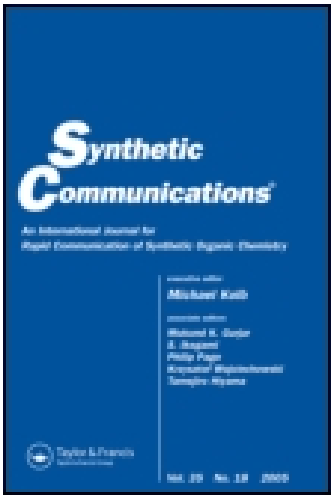

Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Inexpensive and Efficient Synthesis of Propargylic Substituted Active Methylene Compounds Catalyzed by $FeCl_3$

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Published online: 15 Dec 2010.

To cite this article: Sukhendu Maiti, Srijit Biswas & Umasish Jana (2010) Inexpensive and Efficient Synthesis of Propargylic Substituted Active Methylene Compounds Catalyzed by $FeCl_3$, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 41:2, 243-254, DOI: 10.1080/00397910903534031

To link to this article: http://dx.doi.org/10.1080/00397910903534031

Synthetic Communications®, 41: 243–254, 2011

ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910903534031

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INEXPENSIVE AND EFFICIENT SYNTHESIS OF PROPARGYLIC SUBSTITUTED ACTIVE METHYLENE COMPOUNDS CATALYZED BY $FeCl_3$

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Department of Chemistry, Jadavpur University, Kolkata, West Bengal, India

A highly efficient and practical method for the synthesis of propargylic substituted 1,3-dicarbonyl compounds with direct use of propargylic alcohols in the presence of inexpensive and environmentally benign $FeCl_3$ (5 mol%) has been presented. The reaction works with varieties of substrates at room temperature without an inert atmosphere with an excellent yield. The present method can also be employed for the large-scale synthesis of propargylic substituted active methylene compounds.

Keywords: Atom economical; carbon–carbon bond; iron salt; propargylic alcohols; sustainable chemistry

INTRODUCTION

Because of their efficient transformation into various functional groups,[1,2] the alkynes are important building blocks in the synthesis of natural products, drug candidates, and material science.[3] Consequently, a wide variety of strategies have been developed to achieve highly substituted alkynes with the required complexity in the structure. Among the various strategies to construct complex alkynes molecules, propargylic substitution with various nucleophiles has attracted much attention. Traditionally, propargylic substitution is carried out using the Nicholas reaction[4] via cobalt complex–stabilized propargylic carbocation intermediate. However, it has several drawbacks, such as use of a stoichiometric amount of $Co_2(CO)_8$ and a multistep reaction. Thus, to avoid these problems, many methods have been described for the direct substitution of propargylic alcohols in the presence of various transition metals such as ruthenium, rhenium, bismuth, gold, and Brønsted acids.[5] Although these direct substitutions of propargylic alcohols are attractive processes in organic synthesis because of easy availability of the substrates, the reaction is also highly atom economical as the water is the only by-product.[6] However, compared to heteroatom-centered nucleophiles such as alcohols, thiols, amides, and so on, carbon-centered nucleophiles were unfortunately limited to allylsilanes and electron-rich aromatic compounds.

Received August 23, 2009.
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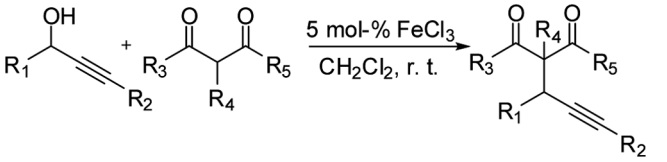


Scheme 1. Reaction of propargylic alcohols with 1,3-dicarbonyl compounds.

On the other hand, alkylation of 1,3-dicarbonyl compounds is very important and a fundamental reaction in organic synthesis. Recently, a number of methods have been developed for the synthesis of substituted active methylene compounds by the direct substitution of alcohol in the presence of a catalytic amount of transition metal and Lewis and Brønsted acids. However, such a strategy has been applied mostly to the synthesis of allylic- and benzylic-substituted 1,3-dicarbonyl compounds,[7] and the synthesis of propargylic substituted 1,3-dicarbonyl compounds has been little explored. The reagents available to effect this substitutions are $Yb(OTf)_3$,[8] $InCl_3$,[9] *p*-toluenesulfonic acid (PTS),[10] ruthenium(II) with trifluoroacetic acid,[11] copper(II) triflate,[12] and phosphomolybdic acid supported on silica gel (PMA/SiO_2).[13] Most of these reagents have been used for the one-pot synthesis of furan derivatives, and only a few have been demonstrated for the synthesis of propargylic substituted active methylene compounds. Recently, Cheng and Bao reported synthesis of these compounds using 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) via an oxidative cross-coupling reaction.[14] Although these methods are suitable for certain synthetic reaction conditions, many of these procedures are associated with one or more disadvantages such as long reaction time; use of expensive, toxic, and moisture-sensitive reagents; poor yield; requirement of excess of reagents or catalysts; and harsh reaction conditions.

The development of sustainable, environmentally benign C-C bond-forming processes is one of the fundamental goals in organic chemistry. As a result, iron-catalyzed reactions have received considerable attention because they are less expensive, readily available, environmentally benign, and perform many useful organic transformations under mild conditions.[15] Considering the significance of direct substitution of alcohols, several researchers[7b,16,17] have demonstrated efficient iron salts–catalyzed direct substitution of alcohols with various nucleophiles. In continuation of our previous work on the direct substitution of benzylic and allylic alcohols with active methylene compounds,[7b] we report herein an efficient synthesis of propargylic substituted 1,3-dicarbonyl compounds under mild conditions by direct substitution of propargylic alcohols in the presence of catalytic $FeCl_3$ (Scheme 1).

RESULTS AND DISCUSSION

Although propargylic substitution reactions between various nucleophiles with propargylic acetate[18] and alcohols[16a,16d,17a] in the presence of iron salts have been reported recently, the synthesis of propargylic substituted 1,3-dicarbonyl compounds

by the direct substitution of propagylic alcohols has not been reported. Thus, encouraged by our previous work, we decided to study systematically the reaction between various active methylene compounds and propargylic alcohols to synthesize the propargylic substituted active methylene compounds.[19]

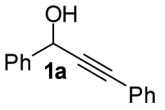
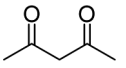
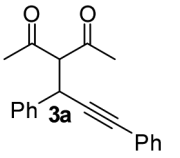
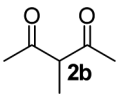
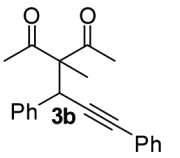
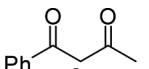
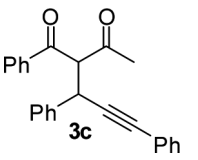
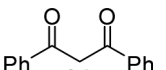
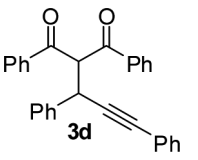
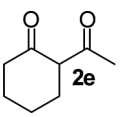
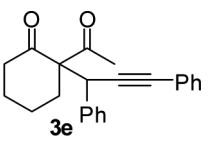
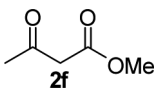
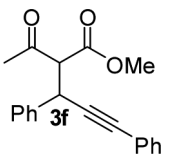
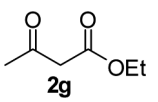
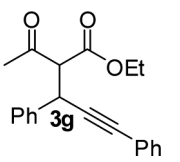
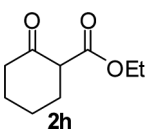
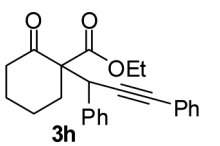
First, we investigated the model reaction of active methylene compound **2a** with propargylic alcohol **1a** using $FeCl_3$ under different reaction conditions to standardize the reaction condition. The reaction worked well in various solvents such as dichloromethane, dichloroethane, nitromethane, and acetonitrile with comparable yield at room temperature without an inert atmosphere. The reaction was sluggish in toluene solvent at room temperature but completed within a few minutes under reflux.[20] Dichloromethane was found to be the most effective solvent in this reaction in terms of time and yield of the propargylic substituted products. Moreover, we also observed that anhydrous $FeCl_3$ gave slightly better yield compared to the hydrated $FeCl_3$. The reaction was reasonably fast and clean, and 5 mol% of $FeCl_3$ was sufficient for complete conversion of reactants to product in dichloromethane solvent with an excellent yield of **3a** (92%).

Having optimized the reaction conditions, we then explored the generality and efficiency of this reaction between various active methylene compounds and secondary propargylic alcohol **1a**. In general, the reaction proceeded smoothly for all cases in very good to excellent yields within a short period of time with complete regioselectivities with respect to both of the reactants. The results are summarized in Table 1. The procedure worked efficiently for both acyclic (Table 1, entries 1–4) and cyclic (Table 1, entry 5) β-diketones. Moreover, methyl substituted β-diketone **2b** (Table 1, entry 2) also reacted smoothly with alcohol **1a** and gave the greatest yield of the product **3b** (90%).

Furthermore, β-ketoesters also reacted smoothly at room temperature with propargylic alcohol **1a** to produce the corresponding desired product in 88–92% yields (Table 1, entries 6–8). The $FeCl_3$-catalyst propargylation reaction also worked efficiently for the synthesis of propargylic substituted coumarin **3i** in good yield (77%) in 1:1 dichloromethane and 1,4-dioxane solvent at 50 °C (Table 1, entry 9). Synthesis of substituted coumarins is very important in organic synthesis because of their biological significance and their unique role as a valuable synthetic intermediate in pharmaceuticals.[21] However, the synthesis of substituted coumarines mostly relied on the alkylation of 4-hydroxy coumarine using alkyl halide in the presence of a base or in the presence of transition metals. Moreover, alkyne substituted coumarins would be valuable intermediates because of their further synthetic manipulation.

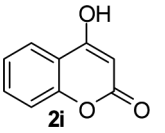
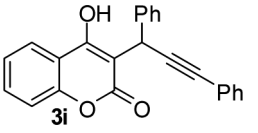
Encouraged by these results, we subsequently tested this reaction for various substituted propargylic alcohols, and the results are summarized in Table 2. Both electron-rich and moderately electron-poor propargylic alcohols reacted efficiently with various 1,3-dicarbonyl compounds, affording the corresponding propargylated products in good yields. Functional groups, such as chloride, methoxy, and nitro, in propargylic alcohols did not affect the formation of the products under the reaction conditions. More interestingly, heterocylic molecules such as thiophene substituted propargylic alcohols also reacted smoothly with β-diketones, such as **2a** and **2d**, and gave the desired products **3p** and **3q** in good yields (Table 2, entries 7 and 8) without formation of any side product. It is interesting to note that acid-sensitive

Table 1. $FeCl_3$-catalyzed propargylic substitution between propargyl alcohol **1a** and various active methylene compounds **2**

Entry	1	2	Time	Product	Yields (%)[a]	Ref.
1			2		92	8
2	**1a**		2		90	8
3	**1a**		2		92	10
4	**1a**		2		94	8
5	**1a**		2		90	10
6	**1a**		3		90[b]	—
7	**1a**		3		88[b]	8
8	**1a**		3		92[b]	—

(*Continued*)

Table 1. Continued

Entry	1	2	Time	Product	Yields (%)[a]	Ref.
9	**1a**	 **2i**	3	 **3i**	77[c]	8

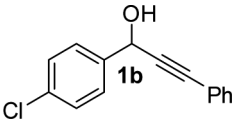
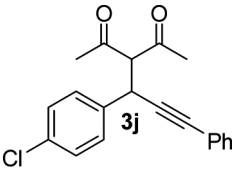
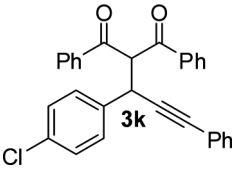
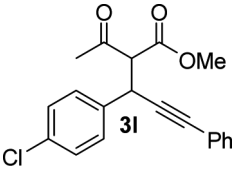
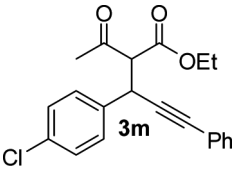
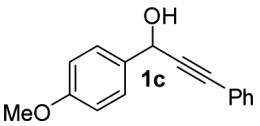
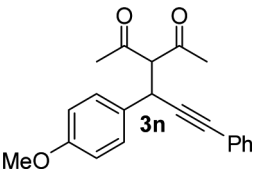
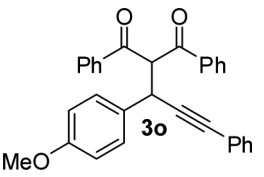
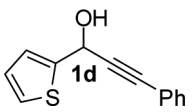
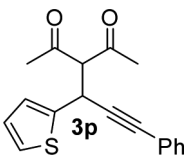
[a]The yields refer to pure isolated products obtained after column chromatography and characterized by spectral data.
[b]1.2 eq. alcohol was used.
[c]The reaction was carried out in 1:1 dichloromethane/1,4 dioxan solvent at 50 °C.

secondary aliphatic alcohol **1f** (Table 2, entry 11) also participated in this reaction, but the reaction was sluggish at room temperature in CH_2Cl_2 solvent. However, the desired product **3t** was obtained in 63% yield in nitromethane solvent at 60 °C. After demonstrating the generality of this reaction for secondary propargylic alcohols and active methylene compounds under iron-salt catalysis, we studied the reaction of tertiary propargylic alcohol. We have observed that in contrast to the $Yb(OTf)_3$-catalyzed reaction, which gave allene derivatives,[8] for the same substrate the iron salt–catalyzed reaction produced only the conjugated diene-dione **3v** in 90% yield (Table 2, entry 13). This product was possibly formed via allenylation of 1,3-diketones followed by isomerization of the double bond, leading to the most stable conjugated carbonyl compound. This reaction can be regarded as an alternative of classical base-catalyzed Knoevenagel reaction between active methylene compounds and α,β-unsaturated carbonyl compounds for the synthesis of diene-dione, and this structural motif is a very useful intermediate for the further synthetic transformations such as Diels–Alder and Michael additions.[22] However, the primary propargylic alcohol **1i** did not react under the similar reaction conditions, even at higher temperature. This experimental observation suggested that a propargylic carbocation intermediate is involved during the course of the reaction. However, because of the instability of the primary carbocation, the alcohol **1i** did not react.

Finally, to investigate the efficiency of this methodology on a multigram scale, we conducted a reaction between propargylic alcohol **1a** (1.65 g, 7.96 mmol) and active methylene compound **2d** (1.78 g, 7.96 mmol). Significantly, we observed that this reaction also afforded the desire product **3d** with excellent yield, 91% (3.00 g, 7.24 mmol), almost same as that of the small-scale (1 mmol) reaction.

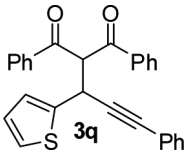
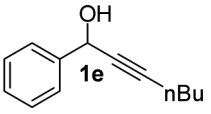
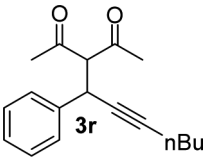
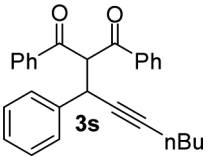
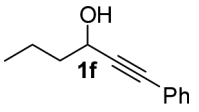
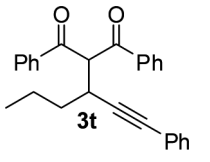
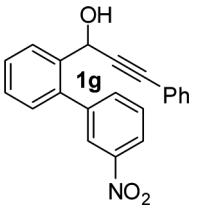
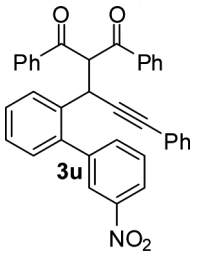
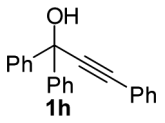
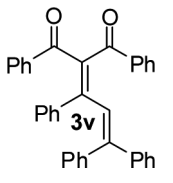
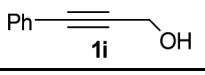
In conclusion, we have developed an efficient method for the synthesis of propargylic substituted active methylene compounds in the presence of $FeCl_3$ (5 mol%) by the direct use of propargylic alcohols (highly atom economical). The present method has many advantages over the previously reported methods, such as mild reaction conditions, operational simplicity, good yields, inexpensive components, and use of nontoxic iron salt as a catalyst [compared to $Yb(OTf)_3$ and *p*-TsOH]. Functional groups such as chloride, methoxy, nitro, ester, triple bond, and ketones remained unaffected under the reaction conditions. The reaction also worked with similar efficiency on a moderate scale at room temperature. Additionally, this method was also efficient for the synthesis of propargylic substituted 4-hydroxy

Table 2. $FeCl_3$-catalyzed propargylic substitution between propargyl alcohol **1** and various active methylene compounds **2**

Entry	1	2	Time (h)	Product	Yields (%)[a]	Ref.
1		**2a**	2		90	8
2	**1b**	**2d**	2		92	8
3	**1b**	**2f**	3		84[b]	—
4	**1b**	**2g**	3		82[b]	—
5		**2a**	1.5		90	14
6	**1c**	**2d**	1.5		94	14
7		**2a**	2		85	—

(*Continued*)

Table 2. Continued

Entry	1	2	Time (h)	Product	Yields (%)[a]	Ref.
8	**1d**	**2d**	2		88[b]	8
9		**2a**	2		85[b,c]	8
10	**1e**	**2d**	2		88[b,c]	8
11		**2d**	3		63[b,c]	8
12		**2d**	2		93	—
13		**2d**	2		90	10
14		**2d**	6	—	NR[e]	

[a]The yields refer to pure isolated product obtained after column chromatography and characterized by spectral data.

[b]1.2 eq. alcohol was used.

[c]The reaction worked in nitromethane solvent.

[d]The reaction worked at 60 °C in nitromethane solvent.

[e]Room temperature for 3 h, then reflux for 5 h.

coumarin derivatives. Thus, we believe that the present method would be an attractive and environmentally friendly alternative process for the synthesis of propargylic substituted active methylene compounds and related applications both in academic and industrial applications.

EXPERIMENTAL

Representative Experimental Procedure for the Synthesis of 3-(1,3-Diphenyl-2-propynyl)pentane-2,4-dione (3a)[8]

Anhydrated $FeCl_3$ (8 mg, 0.05 mmol) was added to a stirred solution of alcohol **1a** (208 mg, 1 mmol) and acetyl acetone **2a** (100 mg, 1 mmol) in dichloromethane (3 mL), and the resulting mixture was stirred vigorously at room temperature for a set period of time. After completion of the reaction [by thin-layer chromatography (TLC)], dichloromethane was evaporated under reduced pressure, and the residue was purified by silica gel (60–120 mess) column chromatography using 5–10% ethyl acetate–petroleum ether solution (v/v) to afford the desired product **3a** as a white solid (267 mg, 0.92 mmol, 92%), mp 91–92 °C. IR (KBr) 1722, 1701, 1359, 754, 690 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 1.94 (s, 3H), 2.40 (s, 3H), 4.23 (d, $J = 10.9$ Hz, 1H), 4.68 (d, $J = 10.9$ Hz, 1H), 7.28–7.43 (m, 10H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 28.8, 31.1, 38.1, 75.6, 77.5, 88.1, 122.7, 127.8, 128.2, 128.3, 128.4, 128.9, 131.6, 138.2, 201.6, 201.6 ppm.

Methyl 2-Acetyl-3,5-diphenylpent-4-ynoate (3f)

Alcohol **1a** (250 mg, 1.2 mmol) and 1,3-dicarbonyl compound **2d** (116 mg, 1 mmol) in dichloromethane (3 mL) and anhydrated $FeCl_3$ (8 mg, 0.05 mmol) yielded a sticky yellowish liquid (90%, 1:1 mixture of two diastereoisomers). IR (neat) 1743, 1712, 1491, 758, 692 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 2.01 (s, 3H), 2.44 (s, 3H), 3.55 (s, 3H), 3.82 (s, 3H), 4.01–4.12 (m, 2H), 4.63–4.68 (m, 2H), 7.27–7.47 (m, 20H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 30.0, 30.7, 38.0, 52.5, 52.8, 66.5, 66.7, 84.6, 84.9, 88.0, 88.4, 122.8, 123.0, 127.8, 128.2, 128.2, 128.3, 128.3, 128.7, 128.8, 131.7, 138.2, 167.3, 167.6, 200.3, 200.7 ppm.

Ethyl 1-(1,3-Diphenylprop-2-ynyl)-2-oxocyclohexanecarboxylate (3h)

Product **3h** (92%, 1:2 mixture of two diastereoisomers). Diastereomer 1 (31%): obtained as a white solid, mp 109–111 °C. IR (neat) 1709, 1491, 1229, 754 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 1.27 (t, $J = 7.1$ Hz, 3H), 1.45–1.55 (m, 2H), 1.76–1.84 (m, 2H), 1.90–1.97 (m, 1H), 2.34–2.51 (m, 3H), 4.21–4.28 (q, 2H), 4.93 (s, 1H), 7.24–7.35 (m, 6H), 7.41–7.44 (m, 2H), 7.55 (d, $J = 7.7$ Hz, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.0, 22.4, 26.5, 32.6, 41.3, 41.5, 61.7, 65.9, 76.6, 84.3, 88.7, 123.3, 127.3, 127.8, 127.9, 128.1, 130.6, 131.6, 137.0, 169.5, 204.8 ppm. HRMS: m/z calcd. for $C_{24}H_{24}NaO_3$: 383.1624; found: 383.1628.

Diastereomer 2 (61%): obtained as a pale yellowish sticky liquid. IR (neat) 1717, 1491, 1229, 758 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 1.15 (t, $J = 7.1$ Hz, 3H), 1.65–1.73 (m, 2H), 1.76–1.89 (m, 1H), 2.01–2.05 (m, 1H), 2.17–2.38 (m, 2H),

2.54–2.63 (m, 2H), 4.01–4.04 (q, 2H), 4.93 (s, 1H), 7.27–7.36 (m, 8H), 7.40–7.45 (m, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.8, 22.5, 26.6, 31.2, 41.4, 42.0, 61.5, 65.9, 84.9, 88.9, 123.5, 127.6, 127.9, 128.1, 128.1, 129.2, 131.7, 137.2, 168.9, 204.4 ppm. HRMS: m/z calcd. for $C_{24}H_{24}NaO_3$: 383.1624; found: 383.1623.

Methyl 2-Acetyl-3-(4-chlorophenyl)-5-phenylpent-4-ynoate (3l)

Sticky yellowish liquid (84%, 1:1 mixture of two diastereoisomers). IR (neat) 1748, 1721, 1489, 1244, 758 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.07 (s, 3H), 2.45 (s, 3H), 3.58 (s, 3H), 3.81 (s, 3H), 3.97–4.07 (m, 2H), 4.60–4.67 (m, 2H), 7.28–7.42 (m, 18H) ppm.^{13}C NMR ($CDCl_3$, 75 MHz) δ 30.0, 30.7, 37.0, 37.2, 52.6, 52.9, 66.4, 66.4, 85.0, 85.1, 87.5, 87.8, 122.5, 122.8, 128.3, 128.3, 128.5, 128.9, 129.2, 129.6, 129.8, 130.0, 130.2, 131.6, 133.6, 133.6, 133.7, 136.8, 136.9, 167.1, 167.4, 200.0, 200.4 ppm. HRMS: m/z calcd. for $C_{20}H_{17}ClNaO_3$: 363.0764; found: 363.0769.

Ethyl 2-Acetyl-3-(4-chlorophenyl)-5-phenylpent-4-ynoate (3m)

Sticky yellowish liquid (82%, 1:1 mixture of two diastereoisomers). IR (neat) 1744, 1721, 1489, 1242, 758 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.09 (t, $J = 7.1$ Hz, 3H), 1.29 (t, $J = 7.1$ Hz, 3H), 2.07 (s, 3H), 2.43 (s, 3H), 3.95–4.06 (m, 4H), 4.24–4.31 (m, 2H), 4.59–4.67 (m, 2H), 7.26–7.42 (m, 20H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.9, 14.1, 29.9, 30.5, 37.0, 37.2, 61.8, 62.0, 66.6, 84.7, 85.0, 87.6, 87.9, 122.6, 122.8, 128.3, 128.4, 128.5, 128.7, 128.8, 128.9, 129.7, 129.8, 130.2, 131.6, 133.5, 133.6, 136.8, 137.0, 166.7, 166.9, 200.0, 200.4 ppm. HRMS: m/z calcd. for $C_{21}H_{19}ClNaO_3$: 377.0920; found: 377.0920.

3-(3-Phenyl-1-(thiophen-2-yl)prop-2-ynyl)pentane-2,4-dione (3p)

Sticky deep brown liquid (85%). IR (neat) 1701, 1489, 1356, 758 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 2.07 (s, 3H), 2.37 (s, 3H), 4.27 (d, $J = 10.6$ Hz, 1H), 5.03 (d, $J = 10.6$ Hz, 1H), 6.93 (dd, $J = 3.9$, 1.1 Hz, 1H), 7.21–7.23 (m, 1H), 7.28–7.37 (m, 4H), 7.38–7.40 (m, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 28.9, 31.8, 32.9, 75.7, 84.9, 88.4, 122.3, 124.8, 125.1, 126.2, 126.8, 128.2, 128.4, 128.5, 131.6, 141.1, 200.9, 201.2 ppm. HRMS: m/z calcd. for $C_{18}H_{16}NaO_2S$: 319.0769; found: 319.0763.

2-(1-(3′-Nitrobiphenyl-2-yl)-3-phenylprop-2-ynyl)-1,3-diphenylpropane-1,3-dione (3u)

Reaction was performed in nitromethane solvent at room temperature. Pale yellow solid (93%) mp 151–153 °C. IR (neat) 1691, 1662, 1525, 1350, 759 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 5.08 (d, $J = 10.6$ Hz, 1H), 6.06 (d, $J = 10.5$ Hz, 1H), 7.03 (d, $J = 6.7$ Hz, 2H), 7.14–7.22 (m, 4H), 7.26–7.31 (m, 3H), 7.37–7.49 (m, 4H), 7.56–7.61 (m, 1H), 7.64–7.76 (m, 4H), 7.89 (d, $J = 7.5$ Hz, 1H), 8.08 (d, $J = 7.5$ Hz, 2H), 8.30 (s, 2H) ppm.^{13}C NMR ($CDCl_3$, 75 MHz) δ 35.3, 62.1, 85.7, 89.2, 122.3, 122.6, 124.7, 127.5, 127.9, 128.0, 128.1, 128.3, 128.7, 128.8, 128.9, 129.1, 129.2,

130.5, 131.4, 133.4, 133.6, 135.7, 136.0, 136.8, 139.7, 142.5, 148.2, 191.7, 193.5 ppm. HRMS: m/z calcd. for $C_{36}H_{25}NNaO_4$: 558.1681; found; 558.1687.

Moderate-Scale Synthesis of 2-(1,3-Diphenylprop-2-ynyl)-1,3-diphenylpropane-1,3-dione (3b)[8]

Alcohol **1a** (1.65 g, 7.96 mmol), 1,3-dicarbonyl compound **2d** (1.78 g, 7.96 mmol), and anhydrated $FeCl_3$ (64 mg, 0.40 mmol) were treated as described for **3a** to obtain the product **3d** as a pale yellow solid (3.00 g, 7.24 mmol, 91%), mp 156–157 °C.

ACKNOWLEDGMENTS

We gratefully acknowledge the financial and infrastructural support from the University Grants Commission–Center of Advanced Study (UGC-CAS) program of the Department of Chemistry, Jadavpur University. S. M. and S. B. are also thankful to the UGC, Jadavpur University and New Delhi, India, respectively, for their fellowships.

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19. During our study, the $FeCl_3$-catalyzed synthesis of propargylic substituted active methylene compounds by the direct substitution of substituted propargylic alcohols, a tandem $FeCl_3$-catalyzed propargylation–cycloisomerization reaction of tetramethyl silane substituted propargylic alcohols or acetates with 1,3-dicarbonyl compounds for the synthesis of furan derivative was reported. See Ji, W.-H.; Pan, Y.-M.; Zhao, S.-Y.; Zhan, Z.-P. $FeCl_3$-catalyzed propargylation–cycloisomerization tandem reaction: A facile one-pot synthesis of substituted furans. *Synlett.* **2008**, 3046–3052.
20. We anticipated the formation of furan derivative under the refluxing condition during our study of propargylation reaction; however no such furan product was observed for the propargylated product **3a**, even after prolonged heating. The same observation was also reported by Ji et al. (see ref. 19). They concluded that for the cycloisomerization step, alkyne should bear TMS group, or instead of propargylic alcohols propargylic acetate should be used.
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