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Iron(III)-Catalyzed Addition of Benzylic Alcohols to Aryl Alkynes – A New Synthesis of Substituted Aryl Ketones

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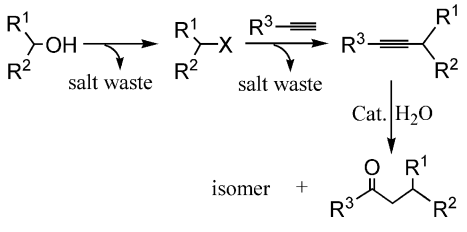
A new, efficient and direct addition of benzylic alcohols with terminal aryl alkynes was developed with the inexpensive, non-toxic, $FeCl_3$ catalyst in nitromethane. The reaction provides a simple method for the synthesis of substituted aryl ketones under mild conditions, and the reaction is highly atom-economical. Several substituted terminal alkynes underwent smooth reaction with various substituted benzylic alcohols. The electron-rich alkynes reacted more efficiently and gave higher yields than did the neutral or electron-deficient alkynes. A wide range of functional groups were tolerated in the developed protocol. The intermediate of this reaction was isolated, and a possible mechanism has been proposed.

Introduction

The regioselective functionalization of asymmetrically substituted alkynes is of fundamental importance in organic synthesis.[1] Those proceeding in an atom-economical manner, in which all the atoms of the reactants end up in the final product, are the most useful in organic synthesis.[2] In particular, the hydration of alkynes to carbonyl compounds is the most typical example of atom-economical transformations since no byproducts are generated. Consequently, a large number of methods have been developed for the hydration of alkynes to synthesize the corresponding carbonyl compounds.[3] Although a wide range of methods and reagents are available to achieve selectively either Markovnikov or anti-Markovnikov products from terminal alkynes.[1,3,4] The hydration of internal alkynes is always problematic, usually giving a mixture of two ketones.[3,5] To avoid this, a few indirect methods for the hydrolysis of internal alkynes with anti-Markovnikov selectivities have been described, which involve a regioselective hydroamination and a subsequent hydrolysis of the generated imine.[6] Very recently, the microwave-assisted, *p*-toluenesulfonic-acid catalyzed, regioselective hydration of an internal alkyne,[7] and a one-pot synthesis of internal alkynes and their hydration have also been described.[8] However, in all these methods, the preparation of internal alkynes is required. Among the methods to synthesize internal alkynes, the palladium-catalyzed, Sonogashira coupling reaction between terminal alkynes and aryl/alkenyl halides is widely used.[9] However, little work has been done on the cross-coupling with benzylic, allylic and propargylic electrophiles.[10] The preparation of internal alkynes still relies on traditional methods that involve either the substitution of alcohol derivatives such as halides and carboxylates with alkynylide anions or the elimination of 1,2-dihalides. These processes require the conversion of alkynes to the corresponding alkynylide anions with stoichiometric amounts of a strong base (e.g. organolithium or organomagnesium reagents). However, the problem associated with all these methods is the production of a large amount waste salts both in the derivatization of alcohols and during the substitution or coupling reaction (Scheme 1), which makes the reaction less atom-efficient. Therefore, an alternative route that avoids all these limitations is highly desirable.



Scheme 1. Hydration of internal alkynes.

The direct utilization of benzylic alcohols as electrophiles for carbon–carbon bond formation would be very useful since it would be both atom-economical and environmentally friendly, as water is the only by-product. However carbon–carbon bond formation with the direct use of alcohols is very difficult because of their poor leaving-group ability, and generally a large excess or stoichiometric amount of reagents are required for the direct substitution of alcohols. Therefore, the development of a catalytic version of this reaction remains a major challenge in modern organic synthe-

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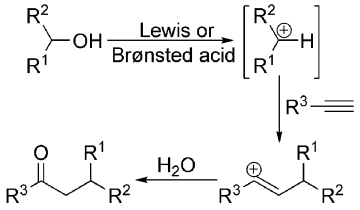
sis. To date, a few catalytic methods have been developed for variety of carbon–carbon and carbon–heteroatom bond formations by direct substitution of alcohols, such as palladium(0), $NaAuCl_4$, $Bi(OTf)_3$, $InCl_3$, $Yb(OTf)_3$, trifluoromethanesulfonic acid, H-montmorillonite and *p*-toluenesulfonic acid.[11] More recently, a direct substitution of benzylic alcohols by alkynyl boron dihalides in the presence of *n*BuLi has also been demonstrated to afford internal alkynes.[12] However, the disadvantages associated with these reagents are moisture sensitivity, high toxicity, low selectivity and relative expense. In order to circumvent these problems, the iron salts have attracted much attention in synthetic organic chemistry, since iron is highly abundant in nature, and consequently, iron and its salts are inexpensive, commercially available and environmentally friendly.[13] Very recently, we[14] and others[15] have demonstrated the use of $FeCl_3$ for the catalytic activation of alcohols towards various nucleophiles. During our study, we anticipated that a new domino reaction between the alkyne and alcohol might be possible with a suitable Lewis- or Brønsted-acid catalyst. The carbon–carbon bond formation in this reaction would be initiated by a carbocation, which would then generate an alkenyl cation. A subsequent nucleophilic attack by hydroxide ion, which represent a novel atom-economical synthesis of substituted ketones (Scheme 2).



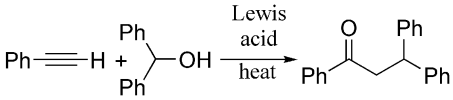
Scheme 2.

Although, the intermolecular electrophilic addition of a carbonium ion to an alkyne is well-known, this transformation has not been much explored in organic synthesis.[16] In this paper, we describe the discovery of the $FeCl_3$-catalyzed, novel, sequential, C–C and C–O bond-forming reactions of benzylic alcohols with aryl acetylenes for the regioselective synthesis of aryl ketones.

Results and Discussion

Although the functionalization of alkynes with $FeCl_3$ has been reported recently,[17] to the best of our knowledge, there is no report of the sequential C–C and C–O bond-forming reactions of benzylic alcohols with aryl acetylenes either with $FeCl_3$ or with any other catalyst.[16a] In our initial studies, phenylacetylene **1a** was treated with benzhydrol **2a** in presence of different catalysts to test the hypothesis. After screening a large number of catalysts under similar conditions (Table 1), we observed that the target ketone was formed in a moderate yield (39%) with anhydrous $FeCl_3$ (15 mol-%) in nitromethane at 80 °C. Further studies indicated that the addition of H_2O (2 equiv.) could improve the yield up to 42%, and the yield was improved up to 45% with hydrated $FeCl_3$ with alcohol **2a** (1.2 equiv.). The other catalysts employed [$Yb(OTf)_3$, *p*-toluenesulfonic acid and $InCl_3$] can also activate benzylic alcohols, but in those cases, the desired product was obtained in low yield. No reaction occurred with transition-metal salts such as those of nickel and copper. However, the reaction with $PdCl_2$ did occur but led to a mixture of products.

Table 1. Reaction of phenylacetylene and benzhydrol with different catalysts.[a]



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

Entry	Catalyst	Yield (%)[b]
1	*p*TsOH·H_2O	16
2	$ZnCl_2$	15
3	$InCl_3$	28
4	$Yb(OTf)_3$	4
5	$FeCl_3$	39
6	$FeCl_3$ + H_2O (2 equiv.)	42
7	$FeCl_3·6H_2O$	45
8	$NiCl_2·6H_2O$	n.r.
9	$Cu(OAc)_2·H_2O$	n.r.
10	$PdCl_2$	0

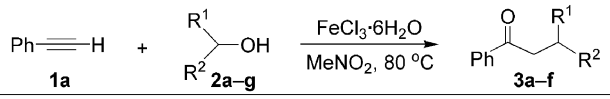
[a] Reaction condition: Phenylacetylene (1 mmol), benzhydrol (1.2 mmol), nitromethane (3 mL), catalyst (10 mol-%), 80 °C, 2 h, and then catalyst (5 mol-%) was again added, and the reaction was heated for 3 h. [b] Pure, isolated yield after column chromatography.

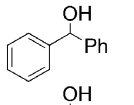
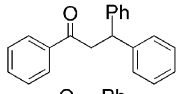
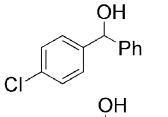
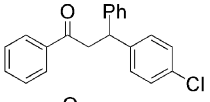
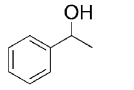
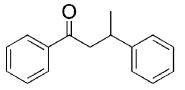
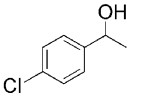
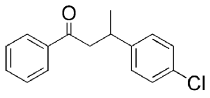
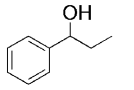
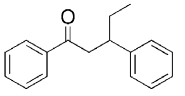
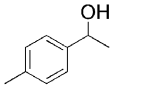
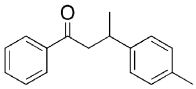
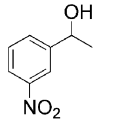
The effect of solvent was also investigated. We found the yield to be highly depended on solvent polarity. Among the various solvents, nitromethane was the most effective. The reaction did not proceed at all in coordinating solvents such as tetrahydrofuran and dimethyl formamide. However, 20% of product was obtained in acetonitrile. Hydrocarbon solvents such as toluene gave a mixture of products, and the desired product was obtained only in trace amount. Dichloromethane and dichloroethane gave only 2–4% of the desired product.[18]

The experimental procedure for this reaction was very simple. The mixture of aryl acetylene and benzylic alcohol in nitromethane was heated at 80 °C with catalytic $FeCl_3·6H_2O$ (15 mol-%) for a set period of time (monitored by TLC) without the removal of air and moisture. The product was then isolated by extraction with ethyl acetate.

Having optimized the reaction conditions, the scope of this new reaction was investigated with various benzylic alcohols with phenylacetylene. The results are summarized in Table 2. In general, the reaction proceeded smoothly and was complete within 2 h to produce various substituted aryl ketones with high Markovnikov selectivity in moderate yield. The regioselectivity may be explained by the formation of the more stable alkenyl carbocation intermediate during the course of the reaction. Both the electron-rich

Table 2. $FeCl_3$-catalysed reaction of phenylacetylene **1** with various benzylic alcohols **2**.[a]



Entry	Alcohol **2a–g**		Product **3a–f**		Yield (%)[b]
1		**2a**		**3a**	45
2		**2b**		**3b**	53
3		**2c**		**3c**	47
4		**2d**		**3d**	51
5		**2e**		**3e**	43
6		**2f**		**3f**	46
7		**2g**	—		n.r.

[a] Reaction conditions: Phenylacetylene **1** (1.0 mmol), benzylic alcohols **2** (1.2 mmol), $FeCl_3·6H_2O$ (0.1 mmol), nitromethane (3 mL), 80 °C, 2 h, and then $FeCl_3·6H_2O$ (0.05 mmol), 3 h. [b] The yields refer to pure isolated product.

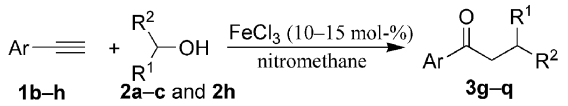
and electron-deficient benzylic alcohols reacted smoothly with phenylacetylene, affording the desired ketones in moderate to good yields. But the reaction did not proceed at all, with the phenyl ring of the benzylic alcohol bearing a strongly electron-withdrawing group such as $-NO_2$ (Table 2, Entry 7). Alcohols that are sensitive to acid-catalyzed dehydration were also tolerated under the present conditions (Table 2, Entries 3–6). It should be noted that besides the formation of the desired ketone, the concomitant formation of a small amount of acetophenone (≈ 6%) by the simple hydration of phenylacetylene[17c] was also observed in the crude ^1H NMR. Although this reaction worked well for a wide range of secondary benzylic alcohols, benzyl alcohol was unchanged even after prolonged reaction times.

Encouraged by these results, we next examined the scope of this domino reaction in various substituted alkynes, which were prepared according to the literature method,[19] and the results are shown in Table 3. The reaction appeared to be quite general with respect to the alkynes. We found that electron-donating groups (such as -OMe, -Me or -OTs, Table 3, Entries 1–8) in phenylacetylene were more beneficial than the presence of weakly electron-withdrawing substituents such as -Cl or -Br (Table 3, Entries 9–11) Interestingly, when we performed the reaction on an electron-rich alkyne such as **1b** under standard conditions (hydrated $FeCl_3$ as the catalyst in $MeNO_2$), we obtained the desired product and a reasonable amount of *p*-methoxy acetophenone.

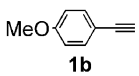
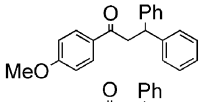
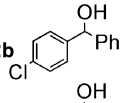
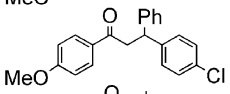
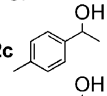
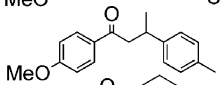
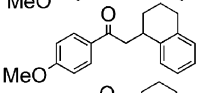
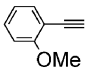
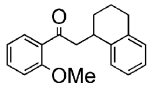
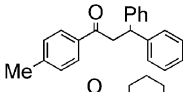
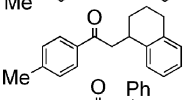
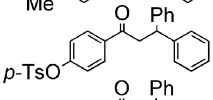
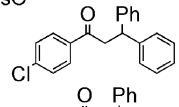
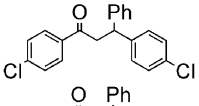
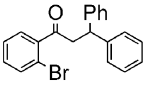
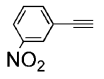
Surprisingly, high yields of the desired product was obtained for electron-rich alkynes (Table 3, Entries 1–4 and 6–7) with anhydrous $FeCl_3$ (10 mol-%) at r.t. However, a sterically hindered alkyne (**1c**) gave moderate yield at 60 °C (Table 3, Entry 5). On the other hand, phenylacetylene bearing the strong electron-withdrawing $-NO_2$ group (Table 3, Entry 12) did not react under the standard conditions. Moreover, internal alkyne such as diphenylacetylene and alkyl alkyne did not give any of the desired ketone.

The mechanism of this reaction can only be speculated (Scheme 3) at present based on experimental observations. We[14] and others[20] have previously observed that with a catalytic amount of $FeCl_3$, benzylic alcohols were rapidly converted to dimeric ether **2b** by eliminating water (Scheme 3). Presumably, in the presence of a nucleophile, the ether is polarized by $FeCl_3$ and generates an incipient benzylic carbocation. The stability of benzylic carbocation is well-documented and has been the subject of theoretical and experimental studies.[21] The nucleophilic attack of the alkyne moiety onto the resulting benzyl carbocation generates more stable alkenyl cation **2c**. And nucleophilic attack of water (which is being generated during ether formation

Table 3. $FeCl_3$-catalyzed reaction of substituted phenylacetylene **1** with various benzylic alcohols **2**.[a]

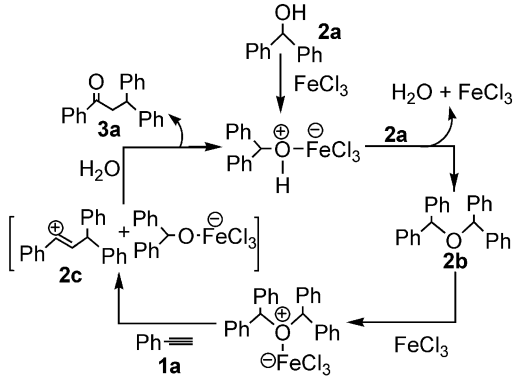


1b–h **2a–c and 2h** **3g–q**

Entry	Nucleophile	Alcohol	Product	Yield (%)[b]
1	 **1b**	**2a** 	**3g** 	80
2	**1b**	**2b** 	**3h** 	62
3	**1b**	**2c** 	**3i** 	63
4	**1b**	**2h** 	**3j** 	79
5	**1c** 	**2h**	**3k** 	48
6	**1d** 	**2a**	**3l** 	55[c]
7	**1d**	**2h**	**3m** 	51
8	*p*-TsO  **1e**	**2a**	**3n** 	58[d]
9	**1f** 	**2a**	**3o** 	42[d]
10	**1f**	**2b**	**3p** 	40[d]
11	**1g** 	**2a**	**3q** 	39[d]
12	**1h** 	**2a**	—	n.r.

[a] Conditions: Alkyne **1** (1.0 mmol), benzylic alcohol **2** (1.2 mmol), anhydrous $FeCl_3$ (0.1 mmol) nitromethane (3 mL), 5 h, r.t. [b] The yields refer to pure isolated product based on alkyne. [c] 4 h at r.t., then 60 °C for 2 h. [d] $FeCl_3 \cdot 6H_2O$ (0.1 mmol), 80 °C for 2 h, catalyst (0.05 mmol), 80 °C for 3 h.

and/or from the hydrated $FeCl_3$ whenever used) onto the alkenyl cation, followed by deprotonation and subsequent tautomerization, leads to the final product **3a**. The generation of the alkenyl cation can be supported by the fact that for the case of electron-rich alkynes, the reaction worked efficiently event at room temperature. Similarly, the generation of the benzylic carbocation from the corresponding alcohols can also be explained from the observations that benzyl alcohol and a benzylic alcohol bearing a $-NO_2$ group did not react. To confirm the formation of the ether intermediate, a separate experiment was performed between ether **2b** and phenylacetylene; we observed that the ether reacted smoothly with phenylacetylene in the presence of $FeCl_3 \cdot 6H_2O$ to produce the desired ketone in a similar yield (≈ 42%) to that obtained when starting from **2a**. The ether was prepared from the alcohol with a catalytic amount of



Scheme 3. Probable mechanism.

$FeCl_3$ (10 mol-%) in nitromethane in the absence of the alkyne at r.t. in quantitative yield. A similar reaction with $InCl_3$ only gave 26% of the desired product. This concluded that $FeCl_3$ is more efficient for this reaction.

Despite the draw back of low yields under the current conditions, the reactions of aryl alkynes with benzylic alcohols are quite remarkable as a synthetic method. In general, the reactions are quite efficient, simple and can be performed in the presence of air and moisture and only a catalytic amount of $FeCl_3$ is necessary. The conditions are very mild, as even the electron-rich alkynes worked at r.t. The reaction did not proceed at all without any catalyst, and a wide range of functional groups such as, -OMe, -Cl, -Br and -OTs can tolerate this method.

Conclusions

In summary, we have developed a novel tandem reaction between terminal aryl acetylenes and benzylic alcohols to synthesize aryl ketones with catalytic $FeCl_3$ with high atom economy. The notable advantages of this method are the operational simplicity (one-pot reaction), mild reaction conditions, direct use of alcohols and the use of inexpensive and non-toxic $FeCl_3$. This method is energy saving, environmentally friendly and provides a straightforward alternative to the classical stepwise method. In addition, due to the easy availability of the starting materials and catalyst, this reaction may prove very useful in organic synthesis. Further studies in this area to explore the mechanism and synthetic applications of this reaction are being carried out in our laboratory.

Experimental Section

General: ^{1}H NMR spectra were recorded with a Bruker 300 (300 MHz) spectrometer as solutions in $CDCl_3$. Chemical shifts are expressed in parts per million (ppm, δ) and are referenced to $CHCl_3$ (δ = 7.26 ppm) as an internal standard. All coupling constants are absolute values and are expressed in Hz. The description of the signals include: s = singlet, d = doublet, t = triplet, m = multiplet and dd = doublet of doublets. ^{13}C NMR spectra were recorded with a Bruker 300 (75 MHz) spectrometer as solutions in $CDCl_3$ with complete proton decoupling. Chemical shifts are expressed in parts per million (ppm, δ) and are referenced to $CHCl_3$ (δ = 77.0 ppm) as an internal standard. High-Resolution Mass Spectra (HRMS) were performed with a Qtof Micro YA263 spectrometer. The molecular fragments are quoted as the relation between mass and charge (m/z). IR (infrared spectroscopy) was recorded with an FT-IR spectrometer, the IR spectra of solids were recorded in KBr and those of oils and liquids were recorded as thin films with KBr. The routine monitoring of reactions was performed with silica gel-coated glass slides (Merck, silica gel G for TLC), which were analyzed with iodine. Solvents, reagents and chemicals were purchased from Aldrich, Fluka, Merck, SRL, Spectrochem and Process Chemicals. Nitromethane was distilled from calcium hydride prior to use. All reactions involving moisture-sensitive reactants were executed with oven-dried glassware. All the benzylic alcohols were prepared either by the reduction of ketones or by a Grignard reaction.

General Procedure for the Addition of Benzylic Alcohols to Alkynes: Representative experimental procedure for the synthesis of 1,3,3-triphenylpropan-1-one (**3a**): A 5 mL screw-cap vial was charged with phenylacetylene (102 mg, 1 mmol), benzhydrol (221 mg, 1.2 mmol) and nitromethane (3 mL). To this stirred solution, $FeCl_3{\cdot}6H_2O$ (27 mg, 0.1 mmol) was added, and the reaction mixture was heated at 80 °C for 2 h. $FeCl_3{\cdot}6H_2O$ (13.5 mg, 0.05 mmol) was added, and heating was continued for another 3 h. The progress of the reaction was followed by TLC. The reaction mixture was allowed to attain r.t. and was then taken up in water (10 mL). The reaction mixture was extracted with ethyl acetate (2 × 25 mL), and the organic phase was dried with anhydrous Na_2SO_4. The solvent was removed under reduced pressure, and the product was purified by silica gel column chromatography (5% ethyl acetate in petroleum spirit) to afford **3a** (129 mg, 0.45 mmol, 45%) as a white solid; m.p. 88 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.75 (d, J = 7.5 Hz, 2 H), 4.84 (t, J = 7.4 Hz, 1 H), 7.15–7.58 (m, 13 H), 7.95 (d, J = 3 Hz, 2 H) ppm.[22]

This procedure was followed for all reactions in Tables 2 and 3 except where otherwise mentioned. The melting points (m.p.) and spectroscopic data (IR, ^{1}H and ^{13}C NMR, HRMS and elemental analysis) for all unknown compounds and only the m.p. and ^{1}H NMR spectroscopic data for known compounds are provided below.

3-(4-Chlorophenyl)-1,3-diphenylpropan-1-one (3b):[23] Alkyne **1a** (102 mg, 1 mmol), alcohol **2b** (263 mg, 1.2 mmol) and hexahydrated $FeCl_3$ (41 mg, 0.15 mmol) in nitromethane (3 mL) were treated as described for **3a** to obtain the product **3b** as a pale yellow oil (170 mg, 0.53 mmol, 53%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.72 (d, J = 7.2 Hz, 2 H), 4.81 (t, J = 7.2 Hz, 1 H), 7.12–7.32 (m, 9 H), 7.43–7.59 (m, 3 H), 7.94 (d, J = 7.7 Hz, 2 H) ppm.

1,3-Diphenylbutan-1-one (3c):[22] Alkyne **1a** (102 mg, 1 mmol) alcohol **2c** (147 mg, 1.2 mmol) and hexahydrated $FeCl_3$ (41 mg, 0.15 mmol) in nitromethane (3 mL) were treated as described for **3a** to obtain the product **3c** as a white solid (105 mg, 0.47 mmol, 47%); m.p. 58–59 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.35 (d, J = 6.7 Hz, 3 H), 3.19 (dd, J = 8.0, 16.4 Hz, 1 H), 3.31 (dd, J = 5.6, 16.4 Hz, 1 H), 3.46–3.57 (m, 1 H), 7.18–7.58 (m, 8 H), 7.93 (d, J = 7.6 Hz, 2 H) ppm.

3-(4-Chlorophenyl)-1-phenylbutan-1-one (3d):[22] Alkyne **1a** (102 mg, 1 mmol), alcohol **2d** (188 mg, 1.2 mmol) and hexahydrated $FeCl_3$ (41 mg, 0.15 mmol) in nitromethane (3 mL) were treated as described for **3a** to obtain the product **3d** as a pale yellow oil (129 mg, 0.51 mmol, 51%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.32 (d, J = 6.8 Hz, 3 H), 3.17 (dd, J = 7.7, 16.7 Hz, 1 H), 3.28 (dd, J = 6.4, 16.6 Hz, 1 H), 3.47–3.56 (m, 1 H), 7.19–7.37 (m, 4 H), 7.42–7.58 (m, 3 H), 7.92 (d, J = 7.3 Hz, 2 H) ppm.

1,3-Diphenylpentan-1-one (3e):[24] Alkyne **1a** (102 mg, 1 mmol), alcohol **2e** (163 mg, 1.2 mmol) and hexahydrated $FeCl_3$ (41 mg, 0.15 mmol) in nitromethane (3 mL) were treated as described for **3a** to obtain the product **3e** as a colorless oil (102 mg, 0.43 mmol, 43%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81 (t, J = 7.5 Hz, 3 H), 1.62–1.67 (m, 1 H), 1.75–1.82 (m, 1 H), 3.2–3.32 (m, 3 H), 7.16–7.32 (m, 5 H), 7.39–7.56 (m, 3 H), 7.91 (d, J = 7.5 Hz, 2 H) ppm.

1-Phenyl-3-*p*-tolylbutan-1-one (3f):[22] Alkyne **1a** (102 mg, 1 mmol), alcohol **2f** (163 mg, 1.2 mmol) and hexahydrated $FeCl_3$ (41 mg, 0.15 mmol) in nitromethane (3 mL) were treated as described for **3a** to obtain the product **3f** as a pale yellow oil (110 mg, 0.46 mmol, 46%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.33 (d, J = 7.0 Hz, 3 H), 2.32 (s, 3 H), 3.17 (dd, J = 8.3, 16.5 Hz, 1 H), 3.29 (dd, J = 5.7, 16.4 Hz, 1 H), 3.42–3.51 (m, 1 H), 7.10–7.19 (m, 4 H), 7.42–7.58 (m, 3 H), 7.94 (d, J = 7.9 Hz, 2 H) ppm.

1-(4-Methoxyphenyl)-3,3-diphenylpropan-1-one (3g):[25] A mixture of alkyne **1b** (132 mg, 1 mmol), alcohol **2a** (221 mg, 1.2 mmol), anhydrous $FeCl_3$ (16 mg, 0.1 mmol) and nitromethane (3 mL) were stirred at r.t. for 5 h, and the product was isolated as described for **3a**. The product **3g** was obtained as a white solid (253 mg, 0.8 mmol, 80%); m.p. 92 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.69 (d, J = 7.2 Hz, 2 H), 3.86 (s, 3 H), 4.83 (t, J = 7.2 Hz, 1 H), 6.91 (d, J = 8.8 Hz, 2 H), 7.17–7.27 (m, 10 H), 7.93 (d, J = 8.8 Hz, 2 H) ppm.

3-(4-Chlorophenyl)-1-(4-methoxyphenyl)-3-phenylpropan-1-one (3h): Alkyne **1b** (132 mg, 1 mmol), alcohol **2b** (262 mg, 1.2 mmol), anhydrous $FeCl_3$ (16 mg, 0.1 mmol) and nitromethane (3 mL) were treated as described for **3g** to obtain the product **3h** as a white solid (218 mg, 0.62 mmol, 62%); m.p. 99 °C. IR (KBr): $\tilde{\nu}$ = 3023, 2838, 1679, 1600, 1510, 1490, 1264, 1246, 1212, 1168, 1027, 986, 838, 822, 701 cm^{-1}. ^{1}H NMR (300 MHz, CDCl3): δ = 3.66 (dd, J = 2.0, 7.1 Hz, 2 H), 3.87 (s, 3 H), 4.80 (t, J = 7.1 Hz, 1 H), 6.92 (dd, J = 1.6, 6.9 Hz, 2 H), 7.19–7.31 (m, 9 H), 7.92 (dd, J = 1.8, 7.0 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 44.2, 45.4, 55.5, 113.8, 126.5, 127.7, 128.6, 129.2, 130.0, 130.3, 132.1, 142.8, 143.9, 163.6, 196.2 ppm. HRMS: calcd. for $C_{22}H_{19}ClNaO_2$ 373.0971; found 373.0978. $C_{22}H_{19}ClO_2$ (350.11): calcd. C 75.32, H 5.46; found C 74.96, H 5.46.

1-(4-Methoxyphenyl)-3-*p*-tolylbutan-1-one (3i): Alkyne **1b** (132 mg, 1 mmol), alcohol **2c** (163 mg, 1.2 mmol), anhydrous $FeCl_3$ (16 mg, 0.1 mmol) and nitromethane (3 mL) were added as described for **3g** to obtain the product **3i** as a pale yellow oil (169 mg, 0.63 mmol, 63%). IR (neat): $\tilde{\nu}$ = 2974, 2933, 1670, 1599, 1508, 1263, 1165, 816, 542 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.31 (d, J = 7.0 Hz, 3 H), 2.32 (s, 3 H), 3.11 (dd, J = 8.5, 16.2 Hz, 1 H), 3.23 (dd, J = 5.6, 16.0 Hz, 1 H), 3.87 (s, 3 H), 6.92 (dd, J = 1.9, 7.0 Hz, 2 H), 7.10–7.19 (m, 4 H), 7.92 (dd, J = 1.9, 6.9 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.0, 22.0, 35.4, 46.8, 55.4, 113.7, 126.7, 129.2, 130.4, 130.4, 135.7, 143.8, 163.4, 197.7 ppm. $C_{18}H_{20}O_2$ (268.35): calcd. C 80.56, H 7.51; found C 80.67, H 7.45.

1-(4-Methoxyphenyl)-2-(1,2,3,4-tetrahydronaphthalen-1-yl)ethanone (3j): Alkyne **1b** (132 mg, 1 mmol), alcohol **2h** (178 mg, 1.2 mmol), anhydrous $FeCl_3$ (16 mg, 0.1 mmol) and nitromethane (3 mL) as described for **3g** to the obtain product **3j** as a pale yellow solid (221 mg, 0.79 mmol, 79%); m.p. 70 °C. IR (KBr): $\tilde{\nu}$ = 2933, 2870, 1669, 1603, 1578, 1509, 1420, 1291, 1256, 1210, 1171, 1030, 810, 751 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.64–1.93 (m, 4 H), 2.77–2.82 (m, 2 H) 3.23–3.27 (m, 2 H), 3.60–3.65 (m, 1 H), 3.88 (s, 3 H), 6.95 (d, J = 8.7 Hz, 2 H), 7.11–7.20 (m, 4 H), 7.98 (d, J = 8.7 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.7, 28.3, 29.7, 33.7, 45.9, 55.5, 113.8, 125.9, 128.5, 129.3, 130.4, 137.3, 140.3, 163.5, 198.0 ppm. HRMS: calcd. for $C_{19}H_{20}NaO_2$ 303.1361; found 303.1360. $C_{19}H_{20}O_2$ (280.37): calcd. C 81.40, H 7.19; found C 81.32, H 7.15.

1-(2-Methoxyphenyl)-2-(1,2,3,4-tetrahydronaphthalen-1-yl)ethanone (3k): Alkyne **1c** (132 mg, 1 mmol), alcohol **2h** (178 mg, 1.2 mmol), anhydrous $FeCl_3$ (16 mg, 0.1 mmol) and nitromethane (3 mL) were treated as described for **3g** to obtain the product **3k** as a pale yellow solid (135 mg, 0.48 mmol, 48%); m.p. 67 °C. IR (KBr): $\tilde{\nu}$ = 2936, 2861, 1671, 1660, 1595, 1484, 1436, 1298, 1250, 1026, 766, 753 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.65–1.92 (m, 4 H), 2.75–2.81 (m, 2 H), 3.28 (dd, J = 9.5, 16.7 Hz, 1 H), 3.38 (dd, J = 4.3, 16.8 Hz, 1 H), 3.53–3.61 (m, 1 H), 3.90 (s, 3 H), 6.96–7.23 (m, 6 H), 7.44–7.50 (m, 1 H), 7.7 (dd, J = 1.7, 7.7 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.8, 28.4, 29.7, 33.7, 51.4, 55.5, 111.5, 120.7, 125.6, 125.7, 128.4, 128.9, 129.1, 130.3, 133.2, 137.3, 140.4, 158.2, 202.2 ppm. HRMS: calcd. for $C_{19}H_{20}NaO_2$ 303.1361; found 303.1360. $C_{19}H_{20}O_2$ (280.37): calcd. C 81.40, H 7.19; found C 81.32, H 7.15.

3,3-Diphenyl-1-*p*-tolylpropan-1-one (3l):[26] A mixture of alkyne **1d** (116 mg, 1 mmol), alcohol **2a** (221 mg, 1.2 mmol), anhydrous $FeCl_3$ (16 mg, 0.1 mmol) and nitromethane (3 mL) were stirred at r.t. for 4 h and then heated at 60 °C for 2 h, and the product was isolated as described for **3a**. The product **3l** was obtained as a white solid (165 mg, 0.55 mmol, 55%); m.p. 86 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.40 (s, 3 H), 3.72 (d, J = 7.3 Hz, 2 H), 4.83 (t, J = 7.3 Hz, 1 H), 7.15–7.28 (m, 12 H), 7.84 (d, J = 8.2 Hz, 2 H) ppm.

2-(1,2,3,4-Tetrahydronaphthalen-1-yl)-1-*p*-tolylethanone (3m): Alkyne **1d** (116 mg, 1 mmol), alcohol **2h** (178 mg, 1.2 mmol), anhydrous $FeCl_3$ (16 mg, 0.1 mmol) and nitromethane (3 mL) were treated as described for **3g** to obtain the product **3m** as a pale yellow oil (135 mg, 0.51 mmol, 51%). IR (neat): $\tilde{\nu}$ = 2929, 2862, 1682, 1607, 1450, 1286, 1180, 806, 751 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.60–1.95 (m, 4 H), 2.42 (s, 3 H), 2.76–2.82 (m, 2 H), 3.26–3.29 (m, 2 H), 3.60–3.65 (m, 1 H), 7.07–7.28 (m, 6 H), 7.89 (d, J = 8.1 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.8, 21.7, 28.3, 29.7, 33.7, 46.2, 125.9, 128.3, 128.5, 129.3, 129.4, 134.9, 137.3, 140.3, 143.9, 199.1 ppm. HRMS: calcd. for $C_{19}H_{20}NaO$ 287.1412; found 287.1410. $C_{19}H_{20}O$ (264.37): calcd. C 86.32, H 7.63; found C 86.30, H 7.42.

4-(3,3-Diphenylpropanoyl)phenyl 4-Methylbenzenesulfonate (3n): Alkyne **1e** (272 mg, 1 mmol), alcohol **2a** (221 mg, 1.2 mmol), hexahydrated $FeCl_3$ (41 mg, 0.15 mmol) and nitromethane (3 mL) were treated as described for **3a** to obtain the product **3n** as a light brown solid (265 mg, 0.58 mmol, 58%); m.p. 171 °C. IR (KBr): $\tilde{\nu}$ = 3048, 2919, 1682, 1598, 1373, 1151, 870, 706, 551 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.45 (s, 3 H), 3.69 (d, J = 7.3 Hz, 2 H), 4.78 (t, J = 7.2 Hz, 1 H), 7.05 (d, J = 8.6 Hz, 2 H), 7.16–7.33 (m, 12 H), 7.70 (d, J = 8.2 Hz, 2 H), 7.86 (d, J = 8.6 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.6, 44.7, 45.8, 122.4, 126.4, 127.7, 128.4, 128.5, 129.7, 129.8, 132.1, 135.5, 143.8, 145.6, 152.9, 196.5 ppm. HRMS: calcd. for $C_{28}H_{24}NaO_4S$ 479.1293; found 479.1232. $C_{28}H_{24}O_4S$ (456.56): calcd. C 73.66, H 5.30; found C 73.64, H 5.42.

1-(4-Chlorophenyl)-3,3-diphenylpropan-1-one (3o):[26] Alkyne **1f** (137 mg, 1 mmol), alcohol **2a** (221 mg, 1.2 mmol), hexahydrated $FeCl_3$ (41 mg, 0.15 mmol) and nitromethane (3 mL) were treated as described for **3a** to obtain the product **3o** as a pale yellow oil (135 mg, 0.42 mmol, 42%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.71 (d, J = 7.3 Hz, 2 H), 4.81 (t, J = 7.2 Hz, 1 H), 7.18–7.36 (m, 10 H), 7.41 (d, J = 8.0 Hz, 2 H), 7.87 (d, J = 8.6 Hz, 2 H) ppm.

1,3-Bis(4-chlorophenyl)-3-phenylpropan-1-one (3p):[26] Alkyne **1f** (137 mg, 1 mmol), alcohol **2b** (263 mg, 1.2 mmol), hexahydrated $FeCl_3$ (41 mg, 0.15 mmol) and nitromethane (3 mL) were treated as described for **3a** to obtain the product **3p** as a pale yellow oil (142 mg, 0.40 mmol, 40%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.67 (d, J = 7.4 Hz, 2 H), 4.78 (t, J = 7.2 Hz, 1 H), 7.17–7.34 (m, 9 H), 7.42 (d, J = 8.3 Hz, 2 H), 7.86 (d, J = 8.6 Hz, 2 H) ppm.

1-(2-Bromophenyl)-3,3-diphenylpropan-1-one (3q): Alkyne **1g** (181 mg, 1 mmol), alcohol **2a** (221 mg, 1.2 mmol), hexahydrated $FeCl_3$ (41 mg, 0.15 mmol) and nitromethane were treated as described for **3a** to obtain the product **3q** as a pale yellow oil (142 mg, 0.39 mmol, 39%). IR (neat): $\tilde{\nu}$ = 3061, 3028, 1660, 1598, 1493, 1448, 1318, 1278, 1211, 1176, 1028, 942, 920, 762, 701, 693 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.74 (d, J = 7.6 Hz, 2 H), 4.74 (t, J = 7.6 Hz, 1 H), 7.02–7.05 (m, 1 H), 7.20–7.32 (m, 10 H), 7.54–8.00 (m, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 46.5, 48.8, 118.4, 126.4, 127.2, 127.8, 128.2, 128.5, 128.9, 129.8, 130.0, 131.4,

132.3, 133.4, 141.8, 143.4, 202.3 ppm. HRMS: calcd. for $C_{21}H_{17}BrNaO$ 387.0360; found 387.0363. $C_{21}H_{17}BrO_2$ (381.27): calcd. C 69.05, H 4.69; found C 69.08, H 4.66.

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[1] a) M. Beller, J. Seayad, A. Tillack, H. Jiao, *Angew. Chem. Int. Ed.* **2004**, *43*, 3368–3398; b) F. Alonson, I. P. Beletskaya, M. Yus, *Chem. Rev.* **2004**, *104*, 3079–3159.

[2] B. M. Trost, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 259–281; B. M. Trost, *Science* **1991**, *254*, 1471–1471.

[3] a) For recent Review see: L. Hintermann, A. Labonne, *Synthesis* **2007**, 1121–1150; b) K. Tani, Y. Kataoka, in *Catalytic Heterofunctionalisation* (Eds.: A. Togni, H. Grützmacher), Wiley-VCH, Weinheim, **2001**, 171–216.

[4] a) A. Labonne, T. Kribber, L. Hintermann, *Org. Lett.* **2006**, *8*, 5853–5856; b) D. B. Grotjahn, *Chem. Eur. J.* **2005**, *11*, 7146–7153; c) D. B. Grotjahn, C. D. Incarvito, A. L. Rheingold, *Angew. Chem. Int. Ed.* **2001**, *40*, 11917–11924; d) T. Suzuki, M. Tokunaga, Y. Wakatsuki, *Org. Lett.* **2001**, *3*, 735–737; e) M. Tokunaga, Y. Wakatsuki, *Angew. Chem. Int. Ed.* **1998**, *37*, 2867–2869 and references cited therein.

[5] a) P. W. Jennings, P. J. W. Hartman, W. C. Hiscox, *Inorg. Chim. Acta* **1994**, *222*, 317–322; b) J. W. Hartman, W. C. Hiscox, P. W. Jennings, *J. Org. Chem.* **1993**, *58*, 7613–7614; c) K. Inu, K. Imai, K. Utimoto, *Tetrahedron Lett.* **1987**, *28*, 3127–3130; d) A. A. Petrov, B. S. Kupin, *Zh. Obsch. Khim.* **1959**, *29*, 3153–3154.

[6] L. Ackermann, L. T. Kaspar, *J. Org. Chem.* **2007**, *72*, 6149–6153 and references cited therein.

[7] G. L. Bras, O. Provot, J.-F. Peyrat, M. Alami, J.-D. Brion, *Tetrahedron Lett.* **2006**, *47*, 5497–5501.

[8] M. Pal, K. Parasuraman, S. Gupta, K. R. Yeleswarpu, *Synlett* **2002**, 1976–1982.

[9] a) K. Sonogashira, in *Comprehensive Organic Synthesis*, vol. 3 (Eds.: B. M. Trost, I. Fleming), Pergamon Press, New York, **1991**, 521; b) K. Sonogashira, Y. Tohda, N. Hagihara, *Tetrahedron Lett.* **1975**, *16*, 4467–4470.

[10] For cross-coupling reactions of terminal alkynes with a benzylic electrophile, see: a) E.-I. Negishi, L. Anastasia, *Chem. Rev.* **2003**, *103*, 1979–2018; b) I. Pérez, J. P. Sestelo, L. A. Sarandeses, *J. Am. Chem. Soc.* **2001**, *123*, 4155–4160; c) M. Qian, E.-I. Negishi, *Tetrahedron Lett.* **2005**, *46*, 2927–2930; d) J. Caeiro, J. P. Sestelo, L. A. Sarandeses, *Chem. Eur. J.* **2008**, *14*, 741–746.

[11] For A few recent examples of the catalytic activation of alcohols, see: a) H. Qin, N. Yamagiwa, S. Matsunga, M. Shibaski, *Angew. Chem. Int. Ed.* **2007**, *46*, 409–413; b) S. Shirakawa, K. Shu, *Org. Lett.* **2007**, *9*, 311–314; c) R. Sanz, A. Martínez, D. Miguel, J. M. Álveraz-Gutiérrez, F. Rodríguez, *Adv. Synth. Catal.* **2006**, *348*, 1841–1845 and references cited therein; d) M. Yasuda, T. Somyo, A. Baba, *Angew. Chem. Int. Ed.* **2006**, *45*, 793–796; e) K. Sonogashira, Y. Inada, Y. Nishibayashi, M. Hidai, S. Uemura, *J. Am. Chem. Soc.* **2002**, *124*, 15172–15173.

[12] G. W. Kabalka, M.-L. Yao, S. Borella, *Org. Lett.* **2006**, *8*, 879–881.

[13] a) D. D. Diaz, P. O. Miranda, J. I. Padrón, V. S. Martin, *Curr. Org. Chem.* **2006**, *10*, 457–476; b) C. Bolm, J. Legros, J. L. Paih, L. Zani, *Chem. Rev.* **2004**, *104*, 6217–6254.

[14] For the $FeCl_3$-catalyzed activation of alcohols, see: a) U. Jana, S. Maiti, S. Biswas, *Tetrahedron Lett.* **2008**, *49*, 858–862; b) U. Jana, S. Biswas, S. Maiti, *Tetrahedron Lett.* **2007**, *48*, 4065–4069; c) U. Jana, S. Maiti, S. Biswas, *Tetrahedron Lett.* **2007**, *48*, 7160–7163.

[15] a) J. Kischel, K. Mertins, D. Michalik, A. Zapf, M. Beller, *Adv. Synth. Catal.* **2007**, *349*, 865–870; b) Z.-P. Zhan, J.-L. Yu, Y.-Y. Cui, R.-F. Yang, W.-Z. Yang, J.-P. Li, *J. Org. Chem.* **2006**, *71*, 8298–8301; c) I. Iovel, M. Kristin, J. Kischel, A. Zapf, B. Mathias, *Angew. Chem. Int. Ed.* **2005**, *44*, 3913–3917.

[16] a) The addition of adamantan-1-ol to acetylene, aliphatic and aromatic alkynes with sulfuric acid leads to the corresponding carbonyl compounds. For example, see: D. R. Kell, F. J. McQuillin, *J. Chem. Soc. Perkin Trans. 1* **1973**, 2100–2103; b) G. V. Roitburd, W. A. Smit, A. V. Semenovaky, A. A. Schegolev, V. F. Kucherov, O. S. Chizhov, V. I. Kadentsev, *Tetrahedron Lett.* **1972**, *13*, 4935–4940; c) F. Marcuzzi, G. Modena, G. Milloni, *J. Org. Chem.* **1982**, *47*, 4577–4579.

[17] a) For the $FeCl_3$-catalyzed coupling of alkynes and arynes, see: R. Li, S. R. Wang, W. Lu, *Org. Lett.* **2007**, *9*, 2219–2222; b) For the $FeCl_3$-catalyzed coupling of alkynes and aldehydes, see: P. O. Miranda, P. Díaz, M. A. Ramírez, V. S. Martín, *J. Org. Chem.* **2005**, *70*, 57–62; c) For the stoichiometric use of $FeCl_3$ for the hydration of alkynes, see; J. P. Damiano, M. Postel, *J. Organomet. Chem.* **1996**, *522*, 303–305.

[18] In dichloromethane and dichloroethane, along with a trace amount of the desired product, a reasonable amount of a vinylic chloride derivative was observed, which is currently under study.

[19] S. Kotha, A. Tafesh, K. Davenport, P. Ortiz, *Indian J. Chem., Ser. B* **2001**, *40*, 1166–1169.

[20] For the $FeCl_3$-catalyzed formation of a benzylic ether from the corresponding alcohols, see: P. Sabhi, N. Iranpoor, F. K. Behbahani, *Tetrahedron* **1998**, *54*, 943–948.

[21] Y. Liu, S. Zhou, G. Li, B. Yan, S. Guo, Y. Zhou, H. Zhang, P. Wang, *Adv. Synth. Catal.* **2008**, *350*, 797–801 and references cited therein.

[22] S. E. Denmark, N. Amishiro, *J. Org. Chem.* **2003**, *68*, 6997–7003.

[23] R. Rendy, Y. Zhang, A. McElrea, A. Gomez, D. A. Klumpp, *J. Org. Chem.* **2004**, *69*, 2340–2347.

[24] A. Hajra, N. Yoshikai, E. Nakamura, *Org. Lett.* **2006**, *8*, 4153–4155.

[25] B. G. Kelly, D. G. Gilheany, *Tetrahedron Lett.* **2002**, *43*, 887–890.

[26] V. D. Orlav, B. Insuasti, K. Kiroga, *Ukrainskii. Khim. Zh. (Russ. Edition)* **1986**, *52*, 316–320.

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