Monatshefte für Chemie - Chemical Monthly
https://doi.org/10.1007/s00706-019-02526-z

ORIGINAL PAPER

A copper-catalyzed reaction between terminal alkynes, acetylenic esters, and oxiranes: efficient synthesis of 2*H*-pyran-4-carboxylate

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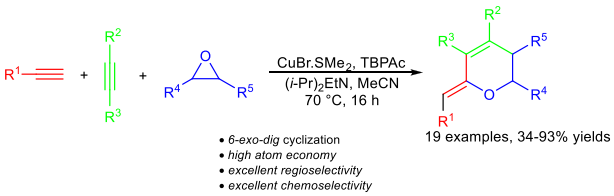
Received: 7 September 2019 / Accepted: 25 November 2019

Abstract

A catalytic reaction between terminal alkynes, acetylenic esters, and oxiranes has been described. This domino transformation serves as a useful sequential and one-pot method for the synthesis of 2*H*-pyran-4-carboxylate skeletons from the readily available starting materials. In situ-generated copper acetylides treated initially with oxiranes in the presence of copper catalysts and tetrabutylphosphonium salts, followed by addition of propiolates after 60 min to form synthetically important heterocycles.

Graphic abstract



Keywords Domino reaction · Three-membered heterocycle · Copper catalysis · Acetylenic ester · Cyclization

Introduction

Synthesis of heterocyclic compounds is a highly demanding field to chemists in the field of organic chemistry (for selected examples of coinage metals-catalyzed synthesis of heterocycles, see [1–3], [4]). A particularly efficient method in this field is transition-metal-catalyzed electrophilic cyclization across C–C triple bonds [5–9]. These catalytic transformations allow the reactions to be performed in mild conditions with the use of starting materials that are not compatible with classical procedures. This is because of exceptional ability of alkynophile metals to activate π-electrons of alkynes towards nucleophilic attacks.

For instance, the copper-catalyzed 1,3-cycloaddition of organic azides and terminal alkynes fix major drawbacks of the thermal versions likes low rate and regioselectivity [10–12]. The great success in copper-catalyzing the Huisgen 1,3-dipolar cycloaddition resulted in enormous attention to explore the precise role of copper salts in activation of alkyne synthon [13, 14]. These studies shed light on the mechanism of activation of alkynes and revealed that the π-electrons of C–C triple bond are strongly coordinated to copper species through the reaction progress. Considering the distortion of π-electron's density across with the C–C triple bond is the origin of a great number of reports featuring synthesis of molecular functionality and complexity using copper acetylides [15–21].

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Published online: 02 January 2020

Based on these findings, we have reported a reaction involving copper acetylides, carbon disulfide, and oxiranes to form 1,4-oxathianes in good yields and excellent regioselectivity [22]. Subsequently, Samzadeh-Kermani and Khalaj independently reported a number of methods featuring synthesis of heterocyclic compounds using metal acetylides, heterocumulenes, and an appropriate third coupling partner [23–26].

Carriera and co-workers have reported the first catalytic additions of copper acetylides on Michael acceptors [27]. While the reaction between metal acetylides and heterocumulenes, imines, and carbonyls has been well documented, the conjugated additions of metal acetylides on activated C–C triple bonds are without precedent. Based on above literatures and in continuation of our reports in copper catalysis [28–30], we became interested to examine the conjugated additions of metal acetylides on acetylenic esters in the presence of oxiranes as third coupling partners toward synthesis of 2*H*-pyran molecules (Scheme 1).

There are many reports in literature featuring synthesis of 2*H*-pyran structures with catalytic reactions being among the most studied procedures [8, 31–33]. Recently, Varmazyar and co-workers have developed a novel catalytic reaction to form 2*H*-pyran from catalytic additions of copper acetylides on oxiranes in the presence of malonates [34]. According to the literature, the regioselectivity in ring opening of three-membered heterocycles relies on substrates' structures, catalysts, and reaction conditions [35–38].

Scheme 1

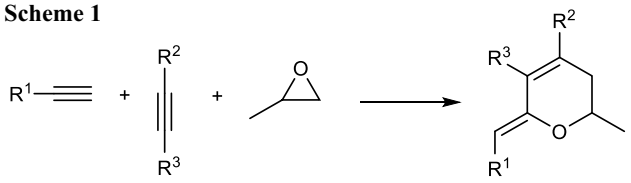
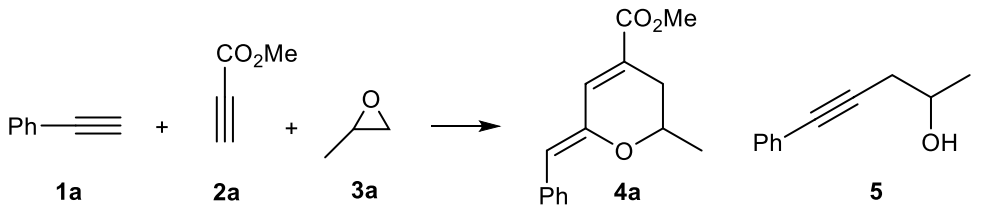


Table 1 Optimization of reaction conditions



1a **2a** **3a** **4a** **5**

Entry	Catalyst	Base	Additive	Solvent	Yield of **4a**/%
1	CuI	$(i\text{-Pr})_2$EtN	TBPAc	MeCN	57
2	$CuBr{\cdot}SMe_2$	$(i\text{-Pr})_2$EtN	TBPAc	MeCN	84
3	Cu_2O	$(i\text{-Pr})_2$EtN	TBPAc	MeCN	67
4	CuCl	$(i\text{-Pr})_2$EtN	TBPAc	MeCN	29
5	$Cu(BF_4)_2$	$(i\text{-Pr})_2$EtN	TBPAc	MeCN	62
6	CuOTf	$(i\text{-Pr})_2$EtN	TBPAc	MeCN	53
7	$Cu(OTf)_2$	$(i\text{-Pr})_2$EtN	TBPAc	MeCN	54
8	$CuBr{\cdot}SMe_2$	$(i\text{-Pr})_2$EtN	TBPAc	THF	64
9	$CuBr{\cdot}SMe_2$	$(i\text{-Pr})_2$EtN	TBPAc	DMF	31
10	$CuBr{\cdot}SMe_2$	$(i\text{-Pr})_2$EtN	TBPAc	HFIP	(61)[a]
11	$CuBr{\cdot}SMe_2$	$(i\text{-Pr})_2$EtN	TBPAc	PEG-400	(73)[a]
12	$CuBr{\cdot}SMe_2$	$(i\text{-Pr})_2$EtN	TBPAc	Toluene	Traces
13	$CuBr{\cdot}SMe_2$	*t*-BuOLi	TBPAc	MeCN	(74)[a]
14	$CuBr{\cdot}SMe_2$	Cs_2CO_3	TBPAc	MeCN	69
15	$CuBr{\cdot}SMe_2$	K_2CO_3	TBPAc	MeCN	21
16	$CuBr{\cdot}SMe_2$	Et_3N	TBPAc	MeCN	18
17	$CuBr{\cdot}SMe_2$	$(i\text{-Pr})_2$EtN	TBPCl	MeCN	15
18	$CuBr{\cdot}SMe_2$	$(i\text{-Pr})_2$EtN	TBPBr	MeCN	31
19	$CuBr{\cdot}SMe_2$	$(i\text{-Pr})_2$EtN	TMPAc	MeCN	43
20	$CuBr{\cdot}SMe_2$	$(i\text{-Pr})_2$EtN	TEPAc	MeCN	59
21		$(i\text{-Pr})_2$EtN	TBPAc	MeCN	Traces

Reaction conditions: **1a** (1.2 mmol), **3a** (2.0 mmol), catalyst (0.1 mmol), base (1.5 mmol), additive (0.3 mmol), and 4.0 cm^3 solvent were reacted at ambient conditions for 1 h, **2a** (1.0 mmol) was then added and the mixture was stirred at 70 °C for 16 h

[a]The digit in parentheses refer to the yield of **5**

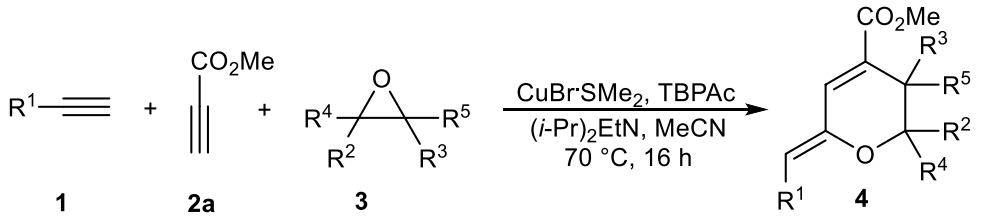
Results and discussion

We initially examined the reaction of phenyl acetylene (**1a**), methyl propiolate (**2a**), and methyl oxirane (**3a**) under the catalysis of CuI in MeCN at 70 °C (Table 1). The reaction performed without an additive only afforded the desired compound **4a** in 7% yield (not shown in Table 1). Based on the previous reports, we found that tetrabutylphosphonium salts (TBP) effectively activate three-membered heterocycles towards nucleophilic attacks [39, 40]. Additionally, alkylphosphonium salts exhibited good catalyst activity in the presence of propiolates [41]. We believe that the adduct derived from the reaction of metal acetylide and propiolate could not attack on oxirane without a preliminary activation (see Scheme 3). Fortunately, the proposed three-component reaction proceeded cleanly and afforded the targeted compound **4a** in reasonable yield using tetrabutylphosphonium acetate (TBPA) (entry 1). Encouraged by this result, we next examined the efficiency of different catalysts and $CuBr{\cdot}SMe_2$ identified as the optimum choice for the reaction (entries 2–7). It is worth mentioning that the oxidation states of copper salts did not affect the reaction outcome in appreciable manner (entry 6 vs. 7). To further optimize the reaction parameters, we performed the reaction in different solvent and our selected results are shown in Table 1 (entries 8–12). Interestingly, the reaction conducted in hexafluoroisopropanol (HFIP) and PEG-400 (which is known to activate oxiranes through intermolecular H-bonding [34, 42]) formed the direct coupling product **5** in 61% and 73% yields, respectively (entries 10, 11). The reaction was also conducted with different organic and inorganic bases and finally, $(i\text{-Pr})_2\text{EtN}$ was selected as the base of choice based on the cost and efficiency (entries 13–16). To our delight, the use of *t*-BuOLi as an inorganic base resulted in formation of compound **5** in 74% yield (entry 13). The oxygen atom in **3a** would be coordinated preferably to lithium ion, thereby providing the opportunity for the direct attack of copper acetylide on activated oxirane. Inferior results were obtained using tetrabutylphosphonium chloride or bromides as an additive (entries 17, 18). Additionally, the success of the transformation has great dependence on alkyl group of phosphonium salts; as the reaction conducted with tetramethyl- and tetraethylphosphonium acetated afforded **4a** in lower yields (entries 19, 20). As expected, the reaction without copper catalyst was not productive (entry 21). Based on the spectroscopic analyses, all of the reactions proceeded through a 6-*exo* cyclization route. It is worth mentioning that no product arising from the attack of acetylides derived from propiolates are detected in crude reaction mixture analyses. Importantly, without a preliminary activation of oxirane, the reaction proceeded in two-component mode as when all the substrates were charged to the reaction vessel at once, the targeted product **4a** was not detected at all (not shown in Table 1). Additionally, the reaction performed with TBPAc (1.0 mmol) resulted in formations of alkylated products derived from the reaction of terminal alkyne with TBP cation. It is worth mentioning that the reaction exhibited good regioselectivity with respect to the *exo*-double bond to afford (*Z*)-configuration of 6-benzylidene motif.

The generality of the reaction was then evaluated using various terminal alkynes and oxiranes (Table 2). The reaction of 2-methyloxirane (**3a**) proceeded cleanly and afforded the desired compound **4a** in good yield (entry 1). Butyl-linked oxirane **3b** reacted with a partial decrease in yield (entry 2). Oxiranes bearing an additional oxygen atom likes **3c** or **3d** afforded an excellent yield of the corresponding products **4c** and **4d** (entries 3 and 4). An additional oxygen atom presumably acts as an auxiliary catalyst coordination site and thereby, activates oxirane toward subsequent nucleophilic attacks. Expanding the scope of **3** to cyclic oxirane like **3e** was also possible, allowing the formations of fused bicyclic compound **4e** in reasonable yield (entry 5). When phenyl-substituted oxirane **3f** was subjected to the optimum reaction conditions, the benzylic-attacked product **4f** was formed exclusively (entry 6). 4-Chlorophenyl and *p*-tolyl oxiranes (**3g**, **3h**) engaged proficiently in this transformation to furnish corresponding 2*H*-pyran-4-carboxylates **4g**, **4h** in acceptable yields (entries 7 and 8). The reaction with *p*-tolylacetylene (**1b**) afforded an excellent yield (entry 9). It could be deduced that the attack of copper acetylide on propiolate is the rate-determination step of this catalytic reaction. Alkyl terminal alkyne **1c** was also tolerated; however, the reaction required higher temperature to afford the expected product **4j** in good yield (entry 10). It should be noted that highly substituted oxirane 2,2,3,3-tetramethyloxirane (**3i**) only afforded the corresponding compound **4k** in moderate yield (entry 11).

To further demonstrate the utility of the proposed reaction, other propiolates **2b**–**2j** were also examined and the results are shown in Table 3. The reactions of methyl- and *tert*-butyl propiolates (**2b**, **2c**) proceeded smoothly and afforded the desired 2*H*-pyran structures in good yields (entries 1 and 2). The catalytic reaction was partially inhibited by steric hindrance from an additional substituent at the triple bond; as ethyl but-2-ynoate (**2d**) and ethyl 3-phenylpropiolate (**2e**) reacted with a notable decrease in yields (entries 3 and 4). Interestingly, propiolamide (**2f**) was also tolerated (entry 5). The tolerance for propiolamide gives further advantage to the present protocol. Additionally, this is in contrast with previous reports which reported that acetylenic esters are protonated upon reaction with amides [41, 43]. Electron-rich terminal alkyne **1d** effectively participated in this domino transformation while, alkyne containing CF_3 as motif only afforded a low yield (entries 6 and 7). It could be

Table 2 Synthesis of functionalized 2*H*-pyran-4-carboxylates with various oxiranes and alkynes

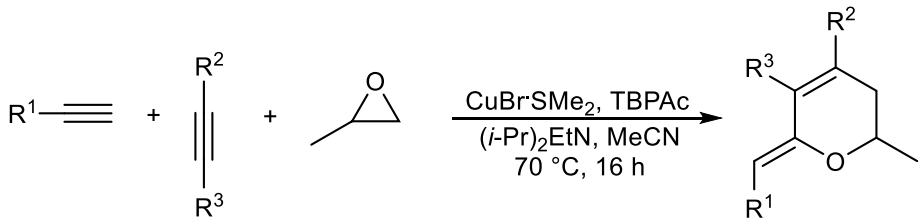


Entry	Alkyne	R^1	Oxirane	R^2,R^3	Yield/%
1	**1a**	Ph	**3a**	Me, H, H, H	**4a**, 84
2	**1a**	Ph	**3b**	*n*-C_4H_9, H, H, H	**4b**, 79
3	**1a**	Ph	**3c**	$PhOCH_2$, H, H, H	**4c**, 93
4	**1a**	Ph	**3d**	Me_2CHOCH_2, H	**4d**, 90
5	**1a**	Ph	**3e**	–$(CH_2)_4$–, H, H	**4e**, 72
6	**1a**	Ph	**3f**	Ph, H, H, H	**4f**, 85
7	**1a**	Ph	**3g**	4-Cl-C_6H_4, H, H, H	**4g**, 87
8	**1a**	Ph	**3h**	4-Me-C_6H_4, H, H, H	**4h**, 67
9	**1b**	4-Me-C_6H_4	**3a**	Me, H, H, H	**4i**, 90
10	**1c**	CH_3OCH_2	**3a**	Me, H, H, H	**4j**, 72[a]
11	**1a**	Ph	**3i**	Me, Me, Me, Me	**4k**, 43

For all entries except stated otherwise: **1** (1.2 mmol), **3** (2.0 mmol), CuBr·SMe_2 (0.1 mmol), (*i*-Pr)$_2$EtN (1.5 mmol), TBPAc (0.3 mmol), in 4.0 cm^3 dry MeCN were stirred at ambient conditions for 1 h, **2a** (1.0 mmol) was then added and the mixture was stirred at 70 °C for 16 h

[a]At 90 °C

Table 3 Synthesis of functionalized 2*H*-pyran-4-carboxylates using various alkynes and propiolates

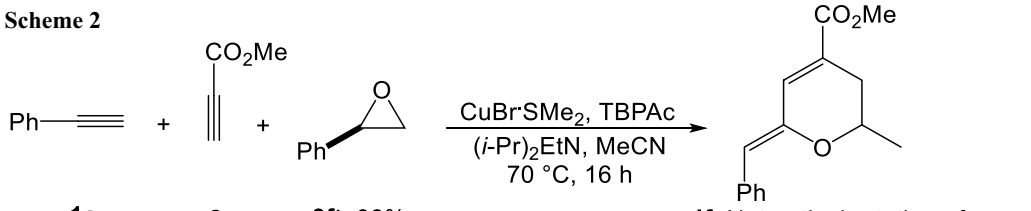


Entry	Alkyne	R^1	Propiolate	R^2, R^3	Yield/ %
1	**1a**	Ph	**2b**	H, CO_2Et	**4l**, 83
2	**1a**	Ph	**2c**	H, CO_2t-Bu	**4m**, 85
3	**1a**	Ph	**2d**	Me, CO_2Et	**4n**, 46
4	**1a**	Ph	**2e**	Ph, CO_2Et	**4o**, 58
5	**1a**	Ph	**2f**	H, $CONH_2$	**4p**, 69
6	**1d**	4-MeO-C_6H_4	**2b**	H, CO_2Et	**4q**, 92
7	**1e**	3-CF_3-C_6H_4	**2b**	H, CO_2Et	**4r**, 34
8	**1f**	*n*-Bu	**2b**	H, CO_2Et	**4s**, 63[a]

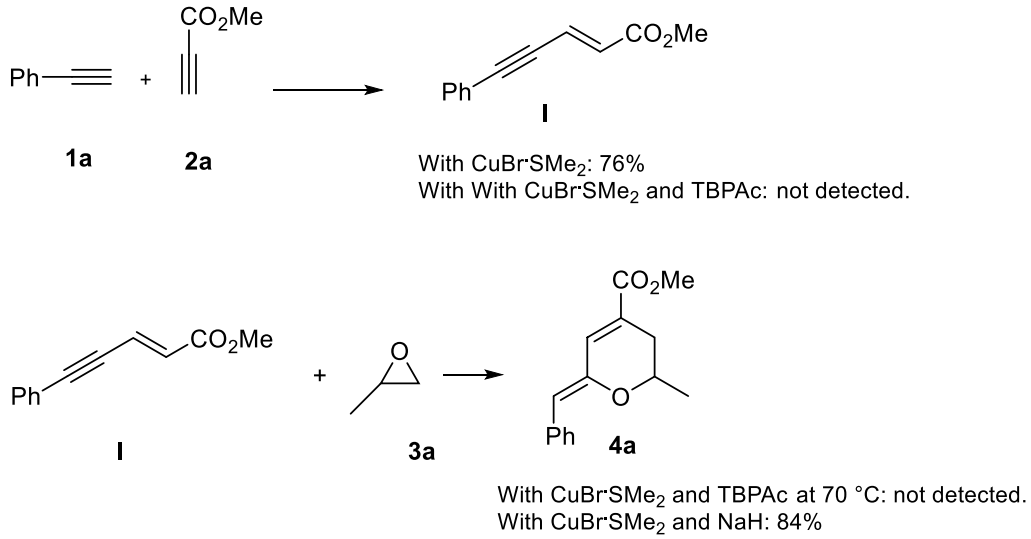
For all entries except stated otherwise: **1** (1.2 mmol), **3a** (2.0 mmol), CuBr·SMe_2 (0.1 mmol), (*i*-Pr)$_2$EtN (1.5 mmol), TBPAc (0.3 mmol), in 4.0 cm^3 dry MeCN were stirred at ambient conditions for 1 h, **2** (1.0 mmol) was then added and the mixture was stirred at 70 °C for 16 h

[a]At 90 °C

Scheme 2



Scheme 3



deduced that the nucleophilic attack of metal acetylide on propiolate is the rate-determination step of this transformation. 1-Hexyne (**1e**) was also tolerated, however, the reaction required higher temperature to give the corresponding product **4s** in reasonable yield (entry 8).

When chiral oxirane **3f′** was used as the substrate, the domino ring opening/cyclization reaction proceeded with racemization at the chiral centre (Scheme 2). This result indicated that the reaction proceeded through a S_N1 pathway using phenyl-substituted oxirane.

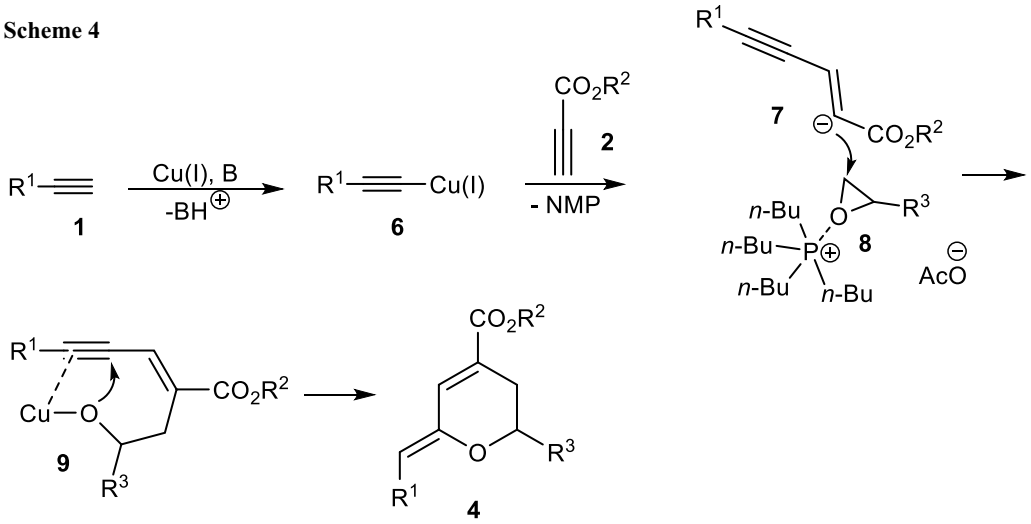
To propose a more reliable mechanism for the formation of **4**, some control experiments were performed and the results are shown in Scheme 3. These results indicate that TBPAc inhibited formation of the compound **I** and instead a polymeric oil was obtained. These findings deduced that in the presence of TBPAc the anionic adduct derived from terminal alkyne and propiolate attacks again on another propiolate while, in the presence of activated oxirane, the reaction proceeded through three-component modes to afford the desired compound **4a**. Additionally, the reaction with compound **I** and **3a** did not afford the desired product **4a** at all while in the presence of a strong base like NaH the reaction formed compound **4a** in good yield. These results are further supported by the fact that the reaction in protic solvents did not afford the targeted product **4a** and instead gave the direct coupling product **5** (see Table 1, entries 10, 11).

Based on previous reports [27, 29, 30], the possible reaction pathway is proposed in Scheme 4. Coordination of copper catalyst with phenyl acetylene in the presence of $(i\text{-Pr})_2$EtN gave copper acetylide **6**. The nucleophilic attack of in situ-generated copper acetylide to the propiolate yielded the adduct **7** which further reacted with activated oxirane (species 8) to form the ring opened-intermediate **9**. The electrophilic cyclization of **9** by the action of copper salt in the presence of $(i\text{-Pr})_2\text{EtNH}^+$ afforded the expected 6-*exo* product **4**.

Conclusion

In summary, we have reported an efficient reaction between terminal alkynes, propiolates, and oxiranes as the third coupling partner in the presence of CuBr·SMe_2 as the catalyst and TBPAc as additive to access synthetically important 2*H*-pyran-4-carboxylate structures. To our knowledge this is the first catalytic additions of copper acetylides on propiolates in the presence of oxiranes. Control experiments indicated that an inert atmosphere together with TBPAc is necessary to furnish the transformation in good yield.

Scheme 4



Experimental

All reactions were carried out in Schlenk tube (25 cm^3) under nitrogen atmosphere. All the reagents, catalysts, and additives were obtained from commercial sources. All the solvents were purchased from PALAENERGY Pure Chemical Industries, and were dried and degassed before use. Melting points were measured with Electrothermal-9100 apparatus. IR spectra were determined on a Nicolet 6700 spectrometer. ^1H and ^{13}C NMR spectra were recorded with Bruker DRX-500 AVANCE instrument; in $CDCl_3$ at 500 and 125 MHz, resp.; δ in ppm, J in Hz. Mass spectra were determined on a EIMS (70 eV): Finnigan-MAT-8430 mass spectrometer. Elemental analyses were performed with a Heraeus Rapid analyser. The results agreed favorably with the calculated values. Silica gel 60 (particle size 63–200 µm or 40–100 mesh) was used for column chromatography (Merck, item number 7734-3). TLC analyses were performed on commercial glass plates bearing a 0.25-mm layer of Merck Silica gel 60 (Merck, item number 116835).

General procedure for the preparation of compounds 4

A Schlenk tube (25 cm^3) equipped with a magnetic stir bar was charged with terminal alkyne (1.2 mmol), $(i\text{-Pr})_2EtN$ (1.5 mmol), $CuBr{\cdot}SMe_2$ (0.1 mmol), TBPAc (0.3 mmol), oxirane (2.0 mmol), and 2.0 cm^3 MeCN. After the mixture was stirred at 25 °C for 1 h, propiolate (1.0 mmol) was added under an inert atmosphere. The tube was evacuated and backfilled with argon (three times). Subsequently, the mixture was stirred for 16 h at appropriate temperature (see Tables 2, 3). After cooling to room temperature, the mixture was passed through silica gel pad and concentrated under reduced pressure. The resulting residue was purified with column chromatography on silica gel (eluent gradient of EtOAc/hexane, see spectroscopic analysis section) to give the corresponding products **4** in the yields listed in Tables 2 and 3.

Methyl 6-benzylidene-2-methyl-3,6-dihydro-2*H*-pyran-4-carboxylate (4a, $C_{15}H_{16}O_3$) The crude product was purified by column chromatography (SiO_2, hexane/EtOAc 9/1, $R_f = 0.29$) affording 0.21 g (84%) of **4a**. Colorless oil; IR (KBr): $\bar{\nu} = 3022, 2970, 1723, 1644, 1465, 1255, 1121\ cm^{-1}$; ^1H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.32$ (3H, d, $^3J = 6.1$ Hz, Me), 2.41 (1H, dd, $^2J = 12.3$ Hz, $^3J = 10.1$ Hz, CH), 2.55 (1H, dd, $^2J = 12.3$ Hz, $^3J = 5.2$ Hz, CH), 3.72 (3H, s, OMe), 4.00–4.05 (1H, m, CH), 5.24 (1H, s, CH), 7.15 (1H, s, CH), 7.32 (1H, t, $^3J = 7.1$ Hz, CH), 7.41 (2H, t, $^3J = 7.2$ Hz, 2 CH), 7.64 (2H, d, $^3J = 7.3$ Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 23.1$ (Me), 40.1 (CH_2), 54.6 (OMe), 81.4 (CH), 87.1 (CH), 124.2 (C), 126.5 (CH), 129.4 (2 CH), 130.7 (2 CH), 133.8 (C), 145.1 (CH), 149.7 (C), 167.2 (C) ppm; EI-MS (70 eV): m/z (%) = 244 (M^+, 1), 229 (12), 177 (23), 100 (65), 91 (43), 77 (100), 54 (48).

Methyl 6-benzylidene-2-butyl-3,6-dihydro-2*H*-pyran-4-carboxylate (4b, $C_{18}H_{22}O_3$) The crude product was purified by column chromatography (SiO_2, hexane/EtOAc 10/1, $R_f = 0.35$) affording 0.23 g (79%) of **4b**. Colorless oil; IR (KBr): $\bar{\nu} = 3014, 2973, 1722, 1651, 1473, 1286, 1095\ cm^{-1}$; ^1H NMR (500.1 MHz, $CDCl_3$): $\delta = 0.91$ (3H, t, $^3J = 6.0$ Hz, Me), 1.35–1.76 (6H, m, 3 CH_2), 2.47 (1H, dd, $^2J = 11.8$ Hz, $^3J = 5.0$ Hz, CH), 2.65 (1H, dd, $^2J = 11.8$ Hz, $^3J = 9.7$ Hz, CH), 3.69 (3H, s, OMe), 4.01–4.05 (1H, m, CH), 5.29 (1H, s, CH), 7.19 (1H, s, CH), 7.31 (1H, t, $^3J = 7.6$ Hz, CH), 7.40 (2H, t, $^3J = 7.6$ Hz, 2 CH), 7.59 (2H, d, $^3J = 7.6$ Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 15.2$ (Me), 28.1 (CH_2), 30.4 (CH_2), 37.9 (CH_2), 41.9 (CH_2), 55.9 (OMe),

80.1 (CH), 94.2 (CH), 122.8 (CH), 126.5 (CH), 128.9 (2 CH), 130.1 (2 CH), 134.8 (C), 144.1 (CH), 148.4 (C), 168.9 (C) ppm; EI-MS (70 eV): *m*/*z* (%) = 286 (M^+, 1), 229 (6), 139 (48), 91 (43), 81 (87), 77 (100), 54 (48).

Methyl 6-benzylidene-2-(phenoxymethyl)-3,6-dihydro-2*H*-pyran-4-carboxylate (4c, $C_{21}H_{20}O_4$) The crude product was purified by column chromatography (SiO_2, hexane/EtOAc 8/1, $R_f = 0.31$) affording 0.31 g (93%) of **4c**. Yellow oil; IR (KBr): $\bar{\nu} = 3030$, 2957, 1726, 1644, 1452, 1256, 1117 cm^{-1}; ^1H NMR (500.1 MHz, $CDCl_3$): $\delta = 2.52$ (1H, dd, $^2J = 12.1$ Hz, $^3J = 9.1$ Hz, CH), 2.69 (1H, dd, $^2J = 12.1$ Hz, $^3J = 5.1$ Hz, CH), 3.79 (3H, s, OMe), 3.95–4.02 (1H, m, CH), 4.29 (1H, dd, $^2J = 11.2$ Hz, $^3J = 8.2$ Hz, CH), 4.36 (1H, dd, $^2J = 11.2$ Hz, $^3J = 5.2$ Hz, CH), 5.34 (1H, s, CH), 6.87 (1H, t, $^3J = 6.9$ Hz, CH), 6.93 (2H, d, $^3J = 6.9$ Hz, 2 CH), 7.09 (1H, s, CH), 7.21 (2H, t, $^3J = 6.9$ Hz, 2 CH), 7.34 (1H, t, $^3J = 7.2$ Hz, CH), 7.43 (2H, t, $^3J = 7.3$ Hz, 2 CH), 7.66 (2H, d, $^3J = 7.3$ Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 36.6$ (CH_2), 54.3 (OMe), 68.8 (CH_2), 81.4 (CH), 95.2 (CH), 114.3 (2 CH), 120.7 (CH), 123.8 (C), 127.1 (CH), 128.8 (2 CH), 129.7 (2 CH), 130.1 (2 CH), 133.1 (C), 145.1 (CH), 147.4 (C), 160.3 (C), 168.9 (C) ppm; EI-MS (70 eV): *m*/*z* (%) = 336 (M^+, 1), 277 (11), 171 (52), 107 (69), 81 (83), 77 (100), 54 (32).

Methyl 6-benzylidene-2-(isopropoxymethyl)-3,6-dihydro-2*H*-pyran-4-carboxylate (4d, $C_{18}H_{22}O_4$) The crude product was purified by column chromatography (SiO_2, hexane/EtOAc 10/1, $R_f = 0.21$) affording 0.27 g (90%) of **4d**. Yellow oil; IR (KBr): $\bar{\nu} = 3038$, 3012, 2958, 1727, 1639, 1542, 1326, 1118 cm^{-1}; ^1H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.21$ (6H, d, $^3J = 6.7$ Hz, 2 Me), 2.45 (1H, dd, $^2J = 11.1$ Hz, $^3J = 7.7$ Hz, CH), 2.67 (1H, dd, $^2J = 11.1$ Hz, $^3J = 5.1$ Hz, CH), 3.61 (3H, s, OMe), 3.70 (1H, dd, $^2J = 11.3$ Hz, $^3J = 8.0$ Hz, CH), 3.84 (1H, dd, $^2J = 11.3$ Hz, $^3J = 5.0$ Hz, CH), 3.90–3.95 (1H, m, CH), 4.02–4.07 (1H, m, CH), 5.23 (1H, s, CH), 7.20 (1H, s, CH), 7.34 (1H, t, $^3J = 6.9$ Hz, CH), 7.42 (2H, t, $^3J = 6.9$ Hz, 2 CH), 7.59 (2H, d, $^3J = 6.9$ Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 21.5$ (2 Me), 36.1 (CH_2), 54.9 (OMe), 69.2 (CH_2), 74.1 (CH), 83.6 (CH), 89.5 (CH), 123.2 (CH), 126.5 (CH), 128.9 (2 CH), 130.8 (2 CH), 133.4 (C), 144.7 (CH), 147.8 (C), 168.2 (C) ppm; EI-MS (70 eV): *m*/*z* (%) = 302 (M^+, 3), 250 (8), 229 (43), 171 (68), 81 (85), 77 (100).

Methyl 2-benzylidene-4a,5,6,7,8,8a-hexahydro-2*H*-chromene-4-carboxylate (4e, $C_{18}H_{20}O_3$) The crude product was purified by column chromatography (SiO_2, hexane/EtOAc 11/1, $R_f = 0.30$) affording 0.20 g (72%) of **4e**. Colorless solid; IR (KBr): $\bar{\nu} = 3033$, 2958, 1725, 1624, 1423, 1238, 1077 cm^{-1}; ^1H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.47$–2.05 (8H, m, 4 CH_2), 2.83–2.88 (1H, m, CH), 3.35–3.40 (1H, m, CH), 3.72 (3H, s, OMe), 5.31 (1H, s, CH), 7.16 (1H, s, CH), 7.32 (1H, t, $^3J = 7.8$ Hz, CH), 7.41 (2H, t, $^3J = 7.8$ Hz), 7.67 (2H, d, $^3J = 7.7$ Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 28.1$ (CH_2), 29.4 (CH_2), 32.7 (CH_2), 34.2 (CH_2), 40.4 (CH), 54.4 (OMe), 81.9 (CH), 91.8 (CH), 127.2 (CH), 129.8 (2 CH), 130.9 (2 CH), 133.5 (C), 135.2 (C), 144.6 (CH), 147.1 (C), 167.0 (C) ppm; EI-MS (70 eV): *m*/*z* (%) = 284 (M^+, 2), 225 (11), 149 (47), 135 (87), 91 (39), 77 (100).

Methyl 6-benzylidene-3-phenyl-3,6-dihydro-2*H*-pyran-4-carboxylate (4f, $C_{20}H_{18}O_3$) The crude product was purified by column chromatography (SiO_2, hexane/EtOAc 8/1, $R_f = 0.27$) affording 0.26 g (85%) of **4f**. Colorless oil; IR (KBr): $\bar{\nu} = 3021$, 2981, 1726, 1632, 1482, 1251, 1092 cm^{-1}; ^1H NMR (500.1 MHz, $CDCl_3$): $\delta = 3.63$ (3H, s, OMe), 4.13–4.18 (1H, m, CH), 4.66 (1H, dd, $^2J = 11.9$ Hz, $^3J = 9.1$ Hz, CH), 4.80 (1H, dd, $^2J = 11.9$ Hz, $^3J = 6.0$ Hz, CH), 5.25 (1H, s, CH), 7.17 (1H, s, CH), 7.23 (2H, d, $^3J = 7.6$ Hz, 2 CH), 7.27 (1H, t, $^3J = 7.5$ Hz, CH), 7.31 (2H, t, $^3J = 7.5$ Hz, 2 CH), 7.36 (1H, t, $^3J = 7.8$ Hz, CH), 7.43 (2H, t, $^3J = 7.8$ Hz, 2 CH), 7.66 (2H, d, $^3J = 7.9$ Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 47.1$ (CH), 54.1 (OMe), 78.7 (CH_2), 95.1 (CH), 126.1 (CH), 127.0 (CH), 128.2 (2 CH), 128.8 (2 CH), 129.4 (2 CH), 130.1 (2 CH), 133.1 (C), 142.3 (C), 144.6 (CH), 145.8 (C), 148.3 (C), 170.5 (C) ppm; EI-MS (70 eV): *m*/*z* (%) = 306 (M^+, 2), 247 (10), 171 (47), 91 (38), 81 (86), 77 (100).

Methyl 6-benzylidene-3-(4-chlorophenyl)-3,6-dihydro-2*H*-pyran-4-carboxylate (4g, $C_{20}H_{17}ClO_3$) The crude product was purified by column chromatography (SiO_2, hexane/EtOAc 7/1, $R_f = 0.34$) affording 0.30 g (87%) of **4g**. Colorless oil; IR (KBr): $\bar{\nu} = 3052$, 2972, 1730, 1648, 1522, 1267, 1076 cm^{-1}; ^1H NMR (500.1 MHz, $CDCl_3$): $\delta = 3.74$ (3H, s, OMe), 4.05–4.11 (1H, m, CH), 4.60 (1H, dd, $^2J = 12.6$ Hz, $^3J = 9.0$ Hz, CH), 4.81 (1H, dd, $^2J = 12.6$ Hz, $^3J = 5.2$ Hz, CH), 5.34 (1H, s, CH), 7.21 (1H, s, CH), 7.35 (1H, t, $^3J = 7.1$ Hz, CH), 7.40 (2H, d, $^3J = 7.1$ Hz, 2 CH), 7.45 (2H, d, $^3J = 7.8$ Hz, 2 CH), 7.52 (2H, t, $^3J = 7.8$ Hz, CH), 7.62 (2H, d, $^3J = 7.2$ Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 43.1$ (CH), 54.1 (OMe), 76.1 (CH_2), 93.2 (CH), 126.9 (CH), 128.1 (2 CH), 128.9 (2 CH), 129.6 (2 CH), 129.9 (2 CH), 132.2 (C), 134.1 (C), 139.1 (C), 142.3 (C), 145.2 (CH), 145.9 (C), 170.9 (C) ppm; EI-MS (70 eV): *m*/*z* (%) = 340 (M^+, 1), 281 (12), 247 (17), 171 (60), 126 (41), 81 (83), 77 (100).

Methyl 6-benzylidene-3-(*p*-tolyl)-3,6-dihydro-2*H*-pyran-4-carboxylate (4h, $C_{21}H_{20}O_3$) The crude product was purified by column chromatography (SiO_2, hexane/EtOAc 9/1, $R_f = 0.25$) affording 0.21 g (67%) of **4h**. Colorless oil; IR (KBr): $\bar{\nu} = 3041$, 2971, 2942, 1726, 1670, 1482,

1252, 1075 cm^{-1}; ^1H NMR (500.1 MHz, $CDCl_3$): $\delta = 2.31$ (3H, s, Me), 3.66 (3H, s, OMe), 3.92–3.98 (1H, m, CH), 4.61 (1H, dd, $^2J = 12.5$ Hz, $^3J = 8.2$ Hz, CH), 4.80 (1H, dd, $^2J = 12.5$ Hz, $^3J = 4.9$ Hz, CH), 5.25 (1H, s, CH), 7.02 (2H, d, $^3J = 7.4$ Hz, 2 CH), 7.17 (2H, d, $^3J = 7.4$ Hz, 2 CH), 7.24 (1H, s, CH), 7.33 (1H, t, $^3J = 7.3$ Hz, CH), 7.44 (2H, d, $^3J = 7.3$ Hz, 2 CH), 7.65 (2H, d, $^3J = 7.1$ Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 22.7$ (CH_3), 40.9 (CH), 55.6 (OMe), 79.8 (CH_2), 89.2 (CH), 126.2 (2 CH), 126.8 (CH), 128.1 (2 CH), 129.8 (2 CH), 130.3 (2 CH), 134.4 (C), 136.1 (C), 137.2 (C), 143.9 (C), 145.1 (CH), 146.3 (CH), 170.1(C) ppm; EI-MS (70 eV): *m/z* (%) = 320 (M^+, 3), 290 (9), 261 (21), 171 (61), 128 (49), 81 (87), 77 (100).

Methyl 6-(4-methylbenzylidene)-2-methyl-3,6-dihydro-2*H*-pyran-4-carboxylate (4i, $C_{16}H_{18}O_3$) The crude product was purified by column chromatography (SiO_2, hexane/EtOAc 8/1, $R_f = 0.32$) affording 0.23 g (90%) of **4i**. Yellow oil; IR (KBr): $\bar{\nu} = 3019$, 2942, 1727, 1621, 1542, 1466, 1258, 1109 cm^{-1}; ^1H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.30$ (3H, d, $^3J = 5.8$ Hz, Me), 2.34 (3H, s, Me), 2.61 (1H, dd, $^2J = 12.5$ Hz, $^3J = 8.2$ Hz, CH), 2.80 (1H, dd, $^2J = 12.5$ Hz, $^3J = 4.9$ Hz, CH), 3.69 (3H, s, OMe), 3.92–3.98 (1H, m, CH), 5.29 (1H, s, CH), 7.25 (1H, s, CH), 7.41 (2H, d, $^3J = 7.4$ Hz, 2 CH), 7.63 (2H, d, $^3J = 7.4$ Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 22.1$ (Me), 24.7 (Me), 40.9 (CH_2), 55.6 (OMe), 82.8 (CH), 93.2 (CH), 122.9 (CH), 128.2 (2 CH), 129.8 (2 CH), 130.5 (C), 138.1 (C), 144.7 (CH), 145.3 (C), 169.3 (C) ppm; EI-MS (70 eV): *m/z* (%) = 258 (M^+, 3), 243 (8), 213 (21), 185 (51), 81 (83), 77 (100).

Methyl 6-(2-methoxyethylidene)-2-methyl-3,6-dihydro-2*H*-pyran-4-carboxylate (4j, $C_{11}H_{16}O_4$) The crude product was purified by column chromatography (SiO_2, hexane/EtOAc 11/1, $R_f = 0.24$) affording 0.15 g (72%) of **4j**. Colorless oil; IR (KBr): $\bar{\nu} = 3042$, 2972, 1728, 1671, 1523, 1471, 1276, 1092 cm^{-1}; ^1H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.28$ (3H, d, $^3J = 6.2$ Hz, Me), 2.58 (1H, dd, $^2J = 12.0$ Hz, $^3J = 8.5$ Hz, CH), 2.79 (1H, dd, $^2J = 12.0$ Hz, $^3J = 5.1$ Hz, CH), 3.46 (3H, s, OMe), 3.64 (3H, s, OMe), 3.91–3.96 (1H, m, CH), 4.17 (2H, s, CH_2), 5.07 (1H, s, CH), 7.21 (1H, s, CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 23.5$ (Me), 40.8 (CH_2), 54.2 (OMe), 57.1 (OMe), 70.1 (CH_2), 82.3 (CH), 111.8 (CH), 123.1 (C), 145.7 (C), 151.2 (C), 169.1 (C) ppm; EI-MS (70 eV): *m/z* (%) = 212 (M^+, 3), 181 (14), 167 (28), 109 (55), 81 (100).

Ethyl 6-benzylidene-2,2,3,3-tetramethyl-3,6-dihydro-2*H*-pyran-4-carboxylate (4k, $C_{19}H_{24}O_3$) The crude product was purified by column chromatography (SiO_2, hexane/EtOAc 8/1, $R_f = 0.31$) affording 0.21 g (43%) of **4k**. Colorless oil; IR (KBr): $\bar{\nu} = 3035$, 2977, 1730, 1601, 1476, 1245, 1187 cm^{-1}; ^1H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.27$ (3H, d, $^3J = 5.7$ Hz, Me), 1.36 (6H, s, 2 Me), 1.45 (6H, s, 2 Me), 4.21 (2H, q, $^3J = 5.7$ Hz, OCH_2), 5.45 (1H, s, CH), 7.05 (1H, s, CH), 7.33 (1H, t, $^3J = 7.8$ Hz, CH), 7.43 (2H, t, $^3J = 7.8$ Hz, 2 CH), 7.61 (2H, d, $^3J = 7.8$ Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 13.9$ (Me), 21.8 (2 Me), 30.1 (2 Me), 53.2 (C), 62.2 (OCH_2), 90.5 (C), 93.1 (CH), 126.4 (CH), 128.9 (2 CH), 129.7 (2 CH), 133.6 (C), 143.4 (CH), 148.2 (C), 149.5 (C), 168.9 (C) ppm; EI-MS (70 eV): *m/z* (%) = 300 (M^+, 1), 255 (5), 225 (32), 199 (48), 109 (87), 77 (100).

Ethyl 6-benzylidene-2-methyl-3,6-dihydro-2*H*-pyran-4-carboxylate (4l, $C_{16}H_{18}O_3$) The crude product was purified by column chromatography (SiO_2, hexane/EtOAc 10/1, $R_f = 0.36$) affording 0.21 g (83%) of **4l**. Colorless oil; IR (KBr): $\bar{\nu} = 3015$, 2951, 1727, 1611, 1547, 1312, 1276, 1032 cm^{-1}; ^1H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.25$ (3H, t, $^3J = 5.6$ Hz, Me), 1.34 (3H, d, $^3J = 5.9$ Hz, Me), 2.53 (1H, dd, $^2J = 12.1$ Hz, $^3J = 9.1$ Hz, CH), 2.74 (1H, dd, $^2J = 12.1$ Hz, $^3J = 5.0$ Hz, CH), 3.97–4.03 (1H, m, CH), 4.12 (2H, q, $^3J = 5.6$ Hz, OCH_2), 5.32 (1H, s, CH), 7.19 (1H, s, CH), 7.35 (1H, t, $^3J = 7.3$ Hz, CH), 7.40 (2H, t, $^3J = 7.3$ Hz, 2 CH), 7.66 (2H, d, $^3J = 7.3$ Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 15.8$ (Me), 23.3 (Me), 40.6 (CH_2), 63.8 (OCH_2), 83.2 (CH), 90.6 (CH), 122.2 (C), 126.9 (CH), 128.7 (2 CH), 129.5 (2 CH), 134.2 (C), 145.7 (CH), 147.6 (C), 170.5 (C) ppm; EI-MS (70 eV): *m/z* (%) = 258 (M^+, 3), 243 (9), 215 (15), 171 (63), 91 (43), 81 (85), 77 (100).

***tert*-Butyl 6-benzylidene-2-methyl-3,6-dihydro-2*H*-pyran-4-carboxylate (4m, $C_{18}H_{22}O_3$)** The crude product was purified by column chromatography (SiO_2, hexane/EtOAc 8/1, $R_f = 0.19$) affording 0.24 g (85%) of **4m**. Pale yellow oil; IR (KBr): $\bar{\nu} = 3022$, 2941, 1729, 1614, 1547, 1287, 1211, 1098 cm^{-1}; ^1H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.30$ (3H, d, $^3J = 5.9$ Hz, Me), 1.52 (9H, s, 3 Me), 2.56 (1H, dd, $^2J = 11.8$ Hz, $^3J = 9.4$ Hz, CH), 2.73 (1H, dd, $^2J = 11.8$ Hz, $^3J = 5.3$ Hz, CH), 4.08–4.14 (1H, m, CH), 5.30 (1H, s, CH), 7.16 (1H, s, CH), 7.34 (1H, t, $^3J = 7.0$ Hz, CH), 7.43 (2H, t, $^3J = 7.0$ Hz, 2 CH), 7.65 (2H, d, $^3J = 7.0$ Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 23.1$ (Me), 30.3 (3 Me), 39.3 (CH_2), 80.2 (C), 82.7 (CH), 90.4 (CH), 122.9 (C), 126.3 (CH), 128.2 (2 CH), 130.1 (2 CH), 134.8 (C), 145.1 (CH), 148.7 (C), 170.1 (C) ppm; MS: *m/z* (%) = 286 (M^+, 4), 271 (9), 215 (18), 125 (60), 91 (32), 81 (88), 77 (100), 58 (90).

Ethyl 6-benzylidene-2,5-dimethyl-3,6-dihydro-2*H*-pyran-4-carboxylate (4n, $C_{17}H_{20}O_3$) The crude product was purified by column chromatography (SiO_2, hexane/EtOAc 12/1, $R_f = 0.24$) affording 0.12 g (46%) of **4n**. Colorless solid; m.p.: 88–90 °C; IR (KBr): $\bar{\nu} = 3031$, 2943, 1724, 1608, 1550, 1302, 1276, 1085 cm^{-1}; ^1H NMR (500.1 MHz, $CDCl_3$): $\delta = 1.20$ (3H, t, $^3J = 5.8$ Hz, Me), 1.29 (3H, d,

^3J = 5.6 Hz, Me), 2.62 (1H, dd, ^2J = 11.8 Hz, ^3J = 9.9 Hz, CH), 2.75 (1H, dd, ^2J = 11.8 Hz, ^3J = 5.8 Hz, CH), 2.83 (3H, s, Me), 3.89–3.94 (1H, m, 1 CH), 4.28 (2H, q, ^3J = 5.8 Hz, CH_2), 5.30 (1H, s, CH), 7.35 (2H, t, ^3J = 7.4 Hz, 2 CH), 7.43 (1H, t, ^3J = 7.4 Hz, CH), 7.61 (2H, d, ^3J = 7.4 Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 10.3 (Me), 13.9 (Me), 24.2 (Me), 38.2 (CH_2), 64.7 (CH_2), 81.1 (CH), 93.5 (CH), 126.7 (CH), 128.2 (2 CH), 129.1 (2 CH), 130.3 (C), 133.8 (C), 151.1 (C), 159.3 (C), 169.2 (C) ppm; MS: *m/z* (%) = 272 (M^+, 1), 257 (17), 229 (9), 215 (34), 171 (66), 81 (85), 77 (100).

Ethyl 6-benzylidene-2-methyl-5-phenyl-3,6-dihydro-2*H*-pyran-4-carboxylate (4o, $C_{22}H_{22}O_3$) The crude product was purified by column chromatography (SiO_2, hexane/EtOAc 8/1, R_f = 0.28) affording 0.19 g (58%) of **4o**. Pale yellow solid; m.p.: 73–75 °C; IR (KBr): $\bar{\nu}$ = 3042, 2951, 1739, 1604, 1554, 1311, 1256, 1051 cm^{-1}; ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 1.14 (3H, t, ^3J = 5.5 Hz, Me), 1.31 (3H, d, ^3J = 5.4 Hz, Me), 2.54 (1H, dd, ^2J = 11.5 Hz, ^3J = 9.2 Hz, CH), 2.66 (1H, dd, ^2J = 11.5 Hz, ^3J = 5.2 Hz, CH), 3.97–4.04 (1H, m, 1 CH), 4.31 (2H, q, ^3J = 5.5 Hz, CH_2), 5.36 (1H, s, CH), 7.20 (2H, d, ^3J = 7.6 Hz, 2 CH), 7.30–7.46 (6H, m, 6 CH), 7.64 (2H, d, ^3J = 7.4 Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 15.9 (Me), 25.1 (Me), 40.5 (CH_2), 64.1 (CH_2), 83.4 (CH), 93.2 (CH), 116.8 (C), 126.3 (CH), 126.8 (CH), 128.5 (2 CH), 128.9 (2 CH), 129.4 (2 CH), 130.1 (2 CH), 133.1 (C), 134.2 (C), 149.3 (C), 157.4 (C), 169.4 (C) ppm; MS: *m/z* (%) = 334 (M^+, 2), 319 (6), 291 (15), 247 (68), 157 (42), 81 (79), 77 (100).

6-Benzylidene-2-methyl-3,6-dihydro-2*H*-pyran-4-carboxamide (4p, $C_{14}H_{15}NO_2$) The crude product was purified by column chromatography (SiO_2, hexane/EtOAc 4/1, R_f = 0.28) affording 0.16 g (69%) of **4p**. Pale yellow solid; m.p.: 84–86 °C; IR (KBr): $\bar{\nu}$ = 3016, 2955, 1637, 1603, 1531, 1308, 1278, 1068 cm^{-1}; ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 1.30 (3H, d, ^3J = 5.6 Hz, Me), 2.58–2.69 (2H, m, 2 CH), 3.93–3.98 (1H, m, CH), 5.32 (1H, s, CH), 6.83 (2H, br s, NH_2), 7.18 (1H, s, CH), 7.37 (2H, t, ^3J = 7.6 Hz, 2 CH), 7.45 (1H, t, ^3J = 7.6 Hz, CH), 7.66 (2H, t, ^3J = 7.6 Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 24.6 (Me), 41.1 (CH_2), 83.3 (CH), 92.7 (CH), 125.8 (CH), 126.7 (CH), 127.2 (2 CH), 129.1 (2 CH), 134.1 (C), 145.7 (CH), 147.1 (C), 173.2 (C) ppm; MS: *m/z* (%) = 229 (M^+, 1), 214 (11), 199 (56), 171 (38), 81 (82), 77 (100).

Ethyl 6-(4-methoxybenzylidene)-2-methyl-3,6-dihydro-2*H*-pyran-4-carboxylate (4q, $C_{17}H_{20}O_4$) The crude product was purified by column chromatography (SiO_2, hexane/EtOAc 8/1, R_f = 0.22) affording 0.26 g (92%) of **4q**. Pale yellow oil; IR (KBr): $\bar{\nu}$ = 3042, 2989, 1724, 1603, 1534, 1264, 1187, 1034 cm^{-1}; ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 1.18 (3H, t, ^3J = 5.7 Hz, Me), 1.28 (3H, d, ^3J = 5.9 Hz, Me), 2.62 (1H, dd, ^2J = 12.8 Hz, ^3J = 5.2 Hz, CH), 2.66 (1H, dd, ^2J = 12.8 Hz, ^3J = 10.0 Hz, CH), 3.90 (3H, s, OMe), 3.95–4.01 (1H, m, 1 CH), 4.27 (2H, q, ^3J = 5.7 Hz, CH_2), 5.30 (1H, s, CH), 7.13 (2H, d, ^3J = 7.8 Hz, 2 CH), 7.19 (1H, s, CH), 7.68 (2H, d, ^3J = 7.8 Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 15.3 (Me), 24.7 (Me), 40.2 (CH_2), 58.3 (OMe), 64.6 (CH_2), 81.6 (CH), 93.8 (CH), 114.5 (2 CH), 122.7 (C), 125.8 (C), 133.2 (2 CH), 144.1 (CH), 160.1 (C), 169.2 (C) ppm; MS: *m/z* (%) = 288 (M^+, 2), 272 (11), 167 (53), 153 (31), 107 (100), 81 (72), 77 (89).

Ethyl 2-methyl-6-[3-(trifluoromethyl)benzylidene]-3,6-dihydro-2*H*-pyran-4-carboxylate (4r, $C_{17}H_{17}F_3O_3$) The crude product was purified by column chromatography (SiO_2, hexane/EtOAc 3/1, R_f = 0.46) affording 0.11 g (34%) of **4r**. Colorless solid; m.p.: 91–93 °C; IR (KBr): $\bar{\nu}$ = 3043, 2989, 1730, 1537, 1521, 1276, 1240, 1082 cm^{-1}; ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 1.13 (3H, t, ^3J = 5.6 Hz, Me), 1.31 (3H, d, ^3J = 5.6 Hz, Me), 2.58 (1H, dd, ^2J = 12.3 Hz, ^3J = 5.5 Hz, CH), 2.74 (1H, dd, ^2J = 12.3 Hz, ^3J = 9.6 Hz, CH), 3.93–4.00 (1H, m, 1 CH), 4.33 (2H, q, ^3J = 5.6 Hz, CH_2), 5.48 (1H, s, CH), 7.17 (1H, t, ^3J = 7.9 Hz, CH), 7.23 (1H, s, CH), 7.41 (1H, d, ^3J = 7.9 Hz, CH), 7.40 (1H, s, CH), 7.53 (1H, s, CH), 7.70 (1H, d, ^3J = 7.9 Hz, CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 15.5 (Me), 22.9 (Me), 40.9 (CH_2), 65.2 (CH_2), 81.9 (CH), 93.2 (CH), 121.2 (C), 123.6 (CH, q, ^3J = 4.8 Hz), 124.5 (CH, q, ^3J = 4.8 Hz), 126.2 (CF_3, q, ^1J = 270.2 Hz), 127.1 (CH), 131.8 (CH), 132.2 (C, q, ^2J = 32.9 Hz), 136.1 (C), 144.1 (CH), 146.8 (C), 170.3 (C) ppm; MS: *m/z* (%) = 326 (M^+, 1), 311 (7), 283 (21), 239 (52), 159 (32), 81 (100).

Ethyl 2-methyl-6-pentylidene-3,6-dihydro-2*H*-pyran-4-carboxylate (4s, $C_{14}H_{22}O_3$) The crude product was purified by column chromatography (SiO_2, hexane/EtOAc 10/1, R_f = 0.36) affording 0.15 g (63%) of **4s**. Colorless oil; IR (KBr): $\bar{\nu}$ = 3018, 2968, 1726, 1534, 1282, 1132, 1108 cm^{-1}; ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 0.89 (3H, t, ^3J = 6.2 Hz, Me), 1.14 (3H, t, ^3J = 5.9 Hz, Me), 1.30 (3H, d, ^3J = 5.6 Hz, Me), 1.37–1.54 (4H, m, 2 CH_2), 2.21–2.32 (2H, m, CH_2), 2.67 (1H, dd, ^2J = 12.0 Hz, ^3J = 9.7 Hz, CH), 2.81 (1H, dd, ^2J = 12.0 Hz, ^3J = 5.7 Hz, CH), 3.18 (1H, dd, ^2J = 12.8 Hz, ^3J = 5.2 Hz, CH), 3.89–3.94 (1H, m, CH), 4.25 (2H, q, ^3J = 5.9 Hz, CH), 4.87 (1H, t, ^3J = 5.2 Hz, CH), 7.21 (1H, s, CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 13.7 (Me), 15.2 (Me), 23.6 (Me), 25.1 (CH_2), 28.3 (CH_2), 35.4 (CH_2), 39.8 (CH_2), 64.7 (CH_2), 83.2 (CH), 110.7 (CH), 122.5 (C), 144.1 (CH), 146.9 (C), 169.1 (C) ppm; MS: *m/z* (%) = 238 (M^+, 1), 223 (9), 195 (25), 151 (58), 81 (100), 71 (83).

Acknowledgements We wish to thank for a grant from Islamic Azad University, South Tehran Branch.

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