.5 mmol) and methyl benzoate **1** (1.1 mmol) at room temperature. After completion of the reaction, a saturated aqueous solution of $NaHCO_3$ was added, and the mixture was extracted with AcOEt two times. The combined extracts were washed with brine, dried ($MgSO_4$), and evaporated to leave the crude product, which was purified by silica gel column chromatography using a mixture of hexane and Et_2O as eluent to give the N-alkylation product **21**.

*4.10.1. N-(2-(2-Hydroxyethyl)phenyl)-4-methylbenzenesulfonamide (**22c**)*

Colorless oil. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 8.47 (s, 1H), 7.61 (d, *J*=8.0 Hz, 2H), 7.47 (dd, *J*=8.0, 1.2 Hz, 1H), 7.24–7.18 (m, 3H), 7.11 (ddd, *J*=7.6, 7.2, 1.2 Hz, 1H), 7.05 (dd, *J*=7.6, 1.6 Hz, 1H), 3.84 (dt, *J*=5.2, 3.6 Hz, 2H), 2.43 (t, *J*=5.2 Hz, 2H), 2.39 (s, 3H), 1.93 (t, *J*=3.6 Hz, 1H). ^{13}C NMR (CDCl$_3$, 100 MHz) δ 143.3, 137.4, 135.8, 133.7, 130.6, 129.4, 127.6, 126.9, 126.0, 124.7, 64.7, 34.4, 21.6. IR (neat) 3496, 3248, 2925, 2882, 1598, 1493, 1401, 1326, 1306, 1289, 1153, 1091, 1047, 922, 813, 755, 706, 660, 626 cm^{-1}. GC–MS (EI) *m*/*z* 291 (M$^+$, 8), 91 (100). HRMS (ESI) calcd for $C_{15}H_{17}NO_3SNa$ ([M+Na]$^+$): 314.0821, found: 314.0820.

*4.10.2. N-(2-(3-Hydroxypropyl)phenyl)-4-methylbenzene-sulfonamide (**22d**)*

Colorless oil. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 8.15 (s, 1H), 7.61 (d, *J*=8.4 Hz, 2H), 7.45 (d, *J*=8.4 Hz, 1H), 7.24–7.14 (m, 3H), 7.12–7.03

(m, 2H), 3.52 (dt, J=5.6, 4.4 Hz, 2H), 2.39 (t, J=6.8 Hz, 2H), 2.38 (s, 3H), 1.86 (t, J=4.4 Hz, 1H), 1.72 (tt, J=6.8, 5.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.3, 137.0, 135.3, 134.1, 130.1, 129.4, 127.0, 127.0, 125.8, 124.2, 59.8, 32.2, 25.8, 21.6. IR (neat) 3499, 3269, 2926, 2876, 1598, 1493, 1438, 1402, 1327, 1306, 1290, 1234, 1184, 1153, 1091, 929, 813, 755, 660 cm^{-1}. GC–MS (EI) m/z 305 (M^+, 6), 91 (100). HRMS (ESI) calcd for $C_{16}H_{19}NO_3SNa$ ($[M+Na]^+$): 328.0978, found: 328.975.

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