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Methyltrifluoromethanesulfonate Catalyst in Direct Nucleophilic Substitution of Alcohols; One-Pot Synthesis of 4*H*-Chromene Derivatives

Srabani Maity, Arnab Roy,[§] Surajit Duari,[§] Subrata Biswas, Asma M. Elsharif, and Srijit Biswas*

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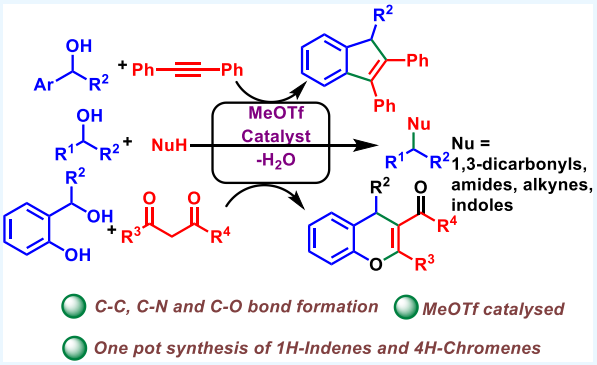
ABSTRACT: The catalytic activity of methyltrifluoromethanesulfonate (MeOTf) has been explored toward direct nucleophilic substitution of the hydroxyl group of nonmanipulated alcohols such as benzylic, allylic, propargylic, and tertiary alcohols with a wide range of uncharged nucleophiles such as 1,3-dicarbonyl compounds, amides, alkynes, and indoles to generate functionalized 1,3-dicarbonyl compounds, amides, alkynes, and indoles, respectively. Thus, the present protocol defines an alternate pathway to construct new C−C, C−N, and C−O bonds with the formation of water as the byproduct under mild conditions without any acids or metals. A completely different mechanism was established through several control experiments to explain the reaction methodology. As an application of the reported protocol, 1*H*-indene derivatives have been synthesized in one pot when benzylic alcohols were subjected to react with internal alkynes. The scope of the reaction has been further extended toward a tandem benzylation−cyclization−dehydration of 1,3-dicarbonyl compounds with 2-hydroxybenzyl alcohols, which furnish biologically important 4*H*-chromene derivatives.



INTRODUCTION

Alcohols are one of the most naturally occurring precursors available in biomass such as cellulose, lignin, steroid, etc.[1] A variety of alcohols are available in nature, and it should be worthy to use these biofeed stocks toward bioactive and value-added chemical production. Due to the poor leaving aptitude of the alcoholic −OH bond, traditional methods of alcohol functionalization involved conversion of the hydroxyl group (−OH) to a better leaving group (such as −OTs), which was reacted with an external nucleophile to furnish the nucleophilic substituted product (Scheme 1A).[2] The overall procedure was time-consuming and involved the use of stoichiometric amounts of extra reagents (such as TsCl, base) as well as generation of a stoichiometric amount of halogenated waste (such as HCl) and acid (such as TsOH) as a byproduct. In this context, it is worth mentioning that direct amination of alcohols has been achieved with specific substrates where transition metal catalysts capable of reversibly borrowing hydrogen were employed (Scheme 1B).[3] In this reaction, the alcohols were oxidized to the corresponding carbonyl compounds by the elimination of hydrogen, forming a metal hydride complex. The generated carbonyl compound was used to undergo the condensation reaction with the amine nucleophile to produce imine. Subsequent reduction of the resulting imine by the metal hydride complex yielded the desired product.

The overall transformation essentially involves a transition metal catalyst such as iridium, ruthenium, rhodium, etc., which can borrow hydrogen from alcohols and also transfer it to imine, yielding the desired products. Although this hydrogen-borrowing methodology has remarkable synthetic utilities, it is limited only to the amination of alcohols, and a transition metal catalyst capable of reversibly borrowing hydrogen is essentially needed to complete the catalytic cycle.

In the last two decades, catalytic nucleophilic substitution of nonmanipulated alcohols has drawn significant attention of researchers, and a number of catalytic methods have been developed toward C−C and C−heteroatom bond formation. Considering the simplicity, generality, and high atom efficiency, recently, the catalytic direct nucleophilic substitution of alcohols has aroused interest and was voted as the second most desired reaction that pharmaceutical companies wanted as a greener alternative.[4] Several catalysts have been developed for this transformation in the literature such as Lewis acid-containing metals, such as boron,[5] iron,[6]

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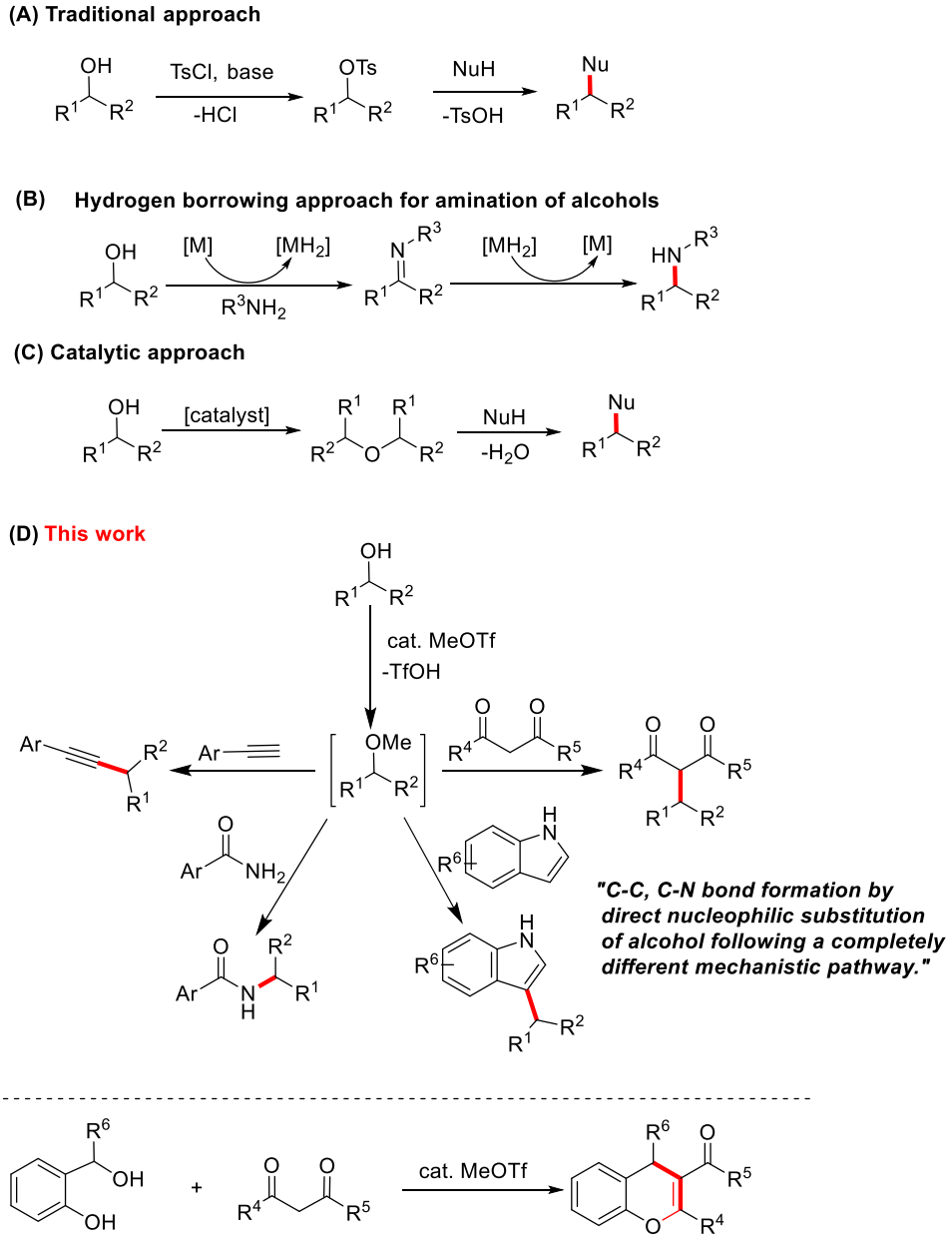
Scheme 1. Previous Reports of Nucleophilic Substitution of Alcohols and This Work



ruthenium,[7] bismuth,[8] indium,[9] and lanthanides (La, Yb, Sc, Hf, Zr),[10] which have been explored as effective catalysts for the direct nucleophilic substitution of alcohols. Also, certain transition metals such as Pd,[11] Co,[12] and Cu[13] have been reported to activate alcohols during nucleophilic substitution reactions (Scheme 1C). In many instances, high reaction temperatures, complex catalytic systems, or expensive metals are involved. There are some metal-free protocols that have been reported recently using molecular iodine[14] and a series of Brønsted acids, *e.g.*, sulfonic acid,[15] Amberlyst-15,[16] H-montmorillonitrite,[17a4e] dodecylbenzenesulfonic acid,[18] *p*-toluenesulfonic acid,[19] triflic acid,[20] and phosphotungstic acid.[21] Besides those, strong and corrosive acids such as perchloric acid[22] and sulfuric acid[23] were also reported to promote the reaction.

Most of the catalytic nucleophilic substitution of non-manipulated alcohols was reported to proceed via the formation of either symmetrical ether or olefin intermediates.[7a10a20,22,24] Importantly, different catalytic protocols were found to preferentially promote reactions involving a specific combination of substrates. For example, catalysts based on Re, Pd, and La were found to favor O-centered nucleophiles, while those of Fe, Bi, and Au gave better results with the S-, C-, and N-centered nucleophiles.[25a] In this context, it remains an important task to develop a general and versatile methodology that would be applicable to almost all kinds of substrates in catalytic nucleophilic substitution of alcohols.

The methylating property of methyl triflate was well known and experimentally established.[24d] Utilizing this inherent property, MeOTf was used as an activator in many reactions where more than an equivalent amount of MeOTf was required to facilitate the reactions.[24ef] In 2017, Zeng and co-workers introduced MeOTf as a catalyst in the Meyer–Schuster rearrangement where the propargyl alcohols got methylated by MeOTf and underwent rearrangement to enable the formation of conjugated *E*-enones and -enals.[24g] Very

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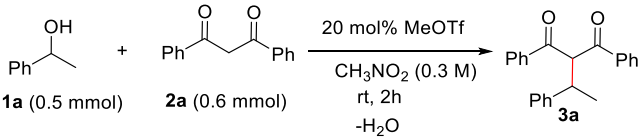
recently, we have reported MeOTf-catalyzed substitution of alcohol followed by O- to N-alkyl group migration generating N-substituted pyridones and the related compound through an entirely different mechanism.[25b] In this report, we wish to disclose our recent development on a generalized MeOTf-catalyzed nucleophilic substitution of alcohols. A completely different mechanism was found to operate where the −OH group of alcohols was converted to the corresponding −OMe group, generating TfOH *in situ*. This methoxy ether underwent a TfOH-catalyzed nucleophilic substitution reaction to yield the product with the regeneration of MeOTf. MeOTf shows its catalytic potential for direct nucleophilic substitution of alcohols with 1,3-dicarbonyls, amides, alkynes, and indoles, and the differential mechanistic aspect is supposed to be the reason for the generality and versatility of the protocol (Scheme 1D). Moreover, the present protocol was equally applicable for one-pot synthesis of biologically relevant 4*H*-chromene derivatives[26,27] from 2-hydroxybenzyl alcohols and 1,3−dicarbonyl compounds.

RESULTS AND DISCUSSION

To explore the catalytic activity of MeOTf toward direct nucleophilic substitution of alcohols, 1-phenylethanol (**1a**) and 1,3-diphenylpropane-1,3-dione (**2a**) were chosen as model electrophilic and nucleophilic partners, respectively. Several solvents were employed to optimize the reaction conditions (Table 1). The reaction was found to proceed in hexane, DCE,

Table 1. Optimization of Reaction Parameters[a]



Reaction Conditions A

entry	deviation from reaction conditions A	yield (%)[b]
1	none	98
2	10 mol % MeOTf instead of 20 mol % MeOTf	75
3	15 mol % MeOTf instead of 20 mol % MeOTf	80
4	hexane instead of CH_3NO_2	60
5	DCM instead of CH_3NO_2	20
6	toluene instead of CH_3NO_2	5
7	DCE instead of CH_3NO_2	40
8	chloroform instead of CH_3NO_2	10
9	1 equiv of **2a** w.r.t. **1a**	90
10	1.5 equiv of **2a** w.r.t. **1a**	98

[a]Reaction conditions: **1a** (1 equiv), **2a** (1.2 equiv), and MeOTf (20 mol %) in nitromethane (0.3 M) at room temperature for 2 h. [b]Yield refers to the pure and isolated product. DCM is dichloromethane. DCE is 1,2-dichloroethane. w.r.t. is with respect to.

DCM, chloroform, and toluene solvents, forming the desired product **3a** in low to moderate yields (5−40%). However, an excellent yield of the product was observed using the nitromethane solvent. Finally, the optimum reaction conditions were found where the reaction between **1a** (1 equiv) and **2a** (1.2 equiv) was performed in the presence of MeOTf (20 mol %) in the nitromethane solvent (0.3 M) at room temperature for 2 h (Table 1, entry 1).

The optimized reaction conditions were applied to a variety of electrophiles and 1,3-dicarbonyl compounds; the results are summarized in Scheme 2. The protocol was found to be general with respect to benzylic, propargylic, allylic, and tertiary alcohols. Secondary benzylic alcohols such as 1-phenylethanol (**1a**) and diphenylmethanol (**1b**) reacted smoothly with 1,3-diphenylpropane-1,3-dione (**2a**), 1-phenylbutane-1,3-dione (**2b**), ethyl 3-oxo-3-phenylpropanoate (**2d**), and pentane-2,4-dione (**2c**) to generate the products **3a, 3b, 3c**, and **3d** in excellent yields (91−100%), respectively. Moreover, propargylic alcohol such as 1,3-diphenylprop-2-yn-1-ol (**1c**) participated in the reaction with **2a** to furnish the desired product **3e** in 98% yields. This method could also be applied to allylic alcohols. Thus, (*E*)-4-phenylbut-3-en-2-ol (**1d**) and 1-phenylprop-2-en-1-ol (**1e**) afforded the desired products **3f** and **3g** when subjected to react with **2a** in moderate to good yields, respectively. Besides secondary alcohols, primary benzylic alcohols were also equally reactive under the present protocol. Phenylmethanol (**1f**) and benzo-[*d*][1,3]dioxol-5-ylmethanol (**1g**) were found to be efficient electrophiles in the reaction with **2a** to generate the corresponding products **3h** and **3i** in 86 and 67% yields, respectively. Most importantly, tertiary butanol (**1h**), which was susceptible to undergo the elimination reaction, successfully underwent the nucleophilic substitution reaction of the hydroxyl group to produce the products **3j** and **3k** in 62 and 65% yields when subjected to react with **2a** and **2d**, respectively. However, a higher reaction temperature (100 °C) and longer reaction time (12 h) were required for these transformations.

To explore the generality and versatility of the MeOTf catalyst, a range of nucleophiles were tested toward nucleophilic substitution of alcohols. Comparatively poor nucleophile amides were found to react smoothly with secondary alcohols as shown in Scheme 3. Secondary alcohol **1a** successfully reacted with benzamide (**2f**), 4-methoxybenzamide (**2g**), 4-chlorobenzamide (**2h**), α, β-unsaturated cinnamide (**2i**), and 4-methylbenzenesulfonamide (**2j**) at 60 °C to afford the expected N-substituted amides (**4a−4e**) in moderate to excellent yields (55−90%). Phenylmethanol (**1f**) was also successfully reacted with 4-fluorobenzamide (**2k**) to produce N-substituted amide **4f** in 82% yield. Unfortunately, inactivated primary alcohols failed to react under our developed conditions, but they showed reactivity with **2j** using MeOTf in the toluene solvent at 120 °C to produced our desired N-substituted amides. Primary alcohols 2-phenylethan-1-ol (**1g**) and 3-phenylpropan-1-ol (**1h**) were subjected to react with **2j** in the toluene solvent at 120 °C for 12 h to afford the expected products **4g** and **4h**, respectively, however, in lower yields (45−40%). To investigate the accessibility of this strategy toward the formation of tertiary amides, **1a** was subjected to react with several secondary amides. When **1a** participated in this protocol with *N*-methylbenzamide (**2r**), generation of tertiary amide **4i** was successfully accessed, however, in a lower yield (42%). Unfortunately, benzanilide failed to afford the desired product with **1a** using this strategy.

Encouraged by the results, we decided to examine the reactivity of alkynes as a nucleophile in catalytic nucleophilic substitution of alcohols (Scheme 4). Delightfully, alkynes were found to show the desired reactivity in the 1,2-dichloroethane solvent. Thus, phenylacetylene (**2l**) reacted with **1a**, 1-(4-bromophenyl)ethan-1-ol (**1i**), and 1-(4-methoxyphenyl)ethan-1-ol (**1j**) to produce the expected products **5a**, **5b**, and **5c** in 60, 71, and 52% yields, respectively, whereas 1-bromo-4-ethynylbenzene (**2m**) was found to react with **1a** to furnish **5d** with a satisfactory yield (50%). However, a completely

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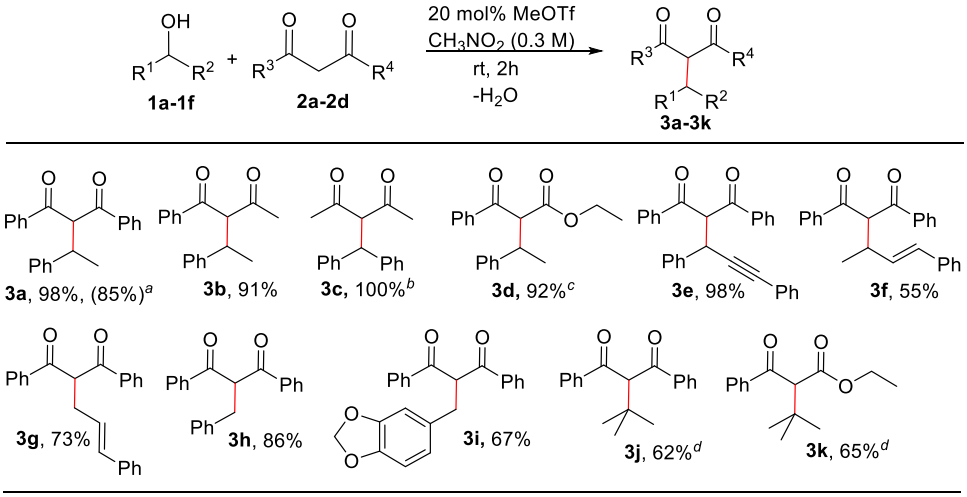
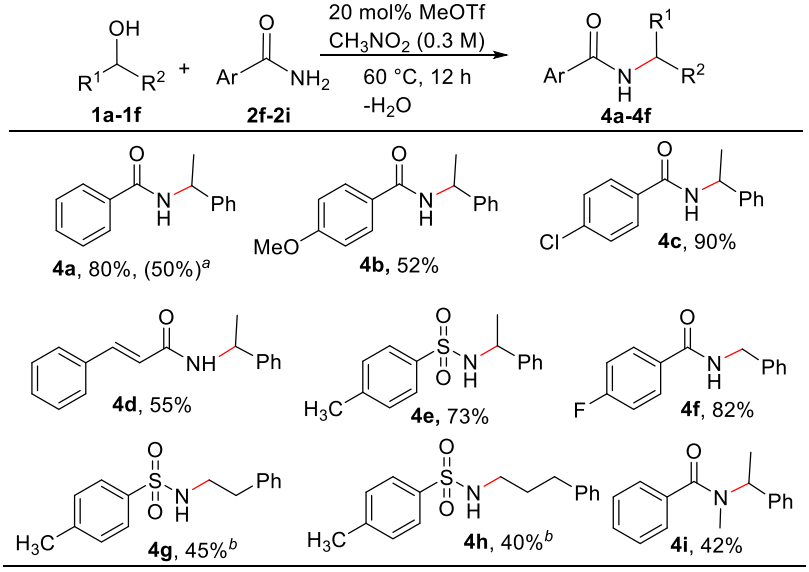
Scheme 2. Substrate Scope of Nucleophilic Substitution of Alcohols by 1,3-Dicarbonyl Compounds*



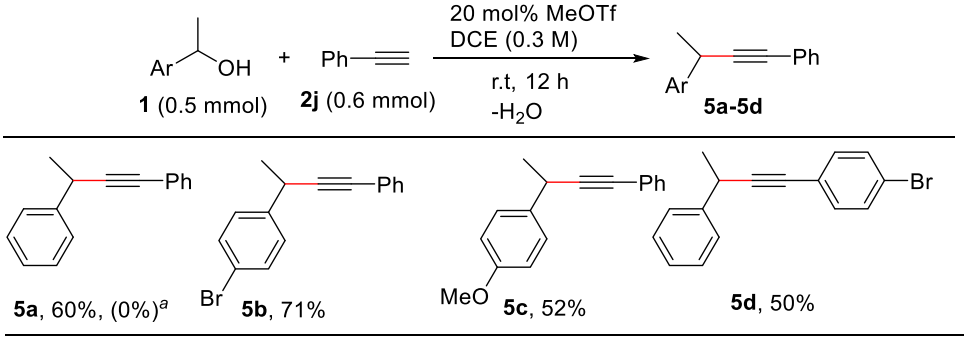
*Reaction conditions: **1** (1 equiv), **2** (1.2 equiv), MeOTf (20 mol %), nitromethane (0.3 M), room temperature, and 2 h. [a]20 mol % TfOH instead of MeOTf. [b]12 h at 90 °C. [c]12 h at 60 °C. [d]12 h at 100 °C.

Scheme 3. Substrate Scope of Nucleophilic Substitution of Alcohols by Amides*



*Reaction conditions: **1** (1 equiv), **2** (1.2 equiv), MeOTf (20 mol %), nitromethane (0.3 M), 60 °C, and 12 h. [a]20 mol % TfOH instead of MeOTf. [b]Toluene (0.3 M), 120 °C, and 12 h.

Scheme 4. Reactivity of Alkynes under the Present Protocol*



*Reaction conditions: **1** (1 equiv), **2** (1.2 equiv), MeOTf (20 mol %), DCE (0.3 M), room temperature, and 12 h. [a]20 mol % TfOH instead of MeOTf.

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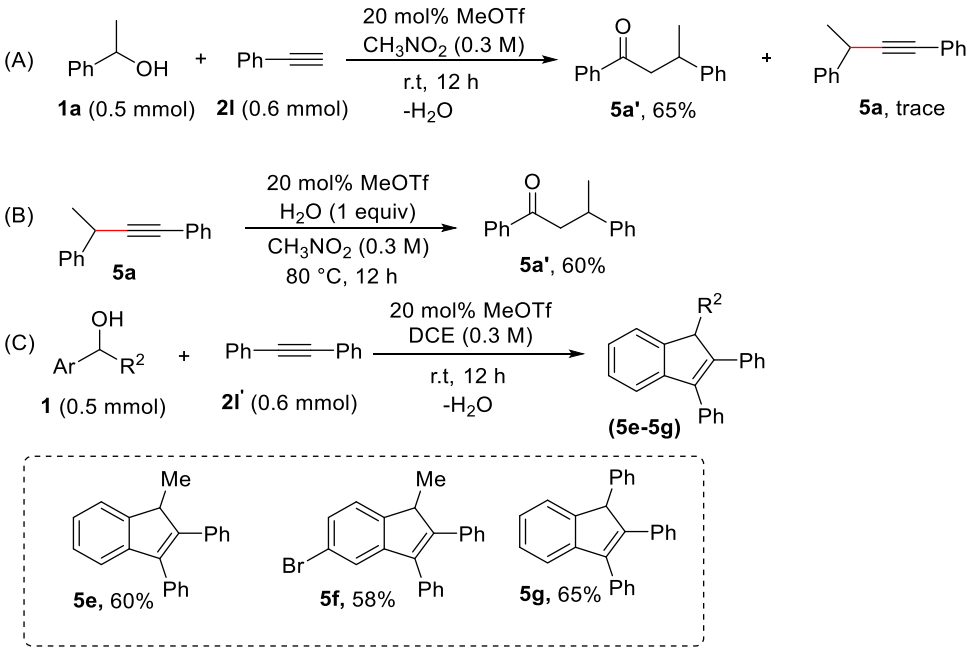
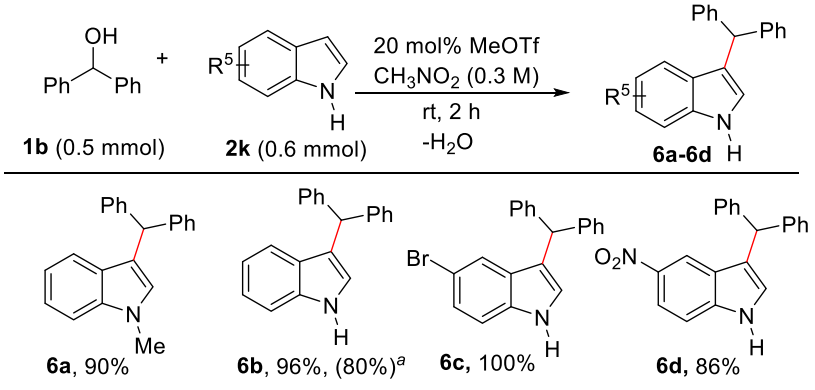
Scheme 5. Reactivity of Alkynes under the Present Protocol



Scheme 6. Reactivity of Indole Derivatives under the Present Protocol*



*Reaction conditions: **1b** (1 equiv), **2** (1.2 equiv), MeOTf (20 mol %), nitromethane (0.3 M), room temperature, and 2 h. [a]20 mol % TfOH instead of MeOTf.

different reactivity was observed in the nitromethane solvent, where phenylacetylene (**2l**) and **1a** generated ketone **5a′** in 65% yield (Scheme 5A). It is worth mentioning that only a trace amount of formation of **5a** was observed in this reaction. To understand the reason why different products were formed in different solvents, we have performed a control experiment (Scheme 5B). When **5a** was subjected to react with H_2O in the presence of the catalyst in the nitromethane solvent, it generated product **5a′**. This experiment showed that the alkyne first underwent nucleophilic substitution with alcohol to produce **5a**, which would further hydrolyze in the nitromethane solvent to generate **5a′**. Formation of different products in different solvents may be attributed to the fact that water/nitromethane formed a homogeneous mixture, whereas water/1,2-dichloroethane did not. For this, availability of the equivalent amounts of water in nitromethane was more than 1,2-dichloroethane, which essentially promoted the hydration of the alkyne bond.[25c]

A completely different reactivity was observed replacing phenylacetylene (**2l**) with the internal alkyne 1,2-diphenylethyne (**2l′**) (Scheme 5C).[25d−f] When **2l′** was subjected to react with **1a** under the present reaction conditions, benzylation followed by cyclization was observed, generating product **5e** in 60% yield. Other secondary benzylic alcohols **1i** and **1b** also successfully took part in the reaction and generated products **5f** and **5g** in 58 and 65% yields, respectively.

Furthermore, the reaction protocol was applied toward nucleophilic substitution of alcohols with indole derivatives, and the results are tabulated in Scheme 6. *N*-Methylindole (**2n**) reacted smoothly with **1b** to produce the expected C_3-alkylated product of indole, **6a**, in 90% yields. Importantly, a chemoselective C-3 functionalization of indoles was observed when alcohols were subjected to react with free indole and the corresponding indole derivatives. Thus, indole (**2o**) successfully reacted with **1b** to furnish the product **6b** chemoselectively, with an excellent yield. Substituted indole derivatives, including 5-bromo-1*H*-indole (**2p**), reacted with **1b** to generate the product **6c** in quantitative yields. Indole derivatives containing an electron-withdrawing nitro group,

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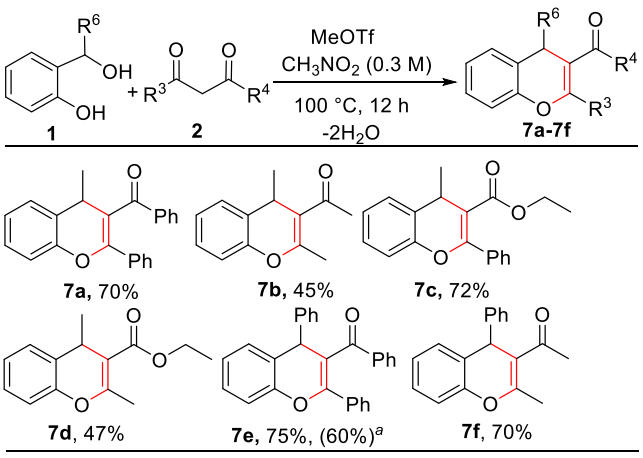
such as 5-nitro-1*H*-indole (**2q**), were also found to generate the product **6d**, all in a bit lower yield.

As an important application, the present protocol was found to be applicable for the direct synthesis of substituted 4*H*-chromene derivatives in one pot, using MeOTf as a catalyst in the nitromethane solvent at 100 °C (Scheme 7). 2-(1-Hydroxyethyl)phenol (**1k**) reacted with 1,3-dicarbonyl compounds, such as **2a**, **2c**, **2d**, and ethyl 3-oxobutanoate (**2e**) under the above-mentioned reaction conditions to produce **7a**, **7b**, **4c**, and **7d** in one pot, in 70, 45, 72, and 47% yields, respectively. 2-(Hydroxyl(phenyl)methyl)phenol (**1l**) also reacted successfully with **2a** and **2c** to produce the corresponding products **7e** and **7f** in 65 and 70% yields, respectively.

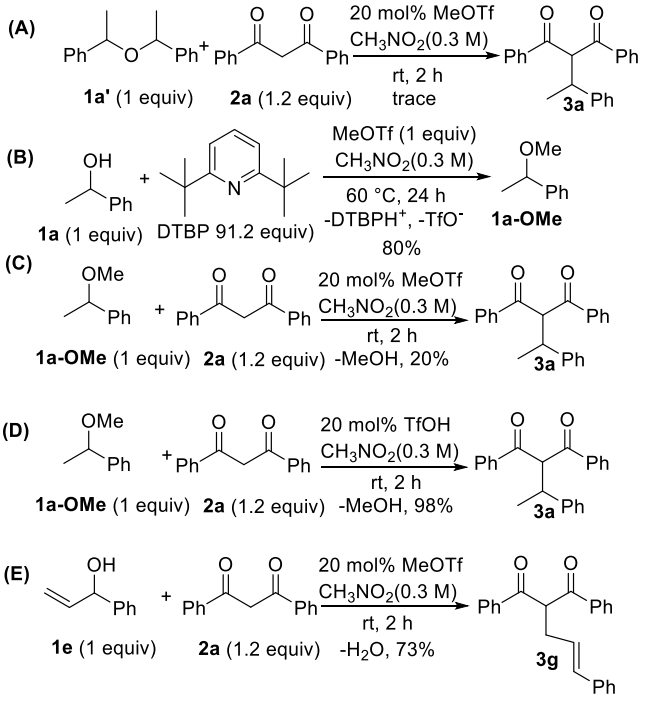
Scheme 7. One-Pot Synthesis of 4*H*-Chromene Derivatives*



*Reaction conditions: **1** (1 equiv), **2** (1.2 equiv), MeOTf (20 mol %), nitromethane (0.3 M), 100 °C, and 12 h. [a]20 mol % TfOH instead of MeOTf.

To emphasize the mechanism, some control experiments were performed taking **1a** and **2a** as model substrates (Scheme 8). It is noteworthy that symmetrical ether and carbocation generated from it were known to be common intermediates in almost all the previous reports.[7a,10a,20,22,24] To investigate the difference in the mechanism that may have operated in MeOTf-catalyzed reactions, symmetrical ether **1a′** was used instead of alcohol **1a** (Scheme 8A). Only a trace amount of product **3a** was formed when **1a′** was subjected to react with **2a** following the optimized conditions. This experimental observation ruled out the possibility of formation of intermediate **1a′** during the course of the reaction. 80% formation of **1a-OMe** was observed when **1a** was subjected to react with MeOTf (1 equiv) in the presence of 2,6-di-*tert*-butylpyridine (DTBP) in nitromethane (Scheme 8B). The presence of DTBP deactivated the *in situ* generation of TfOH, thus allowing for the formation of **1a-OMe**. Importantly, when the methoxy derivative **1a-OMe** was directly used as an electrophile, formation of **3a** was observed in 20% yields using the MeOTf catalyst (Scheme 8C). However, when the same reaction was carried out in the presence of TfOH instead of MeOTf, the yield of **3a** was found to be increased to 98% (Scheme 8D). These experiments proved the dual role of MeOTf. When the reaction was performed between **1e** and **2a** under the optimized reaction conditions, the exclusive formation of **3g** was observed through double-bond migration

Scheme 8. Control Experiments for Mechanistic Investigation



(Scheme 8E). Stereo-electronic factors seemed to have operated in this case, generating the most stable product having the C−C double bond conjugated with the phenyl ring.[20]

Moreover, to explain the superiority of the catalyst in our developed methodology and to establish the fact that the reactions are not promoted by the traces of superacid TfOH, some other control experiments were conducted (Table 2). The reaction of **1a** with **2a** was performed under the same experimental conditions using TfOH and conc.H_2SO_4 (Table 2, entry 1) separately instead of MeOTf, producing the desired product **3a** in 85 and 40% yields, respectively. Similarly, we have also applied these two acids in the reaction between **1a** and **2f** (Table 2, entry 2), resulting in the product **4a** in a lower yield compared to the MeOTf catalyst. The experiment was further extended for alkyne and indole nucleophile. Surprisingly, when **1a** was subjected to react with **2l** using TfOH and conc. H_2SO_4 (Table 2, entry 3), no formation of **5a** was observed. When **1b** underwent nucleophilic substitution with **2n**, the yield of **6a** was reduced in both TfOH (yield 68%) and conc. H_2SO_4 (yield 35%) compared to MeOTf (Table 2, entry 4). Lowering of the yield (45−30%) was also notable for the one-pot synthesis of **7a** from the reaction between **1k** and **2a** (Table 2, entry 5). From these controlled experiments, we can explain that traces of super acids were not involved in these reactions, rather MeOTf activated the alcohol at first and promoted it to react with nucleophiles. These controlled experiments had strongly established the role of MeOTf and its wide range of applicability for the direct nucleophilic substation of nonmanipulated alcohols.

Based on the control experiments and our previous report,[25b] a mechanism of the present protocol has been proposed (Scheme 9). the MeOTf catalyst converted the −OH groups of the alcohols to the corresponding −OMe groups and itself transformed to TfOH. The *in situ* generated TfOH first

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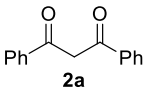
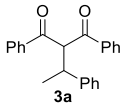
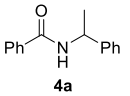
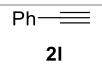
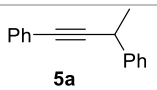
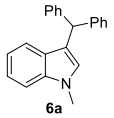
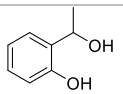
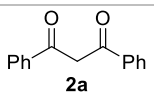
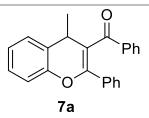
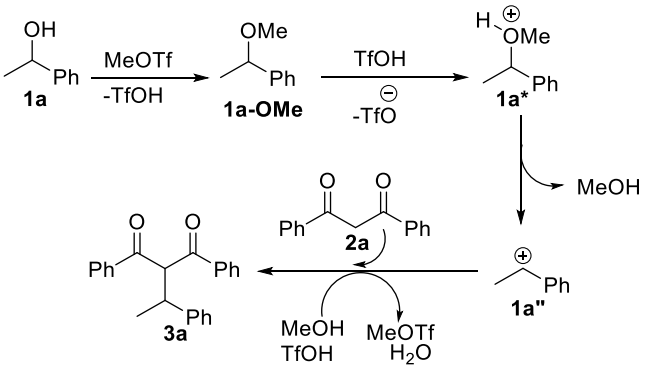
Table 2. Control Experiment to Prove the Catalytic Superiority of MeOTf over TfOH and H_2SO_4*

Entry	Alcohol	Nucleophile	Product	% yield in TfOH	% Yield in H_2SO_4	% Yield in MeOTf
1	 1a	 2a	 3a	85	40	98
2[a]	 1a	 2f	 4a	60	25	80
3[b]	 1a	 2l	 5a	0[c]	0[d]	60
4	 1b	 2n	 6a	68	35	90
5[e]	 1k	 2a	 7a	45	30	70

*Reaction conditions: **1** (1 equiv), **2** (1.2 equiv), catalyst (TfOH/H_2SO_4/MeOTf) (20 mol %), nitromethane (0.3 M), room temperature, and 2 h. [a]60 °C, 12 h. [b]DCE (0.3 M), 12 h. [c]80% formation of the symmetrical ether **1a′** (dr = 1:1) was observed w.r.t **1a**, while remaining starting materials were unreacted. [d]35% formation of symmetrical ether **1a′** (dr = 1:1) was observed w.r.t **1a**, while remaining starting materials were unreacted. [e]100 °C, 12 h.

Scheme 9. Proposed Mechanism of MeOTf-Catalyzed Nucleophilic Substitution of Alcohols



protonated **1a-OMe** to form the protonated species **1***. Elimination of MeOH from **1a*** produced the carbocation **1a″**, which reacted with **2a**, producing the desired product **3a**. The in situ generated MeOH and TfOH reacted to regenerate the MeOTf catalyst. Notably, the experiments in support of the regeneration of the catalyst MeOTf from MeOH and TfOH were already established in our previous work.[25b]

CONCLUSIONS

In conclusion, we have developed a MeOTf-catalyzed strategy for direct nucleophilic substitution of nonmanipulated alcohols by a variety of uncharged nucleophiles. An entirely new mechanism has been proposed, where the alcohol was converted to the corresponding methoxy ether and *in situ* generated TfOH in the presence of catalyst MeOTf. Nucleophilic substitution of the methoxy ether intermediate was catalyzed by the *in situ* generated TfOH, producing the desired product and MeOH. Finally, the catalyst was regenerated from MeOH and TfOH. The developed catalytic protocol is found to be general to almost all kinds of alcohol electrophiles (benzylic, propargylic, allylic, activated primary, and tertiary alcohols) and a variety of C- and N-centered uncharged nucleophiles (1,3-dicarbonyl compounds, amides, alkynes, and N−heterocyclic compounds). Structurally important 4*H*-chromene derivatives have also been synthesized in one pot from 2-hydroxybenzyl alcohols and 1,3-dicarbonyl compounds.

EXPERIMENTAL SECTION

General Considerations. ^1H and ^{13}C NMR spectra were recorded with a 300 and 400 MHz spectrometer as solutions in $CDCl_3$. Chemical shifts are expressed in parts per million (ppm and δ) and are referenced to $CDCl_3$ (δ = 7.28 or 7.18 ppm) as an internal standard. All coupling constants are absolute values and are expressed in Hz. The description of the signals includes s = singlet, d = doublet, t = triplet, q = quadrate, m = multiplet, dd = doublet of doublets, dq = doublet of quadrate, ddd = doublet of doublet of doublets, td = triplet of doublet,

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and brs = broad singlet. ^{13}C NMR spectra were recorded as solutions in $CDCl_3$ with complete proton decoupling. Chemical shifts are expressed in parts per million (ppm, δ) and are referenced to $CDCl_3$ (δ = 77.16 ppm) as an internal standard. The molecular fragments in high-resolution mass spectrometry (HRMS) are quoted as the relation between mass and charge (m/z). The routine monitoring of reactions was performed with a silica gel-precoated Al plate, which was analyzed with iodine and/or ultraviolet (UV light) and ^{1}H NMR analysis of the crude reaction mixture. All reactions were executed with oven-dried glassware without an inert atmosphere.

General Procedure for the Synthesis of 3. Alcohol **1** (0.5 mmol), nucleophile **2** (1,3-dicarbonyl compound, 0.6 mmol), and freshly distilled nitromethane solvent (0.3 M) were taken in a 5 mL VWR reaction vial containing a small magnet without using an inert atmosphere, and then, MeOTf (10 μL, 20 mol %) was added. The cap of the vial was closed, and the reaction mixture was stirred at room temperature for 2 h in an aluminum dry-heating block. After completion of the reaction (by TLC, ^{1}H NMR), the crude reaction mixture was directly purified by column chromatography, using silica gel (100−200 mess) with ethyl acetate/hexane solution to get the desired products **3a**−**3k**.

*1,3-Diphenyl-2-(1-phenylethyl)propane-1,3-dione (**3a**)*.[28a] 1-Phenylethanol **1a** (61 mg, 0.5 mmol), 1,3-dicarbonyl compound **2a** (134 mg, 0.6 mmol), nitromethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **3a** as a white solid (160 mg, 0.49 mmol, 98%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.10−8.06 (m, 2H), 7.80−7.77 (m, 2H), 7.61−7.55 (m, 1H), 7.49−7.41 (m, 3H), 7.33−7.28 (m, 4H), 7.21 (t, J = 7 Hz, 2H), 7.13−7.11 (m, 1H), 5.67 (d, J = 9 Hz, 1H), 4.12 (dq, J = 9, 6 Hz, 1H), 1.39 (d, J = 6 Hz, 3H) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 194.64, 143.83, 137.18, 136.94, 133.56, 133.04, 128.86, 128.84, 128.51, 128.46, 128.41, 127.75, 126.62, 64.93, 41.18, 20.24 ppm.

*1-Phenyl-2-(1-phenylethyl)butane-1,3-dione (**3b**)*.[28a] 1-Phenylethanol **1a** (61 mg, 0.5 mmol), 1,3-dicarbonyl compound **2b** (97 mg, 0.6 mmol), nitromethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **3b** as a white solid (121 mg, 0.45 mmol, 91%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83−7.79 (m, 2H), 7.55−7.48 (m, 1H), 7.40−7.31 (m, 2H), 7.25−7.16(m, 4H), 7.10−7.07 (m, 1H), 4.84 (d, J = 9 Hz, 1H), 3.87 (dq, J = 9, 6 Hz, 1H), 2.27 (s, 3H), 1.33 (d, J = 6 Hz, 3H) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 203.76, 203.25, 195.28, 195.24, 143.45, 143.18, 137.22, 137.04, 133.87, 133.45, 128.90, 128.84, 128.62, 128.48, 128.38, 127.53, 127.39, 127.03, 126.65, 71.52, 70.87, 40.97, 40.38, 29.71, 27.93, 27.54, 21.60, 20.31 ppm.

*3-Benzhydrylpentane-2,4-dione (**3c**)*.[28a] Diphenylmethanol **1b** (92 mg, 0.5 mmol), 1,3-dicarbonyl compound **2c** (60 mg, 0.6 mmol), nitromethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated at 90 °C for 12 h to obtain **3c** as a white solid (133 mg, 0.5 mmol, 100%); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.29 (d, J = 4 Hz, 8H), 7.24−7.21 (m, 2H), 4.86−4.74 (m, 2H), 2.02 (s, 6H) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 203.02, 141.28, 128.96, 127.76, 127.06, 74.55, 51.26, 29.72 ppm.

*Ethyl-2-benzoyl-3-phenylbutanoate (**3d**)*.[10b] 1-Phenylethanol **1a** (61 mg, 0.5 mmol), 1,3-dicarbonyl compound **2d** (115 mg, 0.6 mmol), nitromethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated at 60 °C for 12 h to obtain **3d** (as a mixture of two isomers) as a yellow liquid (136 mg, 0.46 mmol, 92%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16−8.13 (m, 2H), 7.90−7.87 (m, 2H), 7.61−7.52 (m, 1H), 7.51−7.48 (m, 3H), 7.47−7.40 (m, 6H), 7.38−7.22 (m, 5H), 7.17−7.09 (m, 1H), 4.71 (dd, J = 15, 10 Hz, 2H), 4.21 (q, J = 6 Hz, 2H), 3.90−3.83 (m, 4H), 1.42 (d, J = 9 Hz, 3H), 1.30−1.21 (m, 6H), 0.89 (t, J = 6 Hz, 3H) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 193.89, 193.74, 168.72, 168.09, 143.78, 143.45, 136.91,136.74, 133.73, 133.29, 128.85, 128.82, 128.81, 125.54, 128.49, 128.44, 127.75, 127.46, 126.86, 126.56, 61.72, 61.61, 61.36, 61.24, 40.32,39.81, 20.70, 20.31, 14.10, 13.69 ppm.

*2-(1,3-Diphenylprop-2-yn-1-yl)-1,3-dione (**3e**)*.[23] 1,3-Diphenylprop-2-yn-1-ol **1c** (104 mg, 0.5 mmol), 1,3-dicarbonyl compound **2a** (134 mg, 0.6 mmol), nitromethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **3e** as a white solid (203 mg, 0.49 mmol, 98%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.20−8.16 (m, 2H), 7.82−7.79 (m, 2H), 7.63−7.53 (m, 3H), 7.52−7.47 (m, 3H), 7.44−7.30 (m, 4H), 7.23−7.16 (m, 4H), 7.08−7.05 (m, 2H), 5.98 (d, J = 9 Hz, 1H), 5.24 (d, J = 9 Hz, 1H) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 13926, 136.99, 133.57, 133.45, 131.44, 129.12, 128.91, 128.66, 128.60, 128.00, 127.97, 127.49, 122.91, 89.40, 85.13, 63.10, 38.77 ppm.

*(E)-1,3-Diphenyl-2-(4-phenylbut-3-en-2-yl)-propane-1,3-dione (**3f**)*.[28b] (*E*)-4-Phenylbut-3-en-2-ol **1d** (74 mg, 0.5 mmol), 1,3-dicarbonyl **2a** (134 mg, 0.6 mmol), nitromethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **3f** as a white solid (97 mg, 0.27 mmol, 55%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.07−7.97 (m, 4H), 7.61−7.41 (m, 6H), 7.26−7.16 (m, 5H), 6.41 (d, J = 15 Hz, 1H), 6.16 (dd, J = 15, 18 Hz, 1H), 5.38 (d, J = 9 Hz, 1H), 3.73−3.57 (m, 1H), 1.26 (d, J = 9 Hz, 3H) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 195.12, 194.94, 137.14, 137.03, 136.99, 133.57, 133.35, 132.35, 130.56, 128.90, 128.73, 128.75, 128.70, 128.39, 127.23, 126.17, 63.12, 38.61, 18.96 ppm.

*2-Cinnamyl-1,3-diphenylpropane-1,3-dione (**3g**)*.[10b] 1-Phenylprop-2-en-1-ol **1e** (67 mg, 0.5 mmol), 1,3-dicarbonyl compound **2a** (134 mg, 0.6 mmol), nitromethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **3g** as a white solid (124 mg, 0.36 mmol, 73%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.02−7.99 (m, 4H), 7.62−7.57 (m, 2H), 7.51−7.46 (m, 4H), 7.29−7.28 (m, 5H), 6.49 (d, J = 15 Hz, 1H), 6.27 (dt, J = 15, 6 Hz, 1H), 5.38 (t, J = 6 Hz, 1H), 3.73 (dd, J = 15, 6 Hz, 2H) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 195.57, 137.00, 135.95, 133.64, 132.51, 128.97, 128.65, 128.50, 127.38, 126.77, 126.18, 57.18, 32.99 ppm.

*2-Benzyl-1,3-diphenylpropane-1,3-dione (**3h**)*.[28a] Phenylmethanol **1f** (54 mg, 0.5 mmol), 1,3-dicarbonyl compound **2a** (134 mg, 0.6 mmol), nitromethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **3h** as a white solid (100 mg, 0.36 mmol, 73%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.93−7.70 (m, 4H), 7.58−7.54 (m, 2H),7.45−7.40 (m, 4H), 7.29−7.19 (m, 5H), 5.55 (t, J = 6 HZ, 1H), 3.48 (d, J = 6 Hz, 2H) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 195.45, 139.08, 136.02, 133.53, 129.01, 128.85, 128.63, 126.65, 59.04, 35.24 ppm.

*2-(Benzo[d][1,3]dioxol-5-ylmethyl)-1,3-diphenylpropane-1,3-dione (**3i**)*. 2-Benzo[*d*][1,3]dioxol-5-ylmethanol **1g** (54 mg, 0.5 mmol), 1,3-dicarbonyl compound **2a** (134 mg, 0.6 mmol), nitromethane solvent (0.3 M), and MeOTf (10 μL, 0.1

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mmol) were treated following the general procedure to obtain **3i** as a white solid (120 mg, 0.33 mmol, 67%); mp = 120 °C−122 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.91(d, J = 6 Hz, 4H), 7.58−7.53 (m, 2H), 7.46−7.40 (m, 4H), 6.77−6.66 (m, 3H), 5.88 (s, 2H), 5.52 (t, J = 6 Hz, 1H), 3.49 (d, J = 6 Hz, 2H) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 195.43, 147.70, 146.25, 136.01, 133.58, 138.76, 128.90, 128.63, 122.03, 109.52, 108.36, 100.91, 59.26, 34.99 ppm; HRMS (electrospray ionization (ESI)) m/z, $[M + Na]^+$ calculated mass for $C_{23}H_{18}O_4Na^+$: 381.1097; mass found: 381.1085.

*2-(tert-Butyl)-1,3-diphenylpropane-1,3-dione (**3j**).* Tertiary butanol **1h** (37 mg, 0.5 mmol), 1,3-dicarbonyl **2a** (134 mg, 0.6 mmol), nitromethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated at 100 °C for 12 h to obtain **3j** as a white solid (87 mg, 0.31 mmol, 62%); mp = 87 °C−90 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.02−7.99 (m, 4H), 7.59−7.52 (m, 2H), 7.49−7.43 (m, 4H), 5.53 (s, 1H), 1.20 (s, 9H) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 195.12, 138.2, 131.1, 128.8, 128.45, 62.63, 36.32, 29.21 ppm; HRMS (ESI) m/z, $[M + Na]^+$ calculated mass for $C_{19}H_{20}O_2Na^+$: 303.1356; mass found: 303.1355.

*Ethyl-2-benzoyl-3,3-dimethylbutanoate (**3k**).* Tertiary butanol **1h** (37 mg, 0.5 mmol), 1,3-dicarbonyl **2d** (115 mg, 0.6 mmol), nitromethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated at 100 °C for 12 h to obtain **3k** as a white solid (81 mg, 0.33 mmol, 65%); mp = 56 °C−58 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99−7.96 (m, 2H), 7.62−7.56 (m, 1H), 7.52−7.46 (m, 2H), 4.33 (s, 1H), 4.15 (q, J = 6 Hz, 2H), 1.22−1.17(m, 12H) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 195.30, 168.65, 138.30, 133.10, 128.67, 128.26, 61.69, 60.96, 34.75, 28.48. 14.07 ppm; HRMS (ESI) m/z, $[M + Na]^+$ calculated mass for $C_{15}H_{20}O_3$: 271.1305; mass found 271.1388.

*General Procedure for the Synthesis of **4**.* Alcohol **1** (0.5 mmol), nucleophile **2** (amides, 0.6 mmol), and freshly distilled nitromethane solvent (0.3 M) were taken in a 5 mL VWR reaction vial containing a small magnet without using an inert atmosphere, and then, MeOTf (10 μL, 20 mol %) was added. The cap of the vial was closed, and the reaction mixture was stirred at 60 °C for 12 h in an aluminum dry-heating block. After completion of the reaction (by TLC, ^{1}H NMR), the crude reaction mixture was directly purified by column chromatography, using silica gel (100−200 mess) with an ethyl acetate/hexane solution to get the desired products **4a**−**4i**.

*N-(1-Phenylethyl)benzamide (**4a**).*[29a] 1-Phenylethanol **1a** (61 mg, 0.5 mmol), benzamide **2f** (37 mg, 0.6 mmol), nitromethane solvent (1.5 mL), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **4a** as a white solid (90 mg, 0.4 mmol, 80%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.80 (d, J = 7 Hz, 2H), 7.53−7.30 (m, 8H), 6.52(d, J = 6 Hz, 1H), 5.36 (dq, J = 9, 6 Hz, 1H), 1.62 (d, J = 9 Hz, 3H) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 166.64, 143.16, 134.60, 131.49, 128.76, 128.57, 127.47, 126.97, 126.28, 49.25, 21.75 ppm.

*4-Methoxy-N-(1-phenylethyl)benzamide (**4b**).*[29a] 1-Phenylethanol **1a** (61 mg, 0.5 mmol), amide **2g** (91 mg, 0.6 mmol), nitromethane solvent (1.5 mL), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **4b** as a white solid (66 mg, 0.26 mmol, 52%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.78−7.75 (m, 2H), 7.43−7.27 (m, 5H), 6.34(d, J = 6 Hz, 1H), 5.34 (dq, J = 9, 6 Hz, 1H), 3.86 (s, 3H), 1.62 (d, J = 9 HZ, 3H) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 166.12, 162.18, 143.35, 128.75, 128.73, 127.40, 126.86, 126.28, 113.74, 55.41, 49.13, 21.80 ppm.

*4-Chloro-N-(1-phenyl)benzamide (**4c**).*[29a] 1-Phenylethanol **1a** (61 mg, 0.5 mmol), amide **2h** (93 mg, 0.6 mmol), nitromethane solvent (1.5 mL), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **4c** as a white solid (116 mg, 0.45 mmol, 90%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.72−7.70 (m, 2H), 7.40−7.28 (m, 7H), 6.63(d, J = 9 Hz, 1H), 5.31 (dq, J = 9, 6 Hz, 1H), 1.60 (d, J = 9 Hz, 3H) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 165.55, 142.90, 137.2, 132.93, 128.81, 128.40, 127.59, 126.27, 49.40, 21.67 ppm.

*N-(1-Phenylethyl)cinnamide (**4d**).*[29b] 1-Phenylethanol **1a** (61 mg, 0.5 mmol), amide **2i** (88 mg, 0.6 mmol), nitromethane solvent (1.5 mL), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **4d** as a white solid (69 mg, 0.27 mmol, 55%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.69−7.63 (m, 1H), 7.51−7.48 (m, 2H), 7.4−7.28 (m, 8H), 6.45 (d, J = 15 Hz, 1H), 6.04 (d, J = 9 Hz, 1H), 5.31 (dq, J = 9, 6 Hz, 1H), 1.58 (d, J = 9 Hz, 3H) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 165.02, 143.10, 141.27, 134.83, 129.68, 128.81, 128.73, 127.80, 127.45, 126.30, 120.70, 48.98, 21.70 ppm.

*1-Methyl-4-((2-phenylpropyl)sulfonyl)benzene (**4e**).*[29a] 1-Phenylethanol **1a** (61 mg, 0.5 mmol), amide **2j** (102 mg, 0.6 mmol), nitromethane solvent (1.5 mL), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **4e** as a white solid (100 mg, 0.36 mmol, 73%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.67−7.65 (m, 2H), 7.21−7.12 (m, 7H), 5.50 (d, J = 8 Hz, 1H), 4.48 (dq, J = 8 Hz, 1H), 1.43 (d, J = 8 HZ, 3H) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 143.07, 142.22, 137.69, 138.45, 128.49, 127.33, 127.12, 126.18, 53.71, 23.62, 21.51 ppm.

*N-Benzyl-4-fluorobenzamide (**4f**).*[29c] Phenylmethanol (**1f**) (54 mg, 0.5 mmol), amide **2k** (83 mg, 0.6 mmol), nitromethane solvent (1.5 mL), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **4f** as a white solid (93 mg, 0.4 mmol, 82%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89−7.70 (m, 2H), 7.42−7.21 (m, 5H), 7.09 (t, J = 8.6 Hz, 2H), 6.70 (s, 1H), 4.62 (d, J = 5.7 Hz, 2H) ppm; ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 166.44, 166.00, 163.50, 138.10, 130.54, 130.50, 129.41, 129.33, 128.81, 127.89, 127.67, 115.71, 115.49, 44.17 ppm.

*1-Methyl-4-(phenethylsulfonyl)benzene (**4g**).*[29d] 2-Phenylethan-1-ol **1g** (61 mg, 0.5 mmol), amide **2j** (102 mg, 0.6 mmol), toluene solvent (1.5 mL), and MeOTf (10 μL, 0.1 mmol) were treated at 120 °C for 12 h to obtain **4g** as a white solid (60 mg, 0.22 mmol, 45%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77−7.63 (m, 2H), 7.34−7.20 (m, 5H), 7.17−7.07 (m, 2H), 4.23 (t, J = 7.1 Hz, 2H), 2.98 (t, J = 7.1 Hz, 2H), 2.46 (s, 3H) ppm; ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 144.67, 136.21, 132.96, 129.80, 128.92, 128.61, 127.85, 126.89, 70.62, 35.36, 21.65 ppm.

*4-Methyl-N-(3-phenylpropyl)benzenesulfonamide (**4h**).*[29d] 3-Phenylpropan-1-ol **1h** (68 mg, 0.5 mmol), amide **2j** (102 mg, 0.6 mmol), toluene solvent (1.5 mL), and MeOTf (10 μL, 0.1 mmol) were treated at 120 °C for 12 h to obtain **4h** as a white solid (57 mg, 0.20 mmol, 40%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86−7.76 (m, 2H), 7.37 (d, J = 8.1 Hz, 2H), 7.31−7.23 (m, 2H), 7.23−7.16 (m, 1H), 7.13−7.04 (m, 2H), 4.05 (t, J = 6.2 Hz, 2H), 2.75−2.57 (m, 2H), 2.48 (s, 3H), 2.09−1.84 (m, 2H) ppm; ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ

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144.76, 140.39, 133.12, 129.87, 128.49, 128.43, 127.94, 126.16, 69.62, 31.47, 30.47, 21.67 ppm.

*N-Methyl-N-(1-phenylethyl)benzamide (**4i**).*[29e] 1-Phenylethanol **1a** (61 mg, 0.5 mmol), amide **2r** (81 mg, 0.6 mmol), nitromethane solvent (1.5 mL), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **4i** as a colorless oil (50 mg, 0.21 mmol, 42%); ^{1}H NMR (400 MHz, $CDCl_3$, 1:1 mixture of rotamers): δ 7.61−7.05 (m, 10H), 6.20 (brs, 1/2H), 5.10 (brs, 1/2H), 2.82 (s, 3/2H), 2.64 (s, 3/2H), 1.62 (d, *J* = 6.0 Hz, 3H) ppm; ^{13}C{H} NMR (100 MHz, $CDCl_3$, 1:1 mixture of rotamers): δ 172.14, 171.66, 140.14, 136.82, 129.46, 128.64, 127.47, 126.64, 56.43, 50.69, 31.76, 27.88, 17.30, 15.41 ppm.

*General Procedure for the Synthesis of **5**.* Alcohol **1** (0.5 mmol), nucleophile **2** (alkynes, 0.6 mmol), and freshly distilled 1,2-dichloroethane solvent (0.3 M) were taken in a 5 mL VWR reaction vial containing a small magnet without using an inert atmosphere, and then, MeOTf (10 μL, 20 mol %) was added. The cap of the vial was closed, and the reaction mixture was stirred at room temperature for 12 h in an aluminum dry-heating block. After completion of the reaction (by TLC, ^{1}H NMR), the crude reaction mixture was directly purified by column chromatography, using silica gel (100−200 mess) with ethyl acetate/hexane solution to get the desired products **5a**−**5g**.

*But-1-yne-1,3-diyldibenzene (**5a**).*[30a] 1-Phenylethanol **1a** (61 mg, 0.5 mmol), alkyne **2l** (61 mg, 0.6 mmol), 1,2-dichloroethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **5a** as a pale-yellow liquid (62 mg, 0.30 mmol, 60%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50−7.45 (m, 3H), 7.40−7.27 (m, 7H), 4.01 (q, *J* = 6 Hz, 1H), 1.61 (d, *J* = 6 Hz, 3H) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 143.34, 131.63, 128.56, 128.20, 127.75, 126.94, 126.67, 123.74, 92.61, 82.43, 32.48, 24.52 ppm.

*1-Bromo-4-(4-phenylbut-3-yn-2-yl)benzene (**5b**).*[30a] (4-Bromophenyl)ethan-1-ol **1i** (100 mg, 0.5 mmol), alkyne **2l** (61 mg, 0.6 mmol), 1,2-dichloroethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **5b** as a pale-yellow liquid (101 mg, 0.35 mmol, 71%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49−7.44 (m, 2H), 7.41−7.37 (m, 2H), 7.33−7.29 (m, 3H), 6.93−6.89 (m, 2H), 3.97 (q, *J* = 8 Hz, 1H), 3.83 (s, 3H), 1.58 (d, *J* = 8 Hz, 3H) ppm; ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 142.37, 133.68, 131.62, 128.75, 128.26, 127.93, 123.45, 120.45, 91.85, 82.79, 32.03, 24.37 ppm.

*1-Methoxy-4-(4-phenylbut-3-yn-2-yl)benzene (**5c**).*[30b] 1-(4-Methoxyphenyl)ethan-1-ol **1j** (76 mg, 0.5 mmol), alkyne **2l** (61 mg, 0.6 mmol), 1,2-dichloroethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **5c** as a pale-yellow liquid (61 mg, 0.26 mmol, 52%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50−7.44 (m, 4H), 7.37−7.30 (m, 5H),3.96 (q, *J* = 6 Hz, 1H), 3.83 (s, 3H), 1.58 (d, *J* = 6 Hz, 3H) ppm; ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 158.35, 135.50, 131.63, 128.21, 127.91, 127.72, 123.79, 113.93, 92.97, 82.24, 31.66, 24.62 ppm.

*1-Bromo-4-(3-phenylbut-1-yn-1-yl)benzene (**5d**).*[30c] 1-Phenylethanol **1a** (61 mg, 0.5 mmol), alkyne **2m** (70 mg, 0.6 mmol), 1,2-dichloroethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **5d** as a pale-yellow liquid (70 mg, 0.25 mmol, 50%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.47−7.43 (m, 4H), 7.40−7.25 (m, 5H), 3.99 (q, *J* = 9 Hz, 1H), 1.60 (d, *J* = 9 Hz, 3H) ppm; ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 143.03, 133.12, 131.45, 128.51, 127.32, 126.91, 122.70, 121.89, 93.89, 81.39, 32.51, 24.35 ppm.

*1-Methyl-2,3-diphenyl-1H-indene (**5e**).*[30d] 1-Phenylethanol **1a** (61 mg, 0.5 mmol), alkyne **2l′** (106 mg, 0.6 mmol), 1,2-dichloroethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **5e** as a white solid (85 mg, 0.29 mmol, 60%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.60−7.52 (m, 1H), 7.38 (m, *J* = 4.7, 5H), 7.34−7.18 (m, 8H), 4.08 (q, *J* = 8 Hz, 1H), 1.35 (d, *J* = 8 Hz, 3H) ppm; ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 148.49, 147.75, 144.93, 138.40, 135.70, 135.66, 129.58, 129.43, 128.59, 128.09, 127.23, 126.75, 126.69, 125.14, 122.87, 120.41, 45.96, 16.63 ppm.

*5-Bromo-1-methyl-2,3-diphenyl-1H-indene (**5f**).*[30d] (4-Bromophenyl)ethan-1-ol **1i** (100 mg, 0.5 mmol), alkyne **2l′** (106 mg, 0.6 mmol), 1,2-dichloroethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **5f** as a white solid (103 mg, 0.28 mmol, 58%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57−7.30 (m, 8H), 7.30−7.22 (m, 3H), 7.22−7.15 (m, 2H), 4.03 (q, *J* = 8 Hz, 1H), 1.32 (d, *J* = 8 Hz, 3H) ppm; ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 149.26, 147.17, 147.08, 137.55, 135.14, 134.95, 129.44, 129.40, 128.78, 128.17, 127.84, 127.53, 127.12, 124.26, 123.45, 120.76, 45.65, 16.51 ppm.

*1,2,3-Triphenyl-1H-indene (**5g**).*[30d] Diphenylmethanol **1b** (92 mg, 0.5 mmol), alkyne **2l′** (106 mg, 0.6 mmol), 1,2-dichloroethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **5g** as a white solid (110 mg, 0.32 mmol, 65%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.55−7.37 (m, 6H), 7.37−7.28 (m, 4H), 7.28−7.16 (m, 8H), 7.16−7.06 (m, 3H), 5.18 (s, 1H) ppm; ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 148.29, 145.66, 145.07, 139.87, 135.66, 129.60, 129.39, 128.81, 128.75, 128.47, 128.26, 127.93, 127.56, 127.34, 126.99, 126.78, 126.72, 125.80, 124.01, 120.59, 58.07 ppm.

*General Procedure for the Synthesis of **5a′**.* Alcohol **1** (0.5 mmol), nucleophile **2** (alkynes, 0.6 mmol), and freshly distilled dichloroethane solvent (0.3 M) were taken in a 5 mL VWR reaction vial containing a small magnet without using an inert atmosphere, and then, MeOTf (10 μL, 20 mol %) was added. The cap of the vial was closed, and the reaction mixture was stirred at room temperature for 12 h in an aluminum dry-heating block. After completion of the reaction (by TLC, ^{1}H NMR), the crude reaction mixture was directly purified by column chromatography, using silica gel (100−200 mess) with ethyl acetate/hexane solution to get the desired product **5a′**.

*1,3-Diphenylbutan-1-one (**5a′**).*[30e] 1-Phenylethanol **1a** (61 mg, 0.5 mmol), alkyne **2l** (61 mg, 0.6 mmol), nitromethane solvent (1.5 mL), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **5a** as a white solid (72 mg, 0.32 mmol, 65%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99−7.86 (m, 2H), 7.61−7.50 (m, 1H), 7.44 (m, 2H), 7.35−7.24 (m, 5H), 7.22−7.15 (m, 1H), 3.57−3.44 (m, 1H), 3.31 (dd, *J* = 16.5, 5.7 Hz, 1H), 3.18 (dd, *J* = 16.5, 8.3 Hz, 1H), 1.34 (d, *J* = 6.9 Hz, 3H) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 199.13, 146.58, 137.20, 133.00, 128.58, 128.55, 128.09, 126.87, 126.29, 47.04, 35.59, 21.89 ppm.

*General Procedure for the Synthesis of **6**.* Alcohol **1** (0.5 mmol), nucleophile **2** (derivatives of indoles, 0.6 mmol), and freshly distilled nitromethane solvent (0.3 M) were taken in a 5 mL VWR reaction vial containing a small magnet without using an inert atmosphere, and then, MeOTf (10 μL, 20 mol

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%) was added. The cap of the vial was closed, and the reaction mixture was stirred at room temperature for 2 h in an aluminum dry-heating block. After completion of the reaction (by TLC, ^{1}H NMR), the crude reaction mixture was directly purified by column chromatography, using silica gel (100−200 mess) with ethyl acetate/hexane solution to get the desired products **6a**−**6d**.

*3-Benzhydryl-1-methyl-1H-indole (**6a**).*[31a] Diphenylmethanol **1b** (92 mg, 0.5 mmol), *N*-methylindole **2n** (79 mg, 0.6 mmol), nitromethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **6a** as a white solid (134 mg, 0.45 mmol, 90%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35−7.21 (m, 13H), 7.04−7.00 (m, 1H), 6.46 (s, 1H), 5.71 (s, 1H), 3.73 (s, 3H) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 144.16, 137.49, 129.05, 128.77, 128.30, 127.41, 126.21, 121.66, 120.02, 118.86, 118.31, 109.15, 48.83, 32.71 ppm.

*3-Benzhydryl-1H-indole (**6b**).*[31a] Diphenylmethanol **1b** (92 mg, 0.5 mmol), indole **2o** (70 mg, 0.6 mmol), nitromethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **6b** as a white solid (136 mg, 0.48 mmol, 96%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (brs, 1H), 7.41−7.26 (m, 14H), 7.12−7.09 (m, 1H), 6.59 (s, 1H), 5.79 (s, 1H) ppm; ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 144.08, 136.77, 129.14, 128.43, 127.08, 126.38, 124.23, 122.21, 120.02, 119.91, 119.51, 111.22, 48.93 ppm.

*3-Benzhydryl-5-bromo-1H-indole (**6c**).*[31a] Diphenylmethanol **1b** (92 mg, 0.5 mmol), 5-bromo-1*H*-indole **2p** (116 mg, 0.6 mmol), nitromethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **6c** as a white solid (180 mg, 0.5 mmol, 100%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.97 (brs, 1H), 7.43 (s, 1H), 7.36−7.21 (m, 12H), 6.59 (s, 1H), 5.66 (s, 1H) ppm; ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 143.51, 135.31, 128.93, 128.40, 126.43,125.25, 125.06, 122.35, 119.67, 112.74, 84.54 ppm.

*3-Benzhydryl-5-nitro-1H-indole (**6d**).*[31b] Diphenylmethanol **1b** (92 mg, 0.5 mmol), 5-nitro-1*H*-indole **2q** (97 mg, 0.6 mmol), nitromethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **6d** as a white solid (141 mg, 0.43 mmol, 86%); ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.71 (s, 1H), 8.08 (d, *J* = 2.3 Hz, 1H), 7.99−7.96 (m, 1H), 7.56−7.54 (m, 1H), 7.34−7.21 (m, 10H), 7.01−7.00 (m, 1H), 5.85 (s, 1H). 8.65 (d, *J* = 2.2 Hz, 1H), 8.42 (brs, 1H), 8.22 (d, *J* = 2.3 Hz, 1H), 8.16−8.10 (m, 1H), 7.49−7.38 (m, 2H), 7.36−7.30 (m, 3H), 7.28−7.22 (m, 4H), 6.83−6.69 (m, 1H), 5.73 (s, 1H) ppm; ^{13}C{H} NMR (100 MHz, DMSO-d_6): δ 144.13, 140.62, 140.32, 129.00, 128.91, 128.54, 126.85, 126.27, 121.12, 117.15, 116.53, 112.61, 47.84 ppm.

*General Procedure for the Synthesis of **7**.* Alcohol **1** (0.5 mmol), nucleophile **2** (1,3-dicarbonyls, 0.6 mmol), and freshly distilled nitromethane solvent (0.3 M) were taken in a 5 mL VWR reaction vial containing a small magnet without using an inert atmosphere, and then, MeOTf (10 μL, 20 mol %) was added. The cap of the vial was closed, and the reaction mixture was stirred at 100 °C for 12 h in an aluminum dry-heating block. After completion of the reaction (by TLC, ^{1}H NMR), the crude reaction mixture was directly purified by column chromatography, using silica gel (100−200 mess) with ethyl acetate/hexane solution to get the desired products **7a**−**7f**.

*(4-Methyl-2-phenyl-4H-chromen-3-yl)(phenyl)methanone (**7a**).* 2-(1-Hydroxyethyl)phenol **1k** (69 mg, 0.5 mmol), 1,3-dicarbonyl compound **2a** (134 mg, 0.6 mmol), nitromethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **7a** as a colorless liquid (114 mg, 0.35 mmol, 70%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.66−7.63 (m,2H), 7.41−7.38 (m, 2H), 7.31−7.23 (m, 3H), 7.18−7.11 (m, 7H), 4.08 (q, *J* = 9 Hz, 1H), 1.53 (d, *J* = 9 Hz, 3H) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 197.88, 155.88, 150.83, 138.53, 134.12, 132.00, 129.71, 129.31, 127.92, 127.88, 127.50, 126.95, 124.52, 116.32, 115.72, 32.97, 25.21 ppm; HRMS (ESI), *m*/*z*, $[M + H]^+$: calculated mass for $C_{12}H_{19}O_2^+$: 327.1380; mass found 327.1380.

*1-(2,4-Dimethyl-4H-chromen-3-yl)ethan-1-one (**7b**).*[26b] 2-(1-Hydroxyethyl)phenol **1k** (69 mg, 0.5 mmol), 1,3-dicarbonyl compound **2c** (60 mg, 0.6 mmol), nitromethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **7b** as a colorless liquid (50 mg, 0.25 mmol, 50%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.23−7.17(m, 2H), 7.13−7.01 (m, 1H), 7.69−7.98 (m, 1H), 3.91 (q, *J* = 6 Hz, 1H), 2.39 (s, 3H), 2.37 (s, 3H), 1.28 (d, *J* = 6 Hz, 3H) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 198.92, 159.49, 149.98, 127.89, 127.31, 127.16, 124.43, 116.47, 115.94, 30.82, 29.75, 26.08, 20.20 ppm.

*Ethyl-4-methyl-2-phenyl-4H-chromene-3-carboxylate (**7c**).* 2-(1-Hydroxyethyl)phenol **1k** (69 mg, 0.5 mmol), 1,3-dicarbonyl compound **2d** (115 mg, 0.6 mmol), nitromethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **7c** as a colorless liquid (106 mg, 0.36 mmol, 75%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.53−7.44 (m, 5H), 7.27−7.07 (m, 4H), 4.08−4.00 (m, 3H), 1.50 (d, *J* = 6 Hz, 3H), 2.39 (s, 3H), 1.00 (t, *J* = 6 Hz, 3H) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 167.68, 158.81,150.55, 135.54, 129.43, 128.74, 128.09, 127.88, 127.43, 126.88, 124.66, 116.25, 108.85, 60.23, 31.40, 25.72, 13.69 ppm. HRMS (ESI), *m*/*z*, $[M + H]^+$: calculated for $C_{19}H_{20}O_3^+$: 296.1362; mass found 296.1357.

*Ethyl-2,4-dimethyl-4H-chromene-3-carboxylate (**7d**).*[32] 2-(1-Hydroxyethyl)phenol **1k** (69 mg, 0.5 mmol), 1,3-dicarbonyl compound **2e** (78 mg, 0.6 mmol), nitromethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **7d** as a colorless liquid (54 mg, 0.23 mmol, 47%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.21−7.15 (m, 2H), 7.11−7.06 (m, 1H), 6.99−6.95 (m, 1H), 4.33−4.21 (m, 2H), 3.90 (q, *J* = 6 Hz, 1H), 2.42 (s, 3H), 1.36 (t, *J* = 6 Hz, 3H), 1.30 (d, *J* = 6 Hz, 3H) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 167.54, 160.50, 149.99, 128.01, 127.13, 127.08, 124.29, 115.85, 107.28, 60.08, 30.25, 25.91, 19.56, 14.35 ppm.

*(2,4-Diphenyl-4H-chromen-3-yl)(phenyl)methanone (**7e**).*[26b] 2-(Hydroxyl(phenyl)methyl)phenol **1l** (100 mg, 0.5 mmol), 1,3-dicarbonyl **2a** (134 mg, 0.6 mmol), nitromethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **7e** as a white solid (126 mg, 0.32 mmol, 65%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.54−7.45 (m, 4H), 7.41−7.37 (m, 2H), 7.32−7.23 (m, 4H), 7.21−7.05 (m, 9H), 5.37 (s, 1H) ppm; ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 197.36, 155.46, 150.39, 145.30, 138.46, 134.00, 131.77, 129.80, 129.55, 129.35, 129.17, 128.67, 128.14, 127.93, 127.87, 127.69, 126.76, 124.67, 124.66, 116.54, 114.46, 43.95 ppm.

*1-(2-Methyl-4-phenyl-4H-chromen-3-yl)ethan-1-one (**7f**).*[26b] 2-(Hydroxyl(phenyl)methyl)phenol **1l** (100 mg, 0.5 mmol), 1,3-dicarbonyl **2c** (60 mg, 0.6 mmol), nitromethane solvent (0.3 M), and MeOTf (10 μL, 0.1 mmol) were treated following the general procedure to obtain **7f** as a colorless liquid (92 mg, 0.35 mmol, 70%); ^{1}H NMR (300 MHz,

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$CDCl_3$): δ 7.33−7.27 (m, 4H), 7.23−7.14 (m, 3H), 7.08−7.99 (m, 2H), 5.05 (s, 1H), 2.49 (s, 3H), 2.20 (s, 3H) ppm; $^{13}C\{H\}$ NMR (100 MHz, $CDCl_3$); δ 199.13, 159.32, 149.01, 145.83, 128.96, 128.93, 127.69, 127.58, 126.91, 124.89, 124.56, 116.35, 114.18, 42.27, 30.17, 20.19 ppm.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.3c05619.

^1H and ^{13}C NMR spectra of the synthesized compounds **3**, **4**, **5**, **6**, **7**, and **1a-OMe** (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Srijit Biswas − *Department of Chemistry, University of Calcutta, Kolkata 700 009 West Bengal, India*; orcid.org/0000-0003-2363-7381; Email: sbchem@caluniv.ac.in, srijit_biswas@yahoo.co.in

Authors

Srabani Maity − *Department of Chemistry, University of Calcutta, Kolkata 700 009 West Bengal, India*

Arnab Roy − *Department of Chemistry, University of Calcutta, Kolkata 700 009 West Bengal, India*

Surajit Duari − *Department of Chemistry, University of Calcutta, Kolkata 700 009 West Bengal, India*

Subrata Biswas − *Department of Chemistry, University of Calcutta, Kolkata 700 009 West Bengal, India*

Asma M. Elsharif − *Department of Chemistry, Imam Abdulrahman Bin Faisal University, Dammam 31441, Saudi Arabia*

Complete contact information is available at: https://pubs.acs.org/10.1021/acsomega.3c05619

Author Contributions

§A.R. and S.D. contributed equally to this work. S.M. and S.B.* designed the project. S.B.* acquired the research funding, accommodated researchers, and supervised the work. S.M., A.R., S.D., and S.B. investigated the reactions and purified and characterized the products. A.M.E. helped with the formal analysis of the samples and mechanistic investigations. The article and the ESI were prepared mutually by all authors.

Notes

The authors declare no competing financial interest.

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