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PAPER

N-Heterocyclic carbene-catalyzed (NHC) three-component domino reactions: highly stereoselective synthesis of functionalized acyclic ε-ketoesters†

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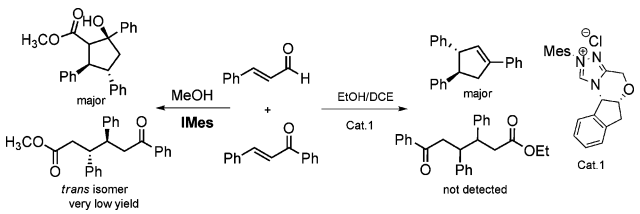
A novel NHC-catalyzed three-component domino strategy to access high functionalized *cis*-ε-ketoesters with excellent yields (up to 98%) and high stereoselectivities (up to 20 : 1) is documented. The title domino reactions are atom economical and work on a broad range of substrates. The relative stereochemistry could be explained by a cascade crossed-benzoin/oxy-Cope rearrangement/esterification process. The thus-obtained products are of potential synthetic value in the drug research and combinatorial chemistry.

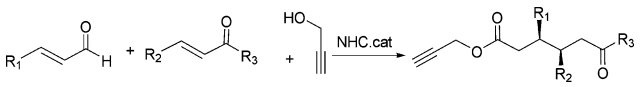
Introduction

Domino reactions have become a fascinating branch of organic chemistry and have been subjected to intensive research in recent years.[1] Such courses of reaction are in sharp contrast to the traditional multi-step processes and manifest their undeniable merits in many ways: 1) they allow for the forming of several bonds in one sequence and hence are of high atom economy; 2) they avoid time-consuming and tedious processes for purification of various precursors; 3) they often proceed with excellent chemoselectivities and high stereoselectivities. Although elegantly performed by nature for billions of years, their applications in the laboratory remain a great challenge due to the lack of sufficient appropriate and efficient catalysts. Thus, considerable efforts have been directed toward the discovery and design of new catalysts with better efficiency and new reactivity. N-heterocyclic carbenes, in free form or generated *in situ*, have emerged as powerful organocatalysts;[2] their applications have led to remarkably fruitful discoveries of novel domino reactions.[3] However, most of them are confined to mono- or two-component reactions, multi-component domino reactions are rarely reported. Recently, Nair and co-workers reported three-component NHC-catalyzed domino reactions with α,β-unsaturated aldehydes, chalcones, and methanol to constitute functionalized cyclopentanes as major products and *trans* acyclic ε-ketoesters as minor ones (Scheme 1).[4] In the course of a mechanistic investigation by Bode and co-workers, the same substrates were subjected to a mixed solvent of ethanol and 1,2-dichloroethane with triazolium as precatalyst, but no ε-ketoesters were observed.[3i] On the other hand, 1,6-dicarbonyl compounds are versatile building blocks in natural products synthesis including prostaglandin A_2(PGA), amphoteronolide B, and bilobalide,[5] but



Scheme 1 Previous work by Nair and Bode.

their synthetic strategies are at present limited, and suffer various drawbacks including the multi-step processes, utility of expensive toxic organometallic reagents, harsh conditions and unsatisfactory total yields.[6] Moreover, stereoselective syntheses of functionalized 1,6-dicarbonyl compounds is far from mature. Therefore, efficient syntheses of 1,6-dicarbonyl compounds and their analogues remain in high demand. Our endeavor in exploring novel domino reactions convinced us that the reaction conditions would exert remarkable influence on the reaction pathway even with identical substrates.[7] Thus we envisioned that the combination of appropriate nucleophiles and catalysts might favor the pathway leading to ε-ketoesters. During our preparation of this manuscript, Nair reported the NHC-mediated stereoselective Michael addition of homoenolate to β-nitrostyrenes.[8] The obtained product remained the *trans* isomer. Herein, we wish to reported novel NHC-catalyzed three-component domino reactions of α,β-unsaturated aldehydes, chalcones, and propargyl alcohol to access to *cis*-ε-ketoesters with high efficiency and stereoselectivities (Scheme 2).



Scheme 2 Three-component domino reactions of α, β-unsaturated aldehydes, chalcones, and propargyl alcohol.

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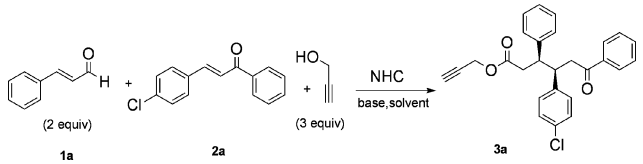
Table 1 Optimization of conditions



Entry[a]	NHC	Base[b]	Solvent	Time/h	Yield (%)[c]
1	**I**	DBU	CH_2Cl_2	10	—
2	**II**	DBU	CH_2Cl_2	10	—
3	**III**	DBU	CH_2Cl_2	2	90
4	**IV**	DBU	CH_2Cl_2	10	65
5	**V**	DBU	CH_2Cl_2	10	Trace
6	**VI**	DBU	CH_2Cl_2	10	75
7	**III**	NEt_3	CH_2Cl_2	10	50
8	**III**	K_2CO_3	CH_2Cl_2	10	20
9	**III**	*t*-BuOK	*t*-BuOH	10	10
10	**III**	DBU	THF	10	20
11	**III**	DBU	$CHCl_3$	10	87
12	**III**	DBU	MeCN	10	85
13	**III**	DBU	Toluene	10	25
14	**III**[d]	DBU	CH_2Cl_2	8	83
15[e]	**III**	DBU	CH_2Cl_2	10	89

[a] All the reactions were conducted at room temperature unless otherwise noted. [b] Base (30 mol%) unless otherwise noted. [c] Isolated yields. [d] **III** (20 mol%) [e] Temperature 0 °C.

Results and discussion

Our studies began with the examination of several readily available NHC precursors for this reaction with the results summarized in Table 1. In the presence of DBU, both imidazolium salt **III** and **VI** (Fig. 1) proved effective catalysts for the conversion, providing ε-ketoester products in 90% and 75% of yields, respectively (entries 3, 6). With triazolium salt **IV**, moderate conversion was observed, however, no redox product of the conjugated aldehyde, as reported earlier, was isolated, which suggested the unique properties of propargyl alcohol.[9] Thiazolium salts **I** and **II** failed to initiate the reaction (entry 1, 2). Investigations on the solvent effect indicated that many common solvents were suitable, among which CH_2Cl_2 was the best option. DBU proved to be effective. With the use of strong base *t*-BuOK, the lactone product from self-condensation of **1a** was isolated with little consumption of chalcone. Decreasing the catalyst loading reduces the yield slightly even with prolonged reaction time (entry 14). The efficiency was not weakened even when the reaction was conducted at low temperature (entry 15). The NMR spectra of the minor isomers were consistent with the major products reported by Nair, which indicated that the major isomers of this reaction adopted the *cis* configuration.

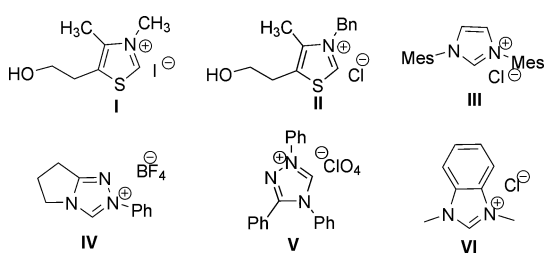
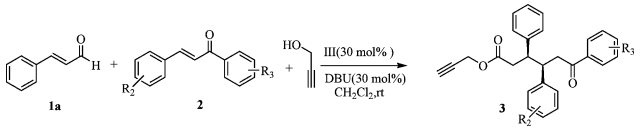


Fig. 1 Structure of several NHC precursors.

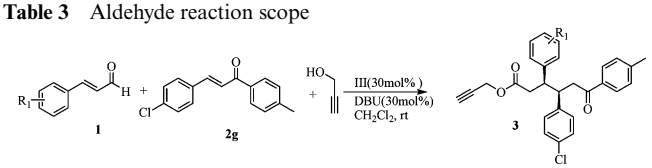
Table 2 α,β-Unsaturated ketone reaction scope



Entry	R_2	R_3	Time/h	Yield (%)[a]	dr[b]
1	*p*-Cl	H	2	93 (**3a**)	4 : 1
2[c]	*p*-F	H	8	85 (**3b**)	1 : 3
3	*p*-NO_2	H	10	51 (**3c**)	3 : 1
4	H	H	8	84 (**3d**)	>20 : 1
5	*p*-CH_3	H	8	80 (**3e**)	10 : 1
6[c]	*m*-F	H	8	63 (**3f**)	1 : 10
7	*p*-Cl	*p*-CH_3	2	91 (**3g**)	12 : 1
8	*p*-Cl	*p*-OCH_3	5	85 (**3h**)	11 : 1
9	H	*p*-Br	6	85 (**3i**)	7 : 1

[a] Isolated yields. [b] Determined by ^{1}H NMR. [c] The *trans*-isomer was obtained.

Table 3 Aldehyde reaction scope



Entry	R_1	Time/h	Yield (%)[a]	dr[b]
1	*p*-CH_3	3	91 (**3i**)	14 : 1
2	*m*-CH_3	3	90 (**3k**)	>20 : 1
3	*o*-CH_3	3	90 (**3l**)	10 : 1
4	*p*-OCH_3	2	98 (**3m**)	>20 : 1
5	*m*-OCH_3	2	95 (**3n**)	10 : 1
6	*p*-F	10	70 (**3o**)	10 : 1
7	*p*-Br	10	75 (**3p**)	>20 : 1
8[c]	*o*-F	10	61 (**3q**)	1 : 7
9	*o*-Cl	10	74 (**3r**)	>20 : 1
10	*p*-Cl	10	80 (**3s**)	10 : 1
11	*o*-OH	24	NR	—
12	*p*-NO_2	10	NR	—

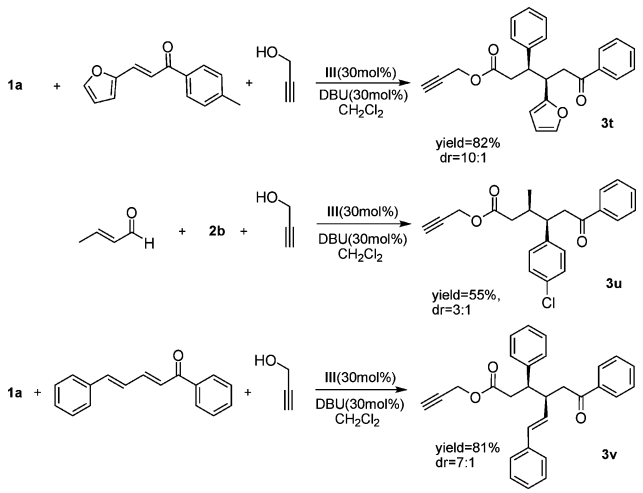
[a] Isolated yields. [b] Determined by ^{1}H NMR. [c] The *trans*-isomer was obtained.

We next examined the scope of this reaction with regard to the chalcone substituents (Table 2). This reaction accommodated both electron-withdrawing and electron-donating groups on the aromatic ring. Electron-withdrawing groups on the β-aromatic ring, with the exception of $-NO_2$ (entry 3), provided the corresponding products with higher yields (entries 1–2, 7–8). α,β-unsaturated aldehydes were then varied in the same reaction conditions (Table 3). The experimental results revealed that various substituted aryl groups were competent substrates.

Cinnamaldehyde derivatives with an electron-donating group strikingly promoted the reaction efficiency, affording corresponding products with excellent yields (up to 98%, Table 3, entries 1–5) and high selectivities in a short time. Electron-withdrawing groups decreased the efficiency but still delivered products in moderate yields with prolonged reaction time (Table 3, entries 6–10). Strong electron-drawing groups, however, were not tolerated in this reaction although the reason remained unclear (entry 12). Compared with that from chalcone, the steric effect stemmed from cinnamaldehyde derivatives was trivial (entries 1–3). Unexpectedly, some of the F-substituted chalcones or cinnamaldehyde

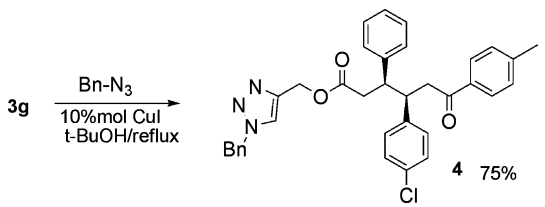
derivatives gave opposite stereochemistry outcomes, leading to the *trans* ε-ketoester (Table 2, entries 2, 6; Table 3, entry 8). This interesting outcome might be accounted for by the strong electon-withdrawing feature of fluorophenyl that favors the Michael addition proposed by Nair.

More importantly, both heterocyclic chalcone and crotonaldehyde were viable and resulted in the desired products **3t** and **3u** in moderate yields. Cinnamylideneacetophenone could also serve as a competent substrate, delivering **3v** in good yield (Scheme 3), which made this reaction a robust one. The structures and configurations of all products were assigned *via* ^{1}H-NMR, ^{13}C-NMR, HRMS and further confirmed according to the related literatures concerned.[3i,4]



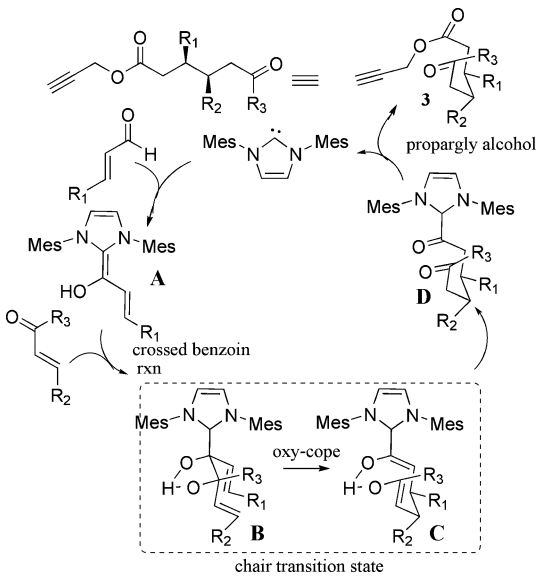
Scheme 3 Further reaction scope.

The introduction of propargyl alcohol as a component not only effectively realized the construction of ε-ketoesters,[10] but also increased the complexity of the products and the synthetic value. Transformation based on alkyne compounds have been subjected to intensive studies, among which the azide-alkyne Huisgen cycloaddition is extremely powerful in combinatorial chemistry and drug discovery.[11] As expected, in the presence of catalytic amount of CuI, **3g** could be readily transformed into desired triazole compound **4** in good yield (Scheme 4).[12]



Scheme 4 The application of the obtained product.

The disparate stereochemical outcome suggested that these reactions might proceed in a pathway that differs from the one proposed by Nair.[4] Enlightened by Bode's mode involving the crossed benzoin/oxy-Cope rearrangement, we proposed a catalytic cycle as follows (Scheme 5). A crossed-benzoin reaction occurred between the catalyst-bound Breslow intermediate **A** and the *trans* chalcone, leading to an intermediate **B** which then underwent an oxy-Cope rearrangement *via* a chair transition state



Scheme 5 Possible mechanism for the formation of **3**.

to give **C**. In the presence of propargyl alcohol, intermediate **C**, *via* rapid tautomerization and protonation, transformed into **D** as a catalyst-bound activated carboxylate which was subsequently trapped by propargyl alcohol, leading to **3** as target product. The *cis*-relative configuration probably arose from the chair transition state. The hydrogen bonds of intermediate **B** not only lock the chair transition state but also disfavor the annulation process proposed by Nair. Furthermore, the minor *trans* isomer may be produced *via* an alternative mechanism featuring conjugate additions of homoenolates to the α,β-unsaturated ketone. For some substrates, the *trans* isomer as major product indicated that these two pathways were competitive and the nature of substrates and nucleophiles were pivotal.

Conclusions

In summary, we have developed a novel NHC-catalyzed three-component domino strategy to access the highly functionalized *cis* ε-ketoester with excellent yields and high stereoselectivities *via* a proposed mechanism featuring a cascade crossed-benzoin/oxy-Cope rearrangement/esterification process. The introduction of propargyl alcohol was critical to establish the feasibility and the stereoselectivity of such domino processes. The obtained product was further functionalized to a useful building block for organic synthesis. More sophisticated and powerful domino reactions are under investigation in our laboratory and will be reported in due course.

Experimental

General

All the reactions are conducted under a dry N_2 atmosphere. All the solvents are commercially available and used without further purification. ^{1}H NMR spectra were recorded on a Bruker 400 MHz spectrometer in chloroform-d. Chemical shifts are reported in ppm with the internal TMS signal at 0.0 ppm as a standard. The data is reported as (s = singlet, d = doublet,

t = triplet, m = multiplet or unresolved, brs = broad singlet, coupling constant(s) in Hz, integration). ^{13}C NMR spectra were recorded on a Bruker 100 MHz spectrometer in chloroform-d. Chemical shifts are reported in ppm with the internal chloroform signal at 77.0 ppm as a standard. The data with * indicate peaks of the minor diastereomer.

To a dry flask filled with nitrogen were added 1,3-dimesityl imidazolium chloride **III** (0.3 mmol), cinnamaldehyde **1a** (1.0 mmol), propargyl alcohol (1.5 mol), and chalcone **2g** (0.5 mmol) in 3 ml dry CH_2Cl_2 under N_2 atmosphere. After stirring for 5 min, DBU (0.3 mmol) was added. This solution was stirred at room temperature until the complete consumption of chalone as monitored by TLC. After the removal of the solvent, the residue was subjected to chromatography on a silica gel (60–120 mesh) column using 12 : 1 petroleum ether–ethyl acetate solvent mixture as eluent to afford **3g** in 93% of yield.

Preparation of prop-2-yn-1-yl 4-(4-chlorophenyl)-6-oxo-3,6-diphenylhexanoate (3a)

White solid, yield (93%). *cis*/*trans* = 4 : 1; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (t, J = 2.4 Hz, 1H), 2.83–2.66 (m, 2H), 3.38–3.25 (m, 2H), 3.59–3.54 (ddd, J_1 = 6.8 Hz, J_2 = 8.8 Hz, 1H), 3.78–3.73 (ddd, J = 6.8 Hz, 1H), 4.59–4.46 (m, 2H), 6.86–6.84 (d, J = 8.4, 2H), 6.90–6.88 (m, 2H), 7.12–7.10 (d, J = 8.8 Hz, 2H), 7.52 (t, J = 7.6 Hz, 1H), 7.85 (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.3, 171.3, 140.8, 140.1, 137.0, 133.0, 130.0, 128.9, 128.5, 128.0, 127.9, 126.7, 126.6, 77.5, 74.8, 51.9, 46.2, 45.1, 41.6, 37.9; IR (KBr): 3292, 2130, 1738, 1682, 1492, 1234, 1147 cm^{-1}; HRMS (MALDI) calcd for $C_{27}H_{23}ClO_3Na$ (M + Na^+): 453.1223; Found: 453.1230; mp = 103–105 °C.

Preparation of prop-2-yn-1-yl 4-(4-fluorophenyl)-6-oxo-3,6-diphenylhexanoate (3b)

White solid, yield (85%); *cis*/*trans* = 1 : 3; ^{1}H NMR (400 MHz, $CDCl_3$), δ 2.35 (t, J = 2.4 Hz, 1H), 2.39* (t, J = 2.4 Hz, 1H), 2.55–2.41 (m, 2H), 2.84–2.67* (m, 2H), 2.89 (dd, J = 2.8, J = 16.4 Hz, 1H), 3.24 (dd, J = 10.4, 17.8 Hz, 1H), 3.32* (dd, J = 8.0, 7.6 Hz, 1H), 3.4 (ddd, J = 4.8, 10.4 Hz, 1H), 3.59 (ddd, J = 3.6,10.8 Hz, 1H), 3.76* (q, J = 6.8 Hz, 1H), 4.40–4.31 (m, 2H), 4.60–4.47* (m, 2H), 6.89–6.81 (m, 2H), 6.98 (t, J = 8.8), 7.34–7.16 (m, 6H), 7.47–7.40 (m, 2H), 7.56–7.52 (m, 2H), 7.63 (d, J = 7.2 Hz, 2H), 7.85* (d, J = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 198.4, 198.1*, 171.2*, 171.1, 126.9, 160.4, 141.6; IR (KBr): 3274, 2132, 1731, 1677, 1510, 1232 cm^{-1}; HRMS (MALDI) calcd for $C_{27}H_{23}FO_3Na$ (M + Na^+): 437.1523; Found: 437.1526; mp = 175–176 °C.

Preparation of prop-2-yn-1-yl 4-(4-nitrophenyl)-6-oxo-3,6-diphenylhexanoate (3c)

Colorless oil, yield (51%); *cis*/*trans* = 4 : 1; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.36* (s, 1H), 2.40 (s, 1H), 2.56 (m, 1H), 2.87–2.71 (m, 2H), 3.00* (d, J = 17.2 Hz, 1H), 3.48–3.44 (m, 2H), 3.61–3.59 (m, 1H), 3.77* (t, J = 10.4 Hz, 1H), 3.90 (d, J = 5.6 Hz, 1H), 4.45–4.32* (m, 2H), 4.62–4.49 (m, 2H), 6.91 (s, 2H), 7.11 (d, J = 7.6 Hz, 2H), 7.17 (s, 2H), 7.56–7.32 (m, 6H), 7.65* (d, J = 6.8 Hz, 2H), 7.86 (d, J = 6.8 Hz, 2H), 7.99 (d, J = 7.2 Hz, 2H), 8.17* (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.5*, 197.4, 170.9, 170.6*, 150.3*, 149.2, 146.9*, 146.5, 140.8*, 139.6, 136.5, 136.4*, 133.4, 133.2*, 129.6, 129.3*, 129.0*, 128.7, 128.6*, 128.5, 128.3, 128.1*, 127.9, 127.8*, 127.6*, 127.2, 123.9*, 123.1, 77.2, 76.9*, 75.0, 74.9*, 52.1, 51.9*, 47.2*, 46.4, 46.3*, 45.2, 43.2*, 41.9, 39.5*, 38.2; IR (KBr): 3290, 2129, 1741, 1685, 1519, 1346, 1148 cm^{-1}; HRMS (MALDI) calcd for $C_{27}H_{23}NO_5Na$ (M + Na^+): 464.1468; Found: 464.1470.

Preparation of prop-2-yn-1-yl 6-oxo-3,4,6-triphenylhexanoate (3d)

Colorless oil, yield (84%). *cis*/*trans*>20 : 1; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (t, J = 2.4 Hz, 1H), 2.85–2.65 (m, 2H), 3.34–3.27 (m, 2H), 3.63–3.58 (ddd, J = 6.8 Hz, 1H), 3.80–3.75 (ddd, J = 6.8, 9.2 Hz, 1H), 4.57–4.45 (m, 2H), 6.94–6.89 (m, 4H), 7.17–7.12 (m, 6H), 7.41 (t, J = 7.6 Hz, 2H), 7.52 (t, J = 7.6 Hz, 1H), 7.85 (d, J = 7.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 198.3, 171.3, 140.8, 140.1, 137.0, 133.0, 130.0, 128.9, 128.5, 128.0, 127.9, 126.7, 126.6, 77.5, 74.8, 51.9, 46.2, 45.1, 41.6, 37.9; IR (KBr): 3297, 2127, 1740, 1682, 1233 cm^{-1}; HRMS (MALDI) calcd for $C_{27}H_{23}NO_5Na$ (M + Na^+): 419.1618; Found: 419.1625.

Preparation of prop-2-yn-1-yl 6-oxo-3,6-diphenyl-4-(*p*-tolyl)hexanoate (3e)

Colorless oil, yield (80%). *cis*/*trans* = 10 : 1; ^{1}H NMR (400 M Hz, $CDCl_3$): δ 7.76 (d, J = 7.4 Hz, 2H), 7.53* (d, J = 7.4 Hz, 2H), 7.42 (t, J = 7.4 Hz, 1H), 7.31* (t, J = 7.7 Hz, 2H), 7.23* (dd, J = 12.1, 4.8 Hz, 1H), 7.13–7.05 (m, 3H), 7.00* (d, J = 7.9 Hz, 2H), 6.88 (d, J = 7.9 Hz, 2H), 6.83 (dd, J = 7.2, 1.9 Hz, 2H), 6.73 (d, J = 8.0 Hz, 2H), 4.46 (dd, J = 15.6, 2.4 Hz, 1H), 4.37 (dd, J = 15.6, 2.4 Hz, 1H), 4.29* (dd, J = 15.6, 2.4 Hz, 1H), 4.21 (dd, J = 15.7, 2.4 Hz, 1H), 3.66 (dd, J = 13.1, 6.7 Hz, 1H), 3.51 (dt, J = 9.1, 6.2 Hz, 1H), 3.21 (dd, J = 7.0, 4.0 Hz, 2H), 2.72 (dd, J = 15.8, 6.4 Hz, 1H), 2.61 (dd, J = 15.8, 9.2 Hz, 1H), 2.28 (t, J = 2.4 Hz, 1H), 2.24* (t, J = 2.4 Hz, 1H), 2.19* (s, 3H), 2.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.5*, 197.3, 170.3, 140.9*, 139.1,138.0*, 136.5, 135.9, 135.3*, 135.0, 131.9, 131.6*, 128.3*, 127.7*, 127.9, 127.8, 127.5, 127.5, 127.2*, 127.1*, 127.1*, 126.9, 126.8, 126.1*, 125.7, 76.4, 75.7, 73.7, 73.6, 50.8, 50.6*, 46.8*, 45.4*, 45.0, 43.6, 42.7*, 40.5, 38.7*, 36.7, 21.6*, 19.9; IR (KBr): 3290, 2129, 1742, 1686, 1449, 1237, 1147 cm^{-1}; HRMS (MALDI) calcd for $C_{28}H_{26}O_3Na$ (M + Na^+): 433.1774; Found: 433.1782.

Preparation of prop-2-yn-1-yl 4-(3-fluorophenyl)-6-oxo-3,6-diphenylhexanoate (3f)

Colorless oil, yield (63%); *cis*/*trans* = 1 : 10; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, J = 7.4 Hz, 2H), 7.46 (t, J = 7.3 Hz, 1H), 7.37–7.29 (m, 6H), 7.28–7.20 (m, J = 13.6, 4.4 Hz, 2H), 7.12 (d, J = 7.6 Hz, 1H), 7.03 (d, J = 9.9 Hz, 1H), 6.93–6.85 (m, J = 8.3, 2.3 Hz, 1H), 4.42 (dd, J = 15.6, 2.4 Hz, 1H), 4.34 (dd, J = 15.6, 2.4 Hz, 1H), 3.63 (td, J = 10.9, 3.1 Hz, 1H), 3.41 (td, J = 10.7, 4.5 Hz, 1H), 3.26 (dd, J = 17.0, 10.4 Hz, 1H), 2.90 (dd, J = 16.9, 3.2 Hz, 1H), 2.54 (dd, J = 15.7, 10.4 Hz, 1H), 2.45 (dd, J = 15.7, 4.6 Hz, 1H), 2.35 (t, J = 2.4 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 198.1, 171.0, 164.1, 161.9, 141.4, 136.8, 132.9, 130.2, 130.1, 128.8, 128.4, 128.2, 127.8, 127.4, 124.1, 115.2, 115.0, 114.0, 113.8, 77.2, 74.7, 51.7, 47.6, 46.4, 43.5, 39.7; IR (KBr): 3296, 2129, 1742, 1680, 1492, 1147 cm^{-1}; HRMS (MALDI) calcd for $C_{27}H_{23}FO_3Na$ (M + Na^+): 437.1523; Found: 437.1526.

Preparation of prop-2-yn-1-yl 4-(4-chlorophenyl)-6-oxo-3-phenyl-6-(*p*-tolyl)hexanoate (3g)

White solid, yield (91%); *cis*/*trans* = 12 : 1; ^{1}H NMR (400 MHz, $CDCl_3$), δ 2.39 (br, 4H), 2.83–2.66 (m, 2H), 3.35–3.22 (m, 2H), 3.58–3.53 (m, 1H), 3.77–3.72 (q, J = 6.4 Hz, 1H), 3.97* (dd, J = 2.4, 15.6 Hz, 1H), 4.23* (dd, J = 2.4, 15.6 Hz, 1H), 4.43–4.28* (m, 2H), 4.59–4.46 (m, 2H), 6.90–6.84 (m, 4H), 7.25–7.10 (m, 8H), 7.50 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.5, 171.1, 144.0, 139.9, 139.4, 134.3, 132.2, 130.2, 129.2, 128.8, 128.1, 128.0, 128.0, 126.9, 76.7, 74.1, 51.9, 46.2, 44.6, 41.6, 38.0, 21.6; IR (KBr): 3295, 2130, 1742, 1681, 1606, 1492, 1148 cm^{-1}; HRMS (MALDI) calcd for $C_{28}H_{25}ClO_3Na$ (M + Na^+): 467.1384; Found: 467.1386; mp: 103–105 °C.

Preparation of prop-2-yn-1-yl 4-(4-chlorophenyl)-6-(4-methoxyphenyl)-6-oxo-3-phenylhexanoate (3h)

Colorless oil, yield (85%); *cis*/*trans* = 11 : 1; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, J = 8.9 Hz, 2H), 7.63* (d, J = 8.9 Hz, 2H), 7.23–7.14 (m, 3H), 7.11 (d, J = 8.4 Hz, 2H), 6.93–6.82 (m, 6H), 6.80 (d, J = 8.9 Hz, 2H), 4.58 (dd, J = 15.6, 2.4 Hz, 1H), 4.49 (dd, J = 15.6, 2.4 Hz, 1H), 4.41 (dd, J = 15.6, 2.5 Hz, 1H), 4.34 (dd, J = 15.7, 2.4 Hz, 1H), 3.85 (s, 3H), 3.80* (s, 3H), 3.75 (q, J = 6.8 Hz, 1H), 3.56 (dt, J = 13.2, 6.5 Hz, 1H), 3.43–3.35* (m, 2H), 3.34–3.19 (m, 2H), 2.81 (dd, J = 15.7, 6.5 Hz, 1H), 2.70 (dd, J = 15.7, 9.0 Hz, 1H), 2.56–2.41* (m, 2H), 2.39 (t, J = 2.4 Hz, 1H), 2.36* (t, J = 2.4 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 196.4, 171.2, 163.5, 139.9, 139.5, 132.2, 130.3, 130.2, 129.9, 128.8, 128.0, 126.9, 113.7, 77.4, 74.8, 55.4, 51.9, 46.2, 44.7, 41.4, 38.0; IR (KBr): 3286, 2127, 1779, 1740, 1673, 1600, 1574, 1258, 1170; HRMS (MALDI) calcd for $C_{28}H_{25}ClO_4Na$ (M + Na^+): 483.1334; Found: 483.1330.

Preparation of prop-2-yn-1-yl 6-(4-bromophenyl)-4-(4-chlorophenyl)-6-oxo-3-phenylhexanoate (3i)

Colorless oil, yield (85%); *cis*/*trans* = 7 : 1; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, J = 8.0 Hz, 2H), 7.55 (d, J = 8.1 Hz, 2H), 7.20–7.11 (m, 6H), 6.95–6.85 (m, 4H), 4.57 (d, J = 15.6 Hz, 1H), 4.48 (d, J = 15.7 Hz, 1H), 4.39* (d, J = 16.1 Hz, 1H), 4.31* (d, J = 15.7 Hz, 1H), 3.80–3.69 (m, 1H), 3.65–3.55 (m, 1H), 3.36–3.21 (m, 2H), 2.82 (dd, J = 15.8, 5.9 Hz, 1H), 2.71 (dd, J = 15.4, 9.0 Hz, 1H), 2.39 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.6*, 197.4, 171.3, 171.2*, 142.0*, 1421.7*, 140.4, 140.1, 135.6, 131.9, 131.6*, 129.6, 129.4*, 128.9, 128.91, 128.9*, 128.8*, 128.5, 128.3, 128.0, 127.3*, 127.1*, 126.9, 126.8, 77.5, 77.3*, 74.9, 74.8*, 51.9, 51.8*, 47.8*, 47.0*, 46.1, 45.1, 43.7*, 41.6, 39.8*, 37.8; IR (KBr): 3293, 2129, 1741, 1687, 1569, 1235, 1147, 702 cm^{-1}; HRMS (MALDI) calcd for $C_{27}H_{23}BrO_3Na$ (M + Na^+): 497.0723; Found: 497.0731.

Preparation of prop-2-yn-1-yl 4-(4-chlorophenyl)-6-oxo-3,6-di-*p*-tolylhexanoate (3j)

Colorless oil, yield (91%); *cis*/*trans* = 7 : 1; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80* (d, J = 8.0 Hz, 2H), 7.75 (d, J = 8.0 Hz, 2H), 7.54* (d, J = 8.0 Hz, 2H), 7.43* (d, J = 8.1 Hz, 2H), 7.37* (d, J = 8.1 Hz, 1H), 7.22–7.16 (m, 2H), 7.12 (d, J = 8.3 Hz, 2H), 6.98 (d, J = 7.7 Hz, 2H), 6.86 (d, J = 8.3 Hz, 2H), 6.77 (d, J = 7.8 Hz, 2H), 4.57 (dd, J = 15.6, 2.0 Hz, 1H), 4.48 (dd, J = 15.6, 2.0 Hz, 1H), 4.44–4.32 (m, 2H), 3.73 (q, J = 8.0 Hz, 1H), 3.58–3.49 (m, 1H), 3.37–3.17 (m, 1H), 2.77 (dd, J = 15.7, 6.4 Hz, 1H), 2.65 (dd, J = 15.7, 8.9 Hz, 1H), 2.38 (s, 4H), 2.27 (s, 3H), 2.31–2.29* (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.7, 171.3, 144.1, 139.5, 136.7, 136.4, 134.5, 132.3, 130.4, 129.3, 128.8, 128.7, 128.2, 128.0, 76.8, 74.9, 51.9, 45.7, 44.6, 41.7, 38.1, 21.7, 21.1. IR (KBr): 3296, 2130, 1741, 1681, 1606, 1491, 1147 cm^{-1}; HRMS (MALDI) calcd for $C_{29}H_{27}ClO_3Na$ (M + Na^+): 481.1541; Found: 481.1547.

Preparation of prop-2-yn-1-yl 4-(4-chlorophenyl)-6-oxo-3-(*m*-tolyl)-6-(*p*-tolyl)hexanoate (3k)

Colorless oil, yield (90%); *cis*/*trans*>20 : 1; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, J = 8.1 Hz, 2H), 7.46* (d, J = 8.1 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 7.03 (d, J = 8.3 Hz, 3H), 6.97 (d, J = 7.9 Hz, 1H), 6.88 (d, J = 7.5 Hz, 1H), 6.78 (d, J = 8.4 Hz, 2H), 6.61 (d, J = 1.3 Hz, 2H), 4.48 (dd, J = 15.6, 2.4 Hz, 1H), 4.40 (dd, J = 15.6, 2.4 Hz, 1H), 4.32* (dd, J = 15.6, 2.4 Hz, 1H), 4.24* (dd, J = 15.6, 2.4 Hz, 1H), 3.66 (q, J = 8.0 Hz, 1H), 3.48–3.40 (m, J = 15.1, 6.4 Hz, 1H), 3.23 (dd, J = 17.0, 6.3 Hz, 1H), 3.13 (dd, J = 17.0, 7.8 Hz, 1H), 2.80* (dd, J = 16.7, 3.2 Hz, 1H), 2.68 (dd, J = 15.7, 6.5 Hz, 1H), 2.59 (dd, J = 15.7, 8.9 Hz, 1H), 2.32–2.27 (m, 4H), 2.24* (br, 6H), 2.13 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 196.9*, 196.6, 170.2, 170.1*, 142.9, 142.6*, 140.4*, 139.9*, 138.7, 138.5, 137.3*, 136.4, 133.4, 133.3*, 131.5*, 131.2, 129.2, 128.7*, 128.6, 128.24, 128.0*, 127.7*, 127.6*, 127.1, 127.1*, 127.0, 126.9*, 126.9, 126.8, 126.6, 124.7, 124.2*, 76.4, 76.3*, 73.8, 73.7*, 50.9, 50.7*, 46.5*, 45.3*, 44.9, 43.5, 42.4*, 40.4, 38.6*, 36.8, 20.6, 20.5*, 20.5*, 20.3; IR (KBr): 3296, 2129, 1741, 1681, 1606, 1491, 1146 cm^{-1}; HRMS (MALDI) calcd for $C_{29}H_{27}ClO_3Na$ (M + Na^+): 481.1541; Found: 481.1547.

Preparation of *cis*-prop-2-yn-1-yl 4-(4-chlorophenyl)-6-oxo-3-(*o*-tolyl)-6-(*p*-tolyl)hexanoate (3l-*cis*)

Colorless oil, yield (80%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, J = 8.1 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 7.09 (t, J = 5.9 Hz, 3H), 7.06–6.99 (m, 3H), 6.96 (d, J = 8.4 Hz, 2H), 4.49 (dd, J = 15.6, 2.4 Hz, 1H), 4.42 (dd, J = 15.6, 2.4 Hz, 1H), 3.85–3.68 (m, 2H), 3.41 (dd, J = 17.1, 7.9 Hz, 1H), 3.33 (dd, J = 17.1, 5.5 Hz, 1H), 2.86–2.70 (m, 2H), 2.39 (s, 3H), 2.36 (t, J = 2.4 Hz, 1H), 2.18 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.6, 171.3, 144.1, 140.7, 139.4, 136.4, 134.3, 132.1, 130.5, 129.7, 129.3, 128.1, 126.9, 126.5, 125.8, 77.2, 74.8, 51.9, 44.8, 41.9, 40.7, 38.1, 21.6, 19.8; IR (KBr): 3295, 2129, 1742, 1680, 1606,1492, 1147 cm^{-1}; HRMS (MALDI) calcd for $C_{29}H_{27}ClO_3Na$ (M + Na^+): 481.1541; Found: 481.1547.

Preparation of *trans*- prop-2-yn-1-yl 4-(4-chlorophenyl)-6-oxo-3-(*o*-tolyl)-6-(*p*-tolyl)hexanoate (3l-*trans*)

Colorless oil, yield (10%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, J = 8.1 Hz, 2H), 7.22–7.02 (m, 10H), 4.32 (dd, J = 15.6, 2.4 Hz, 1H), 4.25 (dd, J = 15.6, 2.4 Hz, 1H), 3.74–3.61 (m, 1H), 3.44 (t, J = 9.6 Hz, 1H), 3.14 (dd, J = 16.3, 10.9 Hz, 1H), 2.76 (dd, J = 16.3, 3.0 Hz, 1H), 2.53–2.41 (m, 1H), 2.37 (dd, J = 15.9, 4.6 Hz, 1H), 2.29–2.24 (m, 4H); HRMS (MALDI) calcd for $C_{29}H_{27}ClO_3Na$ (M + Na^+): 481.1541; Found: 458.1547. ^{13}C NMR (101 MHz, $CDCl_3$): δ 196.81, 178.22, 170.19, 142.74, 139.82, 131.47, 128.67, 128.08, 127.81, 126.93, 125.80, 125.74, 73.72, 50.74, 28.93, 20.54, 19.20; IR (KBr): 3295, 2129, 1742, 1680, 1606,1492, 1147 cm^{-1};

HRMS (MALDI) calcd for $C_{29}H_{27}ClO_3Na$ (M + Na^+): 481.1541; Found: 458.1547.

Preparation of prop-2-yn-1-yl 4-(4-chlorophenyl)-3-(4-methoxyphenyl)-6-oxo-6-(*p*-tolyl)hexanoate (3m)

Colorless oil, yield (98%); *cis*/*trans*>20 : 1 ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, J = 7.8 Hz, 2H), 7.15 (d, J = 7.7 Hz, 2H), 7.05 (d, J = 7.9 Hz, 2H), 6.78 (d, J = 7.9 Hz, 2H), 6.72 (d, J = 8.1 Hz, 2H), 6.65 (d, J = 8.1 Hz, 2H), 4.50 (d, J = 15.6 Hz, 1H), 4.42 (d, J = 15.6 Hz, 1H), 3.68 (s, 3H), 3.67–3.59 (m, 1H), 3.44 (dd, J = 14.2, 6.9 Hz, 1H), 3.19 (qd, J = 17.1, 6.9 Hz, 2H), 2.69 (dd, J = 15.6, 6.3 Hz, 1H), 2.56 (dd, J = 15.5, 9.2 Hz, 1H), 2.32 (s, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 196.6, 170.2, 157.4, 143.0, 138.420, 133.4, 131.3, 131.7, 129.3, 128.8, 128.3, 127.1, 127.0, 112.3, 76.5, 73.8, 54.1, 50.9, 44.3, 43.6, 40.7, 37.3, 20.6; IR (KBr): 3294, 2129, 1741, 1680, 1607, 1512, 1250, 1147 cm^{-1}; HRMS (MALDI) calcd for $C_{29}H_{27}ClO_4Na$ (M + Na^+): 497.1490; Found: 497.1499.

Preparation of prop-2-yn-1-yl 4-(4-chlorophenyl)-3-(3-methoxyphenyl)-6-oxo-6-(*p*-tolyl)hexanoate (3n)

Colorless oil, yield (95%); *cis*/*trans*>10 : 1; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, J = 8.1 Hz, 2H), 7.47* (d, J = 8.1 Hz, 2H), 7.13 (d, J = 8.0 Hz, 2H), 7.04 (d, J = 8.4 Hz, 2H), 7.00 (d, J = 7.9 Hz, 1H), 6.81 (d, J = 8.4 Hz, 2H), 6.62 (dd, J = 8.2, 2.3 Hz, 1H), 6.43 (d, J = 7.6 Hz, 1H), 6.32 (s, 1H), 4.50 (dd, J = 15.6, 2.4 Hz, 1H), 4.42 (dd, J = 15.6, 2.4 Hz, 1H), 4.34* (dd, J = 15.6, 2.4 Hz, 1H), 4.27* (dd, J = 15.7, 2.4 Hz, 1H), 3.70 (s, 3H), 3.67 (dd, J = 13.8, 6.7 Hz, 1H), 3.56 (s, 3H), 3.46 (dt, J = 13.0, 6.6 Hz, 1H), 3.21 (qd, J = 17.1, 7.1 Hz, 2H), 2.82* (dd, J = 16.7, 3.2 Hz, 1H), 2.70 (dd, J = 15.8, 6.5 Hz, 1H), 2.60 (dd, J = 15.8, 8.9 Hz, 1H), 2.46–2.33* (m, 2H), 2.33–2.28 (m, 4H), 2.24* (s, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 196.7*, 196.6, 170.1, 169.9*, 158.8*, 158.1, 143.0, 142.7*, 142.2*, 140.5, 139.8*, 138.5, 133.4, 133.3*, 131.5*, 131.3, 129.2, 128.79*, 128.7*, 128.3, 128.1*, 127.9, 127.8*, 127.1, 127.0, 120.1, 119.4*, 113.3, 113.0*, 111.5, 76.4, 76.4, 76.3*, 76.1, 75.8, 73.9, 73.8*, 54.1*, 54.1, 50.9, 50.7*, 46.6*, 45.1, 43.5, 42.3*, 40.5, 38.6*, 36.9, 20.58, 20.5*; IR (KBr): 3299, 2129, 1741, 1679, 1606, 1490, 1237, 1145 cm^{-1}; HRMS (MALDI) calcd for $C_{29}H_{27}ClO_4Na$ (M + Na^+): 497.1490; Found: 497.1498.

Preparation of prop-2-yn-1-yl 4-(4-chlorophenyl)-3-(4-fluorophenyl)-6-oxo-6-(*p*-tolyl)hexanoate (3o)

Colorless oil, yield (70%); *cis*/*trans* = 10 : 1; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, J = 8.1 Hz, 2H), 7.22 (d, J = 7.9 Hz, 2H), 7.19–7.16 (m, 2H), 7.11 (d, J = 8.4 Hz, 2H), 6.89 (dd, J = 7.2, 1.8 Hz, 2H), 6.85 (d, J = 8.4 Hz, 2H), 4.57 (dd, J = 15.6, 2.4 Hz, 1H), 4.49 (dd, J = 15.6, 2.4 Hz, 1H), 3.75 (q, J = 8.6 Hz, 1H), 3.56 (dt, J = 8.6, 6.5 Hz, 1H), 3.29 (qd, J = 17.1, 7.0 Hz, 2H), 2.86–2.76 (m, 1H), 2.70 (dd, J = 15.7, 8.9 Hz, 1H), 2.38 (br, J = 4.0 Hz, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.6, 171.2, 144.0, 139.9, 139.5, 134.4, 132.3, 130.3, 129.3, 128.8, 128.1, 128.0, 126.9, 77.4, 74.9, 52.0, 46.2, 44.6, 41.6, 38.0, 21.6; IR (KBr): 3298, 2129, 1742, 1682, 1233 cm^{-1}; HRMS (MALDI) calcd for $C_{28}H_{24}ClFO_3Na$ (M + Na^+): 485.1290; Found: 485.1296.

Preparation of prop-2-yn-1-yl 3-(4-bromophenyl)-4-(4-chlorophenyl)-6-oxo-6-(*p*-tolyl)hexanoate (3p)

Colorless oil, yield (75%); *cis*/*trans*>20 : 1; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, J = 8.2 Hz, 2H), 7.22 (d, J = 8.3 Hz, 2H), 7.15 (d, J = 8.1 Hz, 2H), 7.06 (d, J = 8.4 Hz, 2H), 6.77 (d, J = 8.4 Hz, 2H), 6.68 (d, J = 8.4 Hz, 2H), 4.48 (dd, J = 15.6, 2.4 Hz, 1H), 4.41 (dd, J = 15.6, 2.4 Hz, 1H), 3.65 (q, J = 6.8 Hz, 1H), 3.45 (dt, J = 9.3, 6.4 Hz, 1H), 3.27–3.09 (m, 2H), 2.72 (dd, J = 15.8, 6.1 Hz, 1H), 2.57 (dd, J = 15.7, 9.4 Hz, 1H), 2.35–2.27 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 196.3, 169.8, 143.2, 138.2, 137.9, 133.2, 131.5, 130.1, 129.5, 129.2, 128.3, 127.1, 127.1, 119.8, 76.3, 73.9, 51.0, 44.6, 43.7, 40.7, 37.1, 20.6; IR (KBr): 3296, 2129, 1742, 1681, 1491, 1233, 1146 cm^{-1}; HRMS (MALDI) calcd for $C_{28}H_{24}ClBrO_3Na$ (M + Na^+): 545.0489; Found: 545.0492.

Preparation of prop-2-yn-1-yl 4-(4-chlorophenyl)-3-(2-fluorophenyl)-6-oxo-6-(*p*-tolyl)hexanoate (3q)

Colorless oil, yield (63%); *cis*/*trans* = 1 : 7; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75* (d, J = 8.0 Hz, 2H), 7.56 (d, J = 8.0 Hz, 2H), 7.36–7.17 (m, 6H), 7.17–7.00 (m, 4H), 6.96–6.88* (m, J = 8.6 Hz, 4H), 4.54* (d, J = 15.6 Hz, 1H), 4.46–4.31 (m, 2H), 3.79–3.60 (m, 1H), 3.28 (dd, J = 16.7, 10.2 Hz, 1H), 2.87 (dd, J = 16.7, 3.0 Hz, 1H), 2.64 (dd, J = 16.0, 10.2 Hz, 1H), 2.45 (dd, J = 16.0, 4.3 Hz, 1H), 2.39 (s, 4H), 2.34 (s, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.5, 170.9, 162.4, 160.0, 143.8, 140.7, 134.3, 132.7, 129.9, 129.7, 129.4, 129.3, 129.1, 128.9, 128.8, 128.4, 128.3, 128.1, 128.1, 127.9, 124.6, 124.6, 116.0, 115.7, 77.2, 74.7, 51.8, 45.4, 43.2, 38.1, 21.6; IR (KBr): 3296,2129, 1742, 1681,1491, 1233, 1146 cm^{-1}; HRMS (MALDI) calcd for $C_{28}H_{24}ClFO_4Na$ (M + Na^+): 485.1290; Found: 485.1297.

Preparation of prop-2-yn-1-yl 3-(2-chlorophenyl)-4-(4-chlorophenyl)-6-oxo-6-(*p*-tolyl)hexanoate (3r)

Colorless oil, yield (74%); *cis*/*trans*>20 : 1; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, J = 7.6 Hz, 2H), 7.28 (d, J = 5.8 Hz, 1H), 7.21 (d, J = 7.6 Hz, 2H), 7.15–7.04 (m, 4H), 7.01 (d, J = 7.8 Hz, 2H), 6.90 (d, J = 6.2 Hz, 1H), 4.59–4.43 (m, 2H), 4.25–4.11 (m, 1H), 3.96–3.83 (m, 1H), 3.36 (d, J = 6.7 Hz, 2H), 2.89–2.68 (m, 2H), 2.38 (s, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.4, 170.8, 144.0, 139.7, 138.2, 134.6, 134.4, 132.4, 129.9, 129.9, 129.3, 128.2, 128.1, 128.0, 126.5, 77.3, 74.9, 52.1, 43.8, 40.8, 37.4, 29.7, 21.6; IR (KBr): 3298, 2129, 1742, 1681, 1606, 1492, 1240, 1151 cm^{-1}; HRMS (MALDI) calcd for $C_{28}H_{24}Cl_2O_3Na$ (M + Na^+): 501.0995; Found: 501.1009.

Preparation of prop-2-yn-1-yl 3,4-bis(4-chlorophenyl)-6-oxo-6-(*p*-tolyl)hexanoate (3s)

Colorless oil, yield (80%); *cis*/*trans* = 10 : 1; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, J = 8.0 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.14 (t, J = 7.8 Hz, 4H), 6.83 (dd, J = 12.4, 8.4 Hz, 4H), 4.56 (dd, J = 15.6, 2.3 Hz, 1H), 4.49 (dd, J = 15.6, 2.3 Hz, 1H), 3.73 (q, J = 6.8 Hz, 1H), 3.54 (dt, J = 12.9, 6.4 Hz, 1H), 3.35–3.16 (m, 2H), 2.80 (dd, J = 15.7, 6.1 Hz, 1H), 2.65 (dd, J = 15.7, 9.4 Hz, 1H), 2.40 (s, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.4, 170.9, 144.2, 139.2, 138.5, 134.2, 132.7, 132.5, 130.2, 130.1, 129.4, 128.2, 128.2, 128.1, 77.0, 74.9, 52.0, 45.7, 44.5, 41.7, 38.2, 21.7; IR (KBr): 3298,

2129, 1742, 1680, 1606, 1510, 1226, 1148 cm^{-1}, HRMS (MALDI) calcd for $C_{29}H_{27}ClO_4Na$ ($M + Na^+$): 501.0995; Found: 501.1009.

Preparation of prop-2-yn-1-yl 4-(furan-2-yl)-6-oxo-3-phenyl-6-(*p*-tolyl)hexanoate (3t)

Colorless oil, yield (82%); *cis*/*trans* = 10 : 1; ^1H NMR (400 MHz, $CDCl_3$): δ 7.75* (d, J = 8.2 Hz, 2H), 7.62 (d, J = 8.2 Hz, 2H), 7.29–7.25 (m, 1H), 7.24–7.17 (m, 5H), 6.94–6.89 (m, 2H), 6.22 (dd, J = 3.0, 1.9 Hz, 1H), 5.90 (d, J = 3.2 Hz, 1H), 4.58 (dd, J = 15.6, 2.4 Hz, 1H), 4.51 (dd, J = 15.6, 2.4 Hz, 1H), 3.95–3.87 (m, 1H), 3.66–3.58 (m, 1H), 3.23 (dd, J = 17.1, 7.8 Hz, 1H), 3.12 (dd, J = 17.1, 6.2 Hz, 1H), 2.92 (dd, J = 16.0, 6.4 Hz, 1H), 2.84 (dd, J = 16.1, 9.3 Hz, 1H), 2.43–2.37 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.5, 171.3, 154.7, 144.0, 141.2, 140.0, 134.3, 129.3, 128.5, 128.2, 128.1, 128.1, 126.9, 110.2, 107.3, 74.9, 52.0, 45.0, 39.1, 38.9, 37.7, 21.7; IR (KBr): 3290, 2129, 1741, 1681, 1606, 1236, 1149 cm^{-1}, HRMS (ESI) calcd for $C_{26}H_{24}ClO_4Na$ ($M + Na^+$): 423.1567; Found: 423.1564.

Preparation of prop-2-yn-1-yl 3-methyl-6-oxo-4,6-diphenylhexanoate (3u)

Colorless oil, yield (55%); *cis*/*trans* = 3 : 1; ^1H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 7.4 Hz, 0.2H)*, 7.92–7.82 (m, J = 8.4 Hz, 2.5H), 7.59–7.50 (m, J = 7.3 Hz, 1.4H), 7.49–7.39 (m, 2.8H), 7.28–7.17 (m, 3H), 7.13 (t, J = 7.1 Hz, 3H), 4.73–4.64 (m, 2H), 4.62* (dd, J = 7.2, 2.4 Hz, 0.8H), 3.47–3.25 (m, 4H), 2.71–2.43 (m, 2.5H), 2.49–2.25 (m, 2.4H), 2.22–2.11 (m, 2.3H), 2.03* (dd, J = 15.2, 9.3 Hz, 0.4H), 1.07* (d, J = 6.6 Hz, 1H), 0.87 (d, J = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 198.4*, 198.2, 172.0*, 172.0, 141.2*, 140.2, 136.9*, 136.9, 133.2, 132.3*, 129.9, 129.6*, 129.3, 128.6, 128.5, 128.0, 128.0*, 77.6, 75.0, 74.9*,52.0, 51.9*, 45.5*, 44.6, 42.0, 39.5, 39.2*, 35.6, 35.0, 18.1*, 16.9; IR (KBr): 3295, 2128, 1738, 1686, 1491, 1153; HRMS (ESI) calcd for $C_{22}H_{21}ClO_3Na$ ($M + Na^+$): 391.1071; Found: 391.1077.

Preparation of prop-2-yn-1-yl 3-methyl-4-(2-oxo-2-phenylethyl)-7-phenylhept-6-enoate (3v)

Colorless oil, yield (81%). *cis*/*trans* = 7 : 1, ^1H NMR (400 MHz, $CDCl_3$): δ 7.99* (d, J = 7.3 Hz, 2H), 7.85 (d, J = 7.8 Hz, 2H), 7.70* (d, J = 7.8 Hz, 2H), 7.54 (dd, J = 15.9, 8.5 Hz, 2H), 7.43 (t, J = 7.6 Hz, 2H), 7.35–7.23 (m, 7H), 7.15 (d, J = 7.3 Hz, 2H), 6.43 (d, J = 15.9 Hz, 1H), 5.89 (dd, J = 15.8, 9.5 Hz, 1H), 4.61 (dd, J = 15.6, 2.0 Hz, 1H), 4.53 (dd, J = 15.6, 2.1 Hz, 1H), 4.11 (dt, J = 13.8, 7.0 Hz, 1H), 3.57–3.47 (m, 1H), 3.33–3.21 (m, 1H), 3.08 (dd, J = 16.5, 6.2 Hz, 1H), 2.93–2.80 (m, 3H), 2.40 (s, 1H), 2.34* (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 198.7*, 198.5, 171.5*, 171.2, 141.8*, 139.6, 137.1*, 137.0, 136.7*, 133.1, 132.9*, 132.9*, 132.5, 130.7, 128.8, 128.8*, 128.6*, 128.6, 128.5, 128.5*, 128.4*, 128.3, 128.1, 128.1, 128.0, 127.4*, 127.4, 127.2*, 127.0, 126.3, 74.8, 74.7, 51.9, 51.8, 46.1*, 45.4*, 45.0, 42.9, 42.3*, 41.7, 40.0*, 38.0; IR (KBr): 3294, 2128, 1740, 1682, 1149 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{26}O_3Na$ ($M + Na^+$): 445.1774; Found: 485.1780.

Procedure for the preparation of 4

CuI (0.1 mmol) was added to the a suspension of the benzyl azide (1.2 mmol) and ε-ketoester **3g** (1.0 mmol) in 2 ml *t*-BuOH under N_2 atmosphere. This solution was refluxed until the complete consumption of **3g** as monitored by TLC. After the removal of the solvent, the residue was subjected to chromatography on a silica gel (60–120 mesh) column using 15 : 1 petroleum ether–ethyl acetate solvent mixture as eluent to afford **4** as colorless oil in 75% yield.

Colorless oil, yield (75%); ^1H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, J = 7.9 Hz, 2H), 7.34 (d, J = 5.3 Hz, 3H), 7.22 (d, J = 7.5 Hz, 4H), 7.10 (m, J = 12.0, 7.0 Hz, 6H), 6.84–6.77 (m, 4H), 5.42 (s, 2H), 5.14–5.01 (m, 2H), 3.68 (q, J = 6.7 Hz, 1H), 3.50 (dt, J = 12.7, 6.3 Hz, 1H), 3.28 (t, J = 8.6 Hz, 1H), 3.20 (dd, J = 17.2, 7.5 Hz, 1H), 2.76 (dd, J = 15.3, 6.2 Hz, 1H), 2.65 (dd, J = 15.3, 9.6 Hz, 1H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.5, 171.8, 144.1, 143.2, 139.8, 139.4, 134.4, 134.3, 132.3, 130.2, 129.3, 29.1, 128.9, 128.8, 128.1, 128.0, 128.0, 127.9, 126.8, 123.4, 57.7, 54.1, 46.4, 44.5, 41.5, 38.1, 21.5; IR (KBr): 1735, 1680, 1605, 1493, 1226, 1150 cm^{-1}; HRMS (MALDI) calcd for $C_{35}H_{32}ClN_3O_3Na$ ($M + Na^+$): 600.2024; Found: 600.2022.

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