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Radical bromoallylation of alkynes leading to 1-bromo-1,4-dienes

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ABSTRACT

The full scope (30 examples) of the radical bromoallylation of alkynes using allyl bromides was studied. In this reaction, bromine radical adds to alkynes to form vinyl radicals, which then undergo an S_H2' reaction with allyl bromides to produce good yields of 1-bromo-1,4-dienes with the liberation of a bromine radical, which creates a radical chain. The sp^2-carbon–bromine bond of the product dienes was further functionalized via cross-coupling and carbonylation reactions.

1. Introduction

Radical-based allylation reactions,[1] which use allyl-heteroatoms, such as allyltins,[2] allylsulfides,[3] and allylsulfones,[4] have found wide applications in organic synthesis, but relatively little attention has been directed to the development of radical allylation by allyl bromides. The original work dealing with the use of allyl bromides in radical reactions dates to Kharasch's report published in 1949,[5] in which 3-trichloromethylpropene was formed via the addition/elimination sequence of bromotrichloromethane with an allyl bromide under photo-irradiation conditions. In 1993, Singleton and co-workers reported a chain type of radical allylation using allyl halides, but the procedure required the use of hexabutylditin as a chain career.[6] In 1999, Tanko and Sadeghipour reported C–H allylation using allyl bromides and a radical initiator, capitalized on the capability of bromine radicals to abstract hydrogen from cumene, isopropanol and the related compounds, in which the resultant radicals undergo an S_H2' reaction with allylic bromides to give high yields of allylated products.[7] Since bromine radicals are capable of adding to C–C multiple bonds reversibly, we initiated our research based on radical bromoallylation of unsaturated compounds, which turned out to be quite useful in synthesizing a variety of bromine-substituted dienes[8–10] In our first report, we described a radical bromoallylation of arylalkynes with allyl and methallyl bromides, which led to 1-bromo-2-aryl-1,4-dienes.[8] Shortly after the report, we noticed that allyl bromides with an electron-withdrawing group at the 2-position served as excellent UMCT reagents[11] and that alkynes need not be restricted to arylalkynes. In the present study, we disclose the full scope of the bromoallylation chemistry of alkynes, which demonstrates that the approach can be used to synthesize a variety of 1-bromo-substituted 1,4-dienes.[12] Since the 1,4-diene motif is frequently found in a variety of biologically active compounds,[13,14] and thus far a variety of methods are available for the preparation,[15] the present method is unique because the vinyl-bromide moiety of prepared 1-bromo-1,4-dienes can be functionalized further by cross-coupling and carbonylation reactions that lead to a variety of 1-substituted 1,4-dienes (Scheme 1).

2. Results and discussion

Initially, we examined the reaction of phenylacetylene (**1a**) with simple allyl bromide (**2a**) as a model (Table 1). Essentially, no reaction took place when a mixture of **1a** (1.0 mmol), **2a** (2.0 mmol), and V-65 (2,2′-azobis(2,4-dimethylvaleronitrile), 20 mol%) as a radical initiator, was treated at 60 °C for 6 h without a solvent (entry 1). However, the use of a large excess amount (58 equiv) of **2a** gave 1-bromo-1,4-diene (**3aa**) in an 80% yield as a stereoisomeric mixture (*E*/*Z*=23/77) (entry 2). The use of AIBN as a radical initiator at 80 °C was equally effective (entry 3). In these experiments, a careful examination of NMR showed that no regioisomer was formed. Since a large excess of **2a** was necessary to compensate for the modest reactivity of vinyl radicals towards **2a**, which are classified as nucleophilic radicals,[16] we then examined ethyl 2-(bromomethyl)acrylate (**2b**). The reaction of **1a** with a twofold

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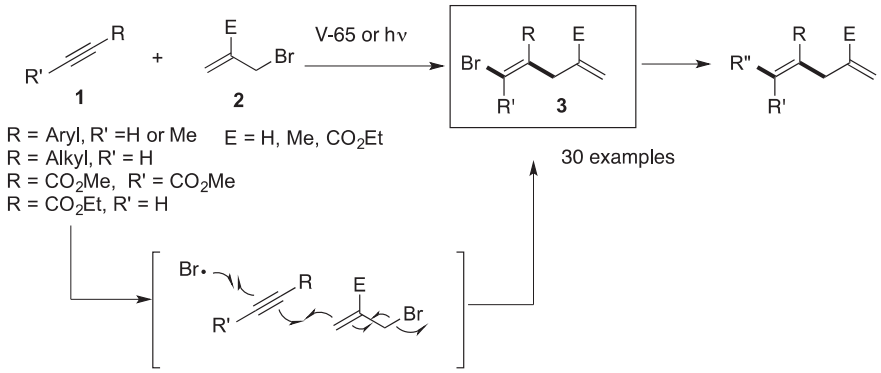
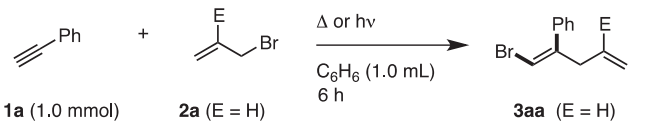
0040-4020/



Scheme 1. Concept: synthesis of substituted 1,4-dienes by radical bromoallylation of alkynes.

Table 1
Reaction conditions for the radical bromoallylation of phenylacetylene (**1a**) with **2a** and **2b**



1a (1.0 mmol) **2a** (E = H) **2b** (E = CO_2Et) **3aa** (E = H) **3ab** (E = CO_2Et)

Entry	Allyl bromide (equiv)	Conditions	Product	Yield (%)[a]	*EIZ*[b]
1	**2a** (2)	V-65 (20 mol %), 60 °C	**3aa**	Trace	—
2[c]	**2a** (58)	V-65 (20 mol %), 60 °C	**3aa**	80[d]	23/77
3[c]	**2a** (58)	AIBN (20 mol %), 80 °C	**3aa**	80[d]	15/85
4	**2b** (2)	AIBN (20 mol %), 80 °C	**3ab**	59	16/84
5	**2b** (2)	Solarbox (Xe, 350 W/m^2)	**3ab**	63	16/84
6	**2b** (4)	Solarbox (Xe, 350 W/m^2)	**3ab**	71	16/84
7[e]	**2b** (4)	Solarbox (Xe, 350 W/m^2)	**3ab**	83[d]	22/78

[a] NMR yield using CH_2Br_2 as an internal standard.
[b] Determined by ^{1}H NMR analysis of the crude reaction mixture.
[c] Without C_6H_6.
[d] Isolated yield after column chromatography on SiO_2.
[e] 12 h.

excess of **2b** delivered the expected bromoallylation product **3ab** in a 59% yield (entry 4). Photoirradiation conditions using a Solarbox equipped with a xenon lamp slightly improved the yield (entry 5). The use of a fourfold excess of **2b** combined with a longer reaction time (12 h) improved the yield of **3ab** to 83% (entry 7). The difference in reactivity observed between **2b** and **2a** is understandable considering the nucleophilic nature of vinyl radicals.

With the optimized conditions in hand, we then explored the scope and limitations of the present bromoallylation reaction, using various alkynes **1a**–**t** and allyl bromides **2a**–**c**, in which thermally initiated conditions (Method A: V-65 (20 mol %), 60 °C, 6 h) were used for **2a** and **2c**, whereas photo-initiation conditions (Method B: Solarbox (Xe, 350 W/m^2), 12 h) were used for **2b** (Table 2). The reaction of arylacetylenes **1a**–**1m** with allyl bromide (**2a**) (method A) gave the corresponding products **3aa**–**3ma** in good yields (entries 1–6, and 8–14). With the exception of 1-naphtylacetylene (**1k**), which gave only an *E*-isomer (entry 12), *Z*-isomers were preferred. The reaction of **1a** with methallyl bromide (**2c**) gave **3ac** in a 95% yield (entry 7). The reaction of electron-deficient alkynes such as ethyl propiolate (**1n**) and dimethyl acetylenedicarboxylate (**1o**) with **2a** gave the corresponding 1,4-dienes **3na** and **3oa** in 86 and 49% yields, respectively (entries 15 and 16).

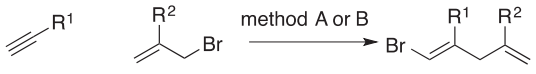
The bromoallylation of arylacetylenes **1a**–**1m** with ethyl 2-(bromomethyl)acrylate (**2b**) under photo-irradiation conditions (method B) worked quite well to give good yields of the corresponding 1-bromo-2-aryl-4-ethoxycarbonyl-1,4-butadienes (entries 17–23). In the reaction of an internal alkyne, 1-phenylpropyne (**1p**), with **2b** proceeded regioselectively to give the bromoallylated product **3pb** in a 57% yield, in which bromine was incorporated into methyl-substituted carbon (entry 24). Compared with arylalkynes, the reactivity of 1-octyne **1q** toward simple allyl bromide **2a** was low. However, the reaction with **2b** took place smoothly to give **3qb** in an 83% yield (entry 25). The reaction of TBS-protected alkyne **1r** with **2b** gave the expected bromo-substituted 1,4-diene **3rb** and the desilylated product 3**rb**′ in 59 and 19% yields, respectively (entry 26). This desilylation reaction was entirely suppressed by the addition of Na_3PO_4 as an HBr scavenger, which gave **3rb** in a 75% yield (entry 27). On the other hand, the reaction of 1-ethynyl-1-cyclohexene (**1s**) with **2b** was sluggish, which gave a 34% yield of product **3sb** with 43% of **1s** remained unreacted (entry 28). The reaction of cyclopropyl acetylene (**1t**) with **2b** gave an 85% yield of **3tb**, in which the cyclopropyl group remained in the product (entry 29). No occurrence of the ring-opening may be attributed to the σ-character of the vinyl radical, which would not interact well with the adjacent cyclopropane ring.

The present alkyne-bromoallylation combines well with radical cascades. The reaction of enyne **4** and **2b** gave cyclopentane **5** bearing bromomethylene and 3-butenyl substituents in the adjacent carbons of the cyclopentane ring in a 76% yield (Scheme 2). The product **5** would be formed through (i) addition of the bromine radical to the alkyne terminus, (ii) 5-*exo* cyclization, (iii) an addition to allyl bromide **2b**, and (iv) β-fragmentation of the bromine radical.

We employed both thermal and photo initiation for this study. As for the thermal initiation with V-65 (Method A), a cyano alkyl radical was generated by the decomposition of V-65, and added to the allyl bromide in an S_H2' manner to form a bromine radical, which initiated the reaction by addition to the C–C triple bond. In the reaction of 1-octyne (**1q**) with **2b** under photo-irradiation conditions (Method B), we detected a small amount of the coupling dimer **6** that was derived from **2b** (Scheme 3). This suggested that in the initiation step, a photo-induced homolysis of the C–Br bond of **2b** would take place to give allyl radical and bromine radical, in which the former dimerizes[17] and the latter acts as a radical initiator via addition to the C–C triple bond. The addition of 10 mol % of a 2,2,6,6-tetramethylpiperidine 1-oxyl free radical (TEMPO) to the reaction completely suppressed the bromoallylation of **1q**, and an allyl TEMPO **7** was isolated. These results support the initiation mechanism based on the photo-induced homolysis of **2b** to generate a bromine radical.

A proposed mechanism for the bromoallylation of alkynes is illustrated in Scheme 4. Irrespective of thermal/V-65 initiation or photo-irradiation, bromine radicals are formed and add to the

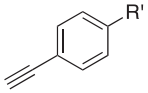
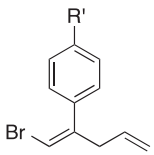
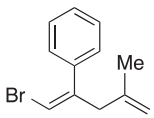
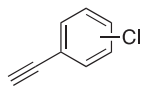
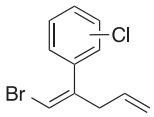
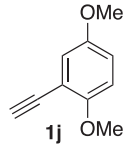
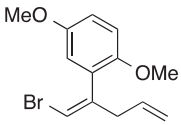
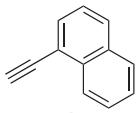
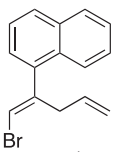
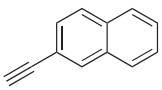
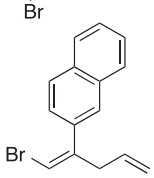
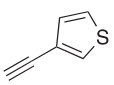
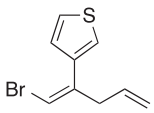
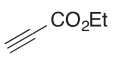
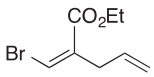
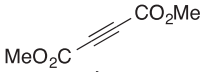
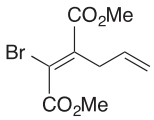
Table 2
Bromoallylation of alkynes leading to 1-bromo-1,4-dienes

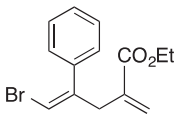
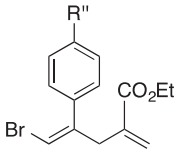
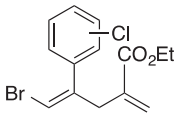
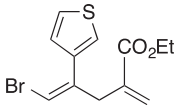
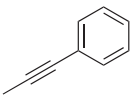
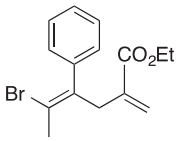
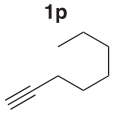
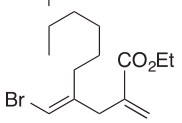
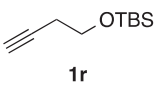
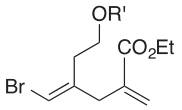
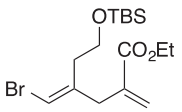
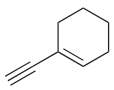
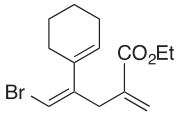
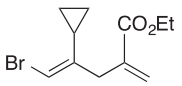


1 **2a** (R^2 = H) **2b** (R^2 = CO_2Et) **2c** (R^2 = Me) **3**

Method A for alkynes **2a** and **2c**: **1** (1.0 mmol), **2** (5 mL), V-65 (20 mol%), 60 °C, 6 h

Method B for **2b**: **1** (1.0 mmol), **2** (4.0 equiv), C_6H_6 (1.0 M),Solarbox (Xe, 350 W/m^2, Pyrex), 12 h

entry	1	3	yield (%)[a]	E/Z[b]
				
1	**1a** (R' = H)		**3aa** (80)	23/77
2	**1b** (R' = Me)		**3ba** (80)	16/84
3	**1c** (R' = OMe)		**3ca** (70)	23/77
4	**1d** (R' = CO_2Et)		**3da** (93)	35/65
5	**1e** (R' = Ac)		**3ea** (94)	27/73
6	**1f** (R' = NO_2)		**3fa** (60)	4/96
7	**1a**		**3ac** (95)	10/90
				
8	**1g** (*o*-Cl)		**3ga** (97)	6/94
9	**1h** (*m*-Cl)		**3ha** (85)	14/86
10	**1i** (*p*-Cl)		**3ia** (81)	18/82
11	 **1j**		**3ja** (90)	6/94
12	 **1k**		**3ka** (83)	99/1
13	 **1l**		**3la** (87)	26/74
14	 **1m**		**3ma** (77)	58/42
15	 **1n**		**3na** (86)	26/74
16	 **1o**		**3oa** (49)	34/66

entry	1	3	yield (%)[a]	E/Z[b]
17	**1a**		**3ab** (83)	22/78
18	**1c** (R'' = OMe)		**3cb** (71)	10/90
19	**1d** (R'' = CO_2Et)		**3db** (73)	20/80
20	**1g** (*o*-Cl)		**3gb** (83)	7/93
21	**1h** (*m*-Cl)		**3hb** (80)	13/87
22	**1i** (*p*-Cl)		**3ib** (82)	13/87
23	**1m**		**3mb** (73)	24/76
24	 **1p**		**3pb** (57)	18/82
25	 **1q**		**3qb** (83)	93/7
26[c]	 **1r**		**3rb** (59) (R' = TBS) **3rb'** (19) (R' = H)	95/5 96/4
27[c, d]	**1r**		**3rb** (75)	91/9
28	 **1s**		**3sb** (34)	24/76
29	 **1t**		**3tb** (85)	12/88

[a] Isolated yield after flash column chromatography on SiO_2 and/or preparative HPLC using $CHCl_3$ as an eluent. [b] The *E/Z* ratio was determined via ^{1}H-NMR analysis of the crude reaction mixture. [c] 18 h. [d] Na_3PO_4 (0.2 equiv).

alkyne terminus to give bromine-containing vinyl radical **A**. The vinyl radical then reacts with **2** to produce radical intermediate **B**, which undergoes β-fission to give 1-bromo-1,4-diene **3** and a bromine radical to sustain the radical chain.[18] Products via *trans*-allylbromination are generally preferred. As we discussed in our preliminary report, this can be explained by the less hindered site attack of allyl bromide towards the vinyl radicals.[8] An exception was the case of 1-naphtylacetylene (**1k**), which gave *E*-isomer of

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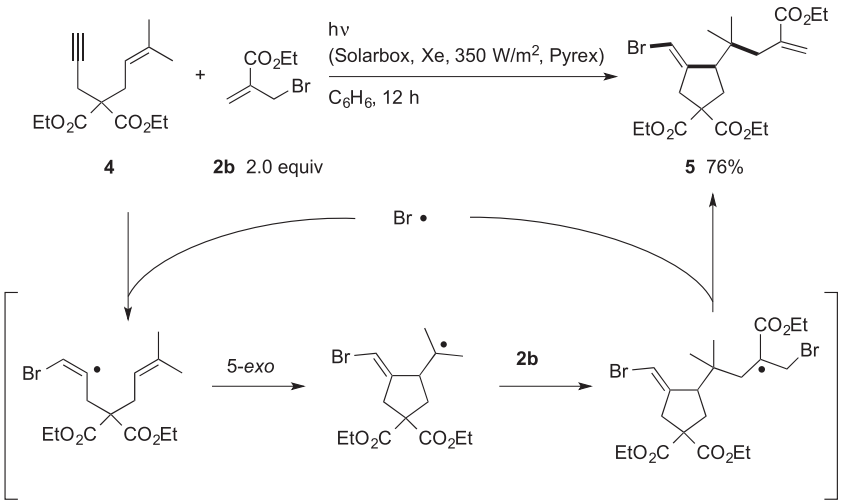
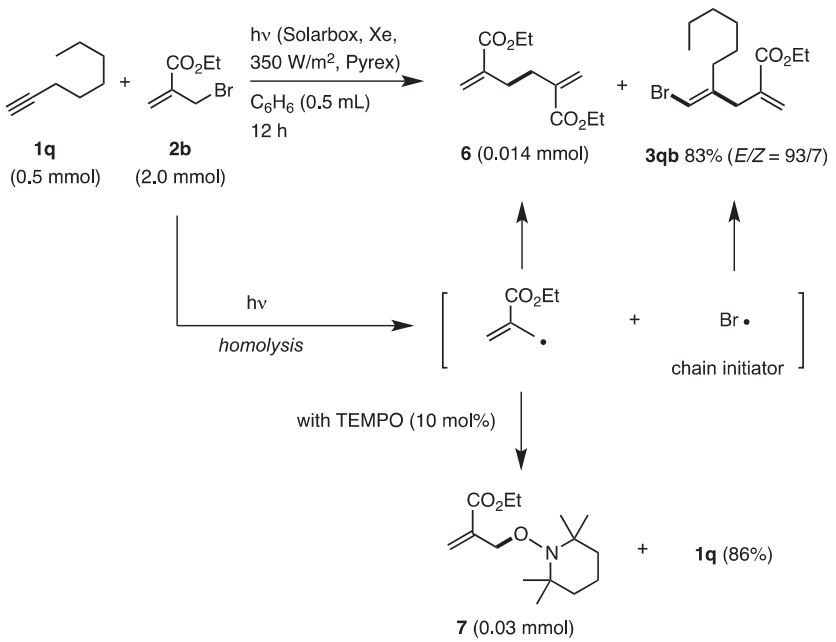


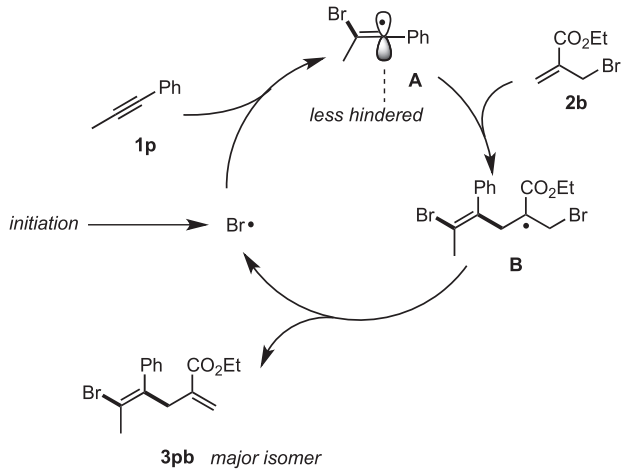
Scheme 2. Cyclizative cascade bromoallylation.



Scheme 3. Radical initiation mechanism under photo-irradiation condition B.

3ka selectively. In this case, the approach of allyl bromide via a similar alignment is difficult, since *peri*-hydrogen would shield the vinyl radical. As the result, *trans* alignment of naphthyl ring and bromine atom would be preferred probably in the transition state where vinyl portion is free of conjugation with the naphthyl ring so as to minimize the steric repulsion.

Since all the diene products **3** involve a vinyl bromide functionality, further chemical transformations to prepare functionalized 1,4-dienes are feasible. Indeed, as we previously discussed in our preliminary work,[8] Pd-catalyzed formic acid reduction, the Sonogashira reaction, and the Suzuki–Miyaura coupling reaction of product **3** all proceeded smoothly to give the corresponding vinyl-substituted compounds. The Pd-catalyzed carbonylation of 1-bromo-1,4-diene **3ab** also took place effectively under carbon monoxide pressure (10 atm) to give α,β-unsaturated ester **8** in a 93% yield.[19] Also, **3ab** underwent carbonylative Suzuki–Miyaura reaction to give α,β-unsaturated ketone **9** in an 83% yield[20] (Scheme 5).



Scheme 4. Radical chain mechanism for the bromoallylation of **1p**.

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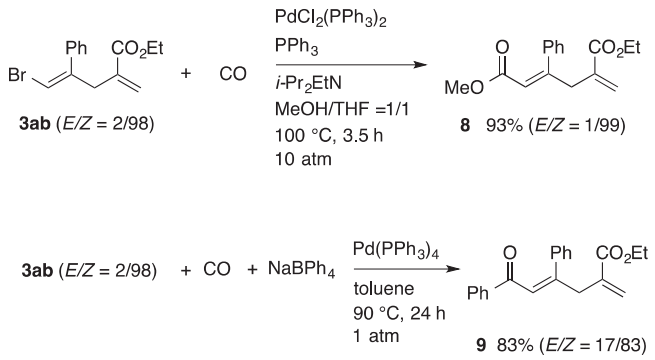

Scheme 5. Carbonyl-functionalization of 1-bromo-1,4-diene **3ab**.

3. Conclusions

We have demonstrated that radical bromoallylation has broad applicability to a variety of substituted alkynes and allyl bromides, and therefore, it is useful in the preparation of a wide range of 1-bromo-substituted-1,4-dienes. The reaction proceeds either under standard thermal initiation using typical diazo initiators such as V-65 or simple irradiation from a xenon lamp with no radical initiator. All these products have C–Br bonds that can be successfully subjected to C–C bond formation reactions such as cross-coupling and carbonylation with CO, serving as a platform to access 1-substituted-1,4-dienes. Since regiochemistry is opposite that of the previously reported Kaneda's Pd-catalyzed bromoallylation reaction,[21] both methods can be used in a complementary fashion.

4. Experimental

4.1. General information

Photoinduced reactions were carried out using a 4 mL screw capped test tube made of Pyrex glass and a solar simulator equipped with a 1500 W xenon lamp (CO.FO.ME.GRA, Milan, Italy, SolarBox 1500e). ^{1}H NMR spectra were recorded with JEOL ECP-500 (500 MHz) and JEOL ECS-400 (400 MHz) spectrometers in $CDCl_3$ and are referenced at 7.26 ppm for solvent peak. ^{13}C NMR spectra were recorded with JEOL ECP-500 (125 MHz) and JEOL ECS-400 (100 MHz) spectrometers in $CDCl_3$ and are referenced at 77.00 ppm for solvent peak. Chemical shifts are reported in parts per million (δ). Splitting patterns are indicated as follows: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sex, sextet; sep, septet; m, multiplet. Infrared spectra were obtained on a JASCO FT/IR-4100 spectrometer; absorptions were reported in reciprocal centimeters. Both conventional and high-resolution mass spectra were recorded with a JEOL MS-700 spectrometer. Melting points were measured by BÜCHI Melting Point B-540. The products were purified by flash column chromatography on silica gel (Kanto Chem. Co. Silica Gel 60N (spherical, neutral, 40–50 μm)) and/or preparative HPLC (Japan Analytical Industry Co., Ltd., LC-908) with GPC columns using distilled $CHCl_3$ as an eluent. Benzene was degassed by argon bubbling for 30 min before use. Compound **4** was synthesized by the reported procedure.[22a] Compound **6** is known in literature.[22b]

4.2. Experimental procedures

*4.2.1. Typical general procedure for bromoallylation of alkynes **1** with **2a** or **2c** (Method A).* To a 20 mL screw capped test tube, ethynylbenzene **1a** (1.0 mmol, 102 mg), 3-bromopropene **2a** (5 mL), and V-65 [2,2′-azobis(2,4-dimethylvaleronitrile)] (0.2 mmol, 50 mg) were added. Then, this test tube was purged with argon and sealed. The mixture was stirred at 60 °C for 6 h under argon atmosphere. The reaction mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography on SiO_2 using hexane to give the corresponding 1-bromo-2-phenyl-1,4-pentadiene **3aa** (179 mg, 80%).

Compound data: **3aa**, **3ba**, **3ca**, **3da**, **3ea**, **3ac**, **3ga**, **3ha**, **3ia**, **3ja**, **3ka**, **3la**, **3ma**, **3na** and **3oa** have already been reported.[8]

*4.2.2. Typical general procedure for bromoallylation of alkynes **1** with **2b** (Method B).* To a 4 mL screw capped test tube made by Pyrex glass, ethynylbenzene **1a** (1.0 mmol, 102 mg), ethyl 2-(bromomethyl)acrylate **2b** (4.0 mmol, 772 mg) and benzene (1 mL) were added. Then, this test tube was purged with argon and sealed. The mixture was irradiated by Solarbox equipped 1500 W xenon lamp (350 W/m^2) with stirring for 12 h. The reaction mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography on SiO_2 using hex/EtOAc (100/1) and preparative HPLC (chloroform) to give the corresponding ethyl 5-bromo-2-methylene-4-phenyl-4-pentenoate **3ab** (245 mg, 83%).

4.3. Characterization data

*4.3.1. 1-Bromo-2-phenyl-1,4-pentadiene (**3aa**).*[8] Obtained as an *E*/*Z* isomeric mixture in a 23/77 ratio (179 mg, 80%), as determined by ^{1}H NMR analysis of the crude reaction mixture. The *E*- and *Z*-isomers of **3aa** were separated using a preparative HPLC. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.2. 1-Bromo-2-(4-tolyl)-1,4-pentadiene (**3ba**).*[8] Obtained as an *E*/*Z* isomeric mixture in a 16/84 ratio (190 mg, 80%), as determined by ^{1}H NMR analysis of the crude reaction mixture. The *E*- and *Z*-isomers of **3ba** were separated using a preparative HPLC. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.3. 1-Bromo-2-(4-methoxyphenyl)-1,4-pentadiene (**3ca**).*[8] Obtained as an *E*/*Z* isomeric mixture in a 23/77 ratio (177 mg, 70%), as determined by ^{1}H NMR analysis of the crude reaction mixture. The *E*- and *Z*-isomers of **3ca** were separated using a preparative HPLC. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.4. 1-Bromo-2-(4-ethoxycarbonylphenyl)-1,4-pentadiene (**3da**).*[8] Obtained as an *E*/*Z* isomeric mixture in a 35/65 ratio (275 mg, 93%), as determined by ^{1}H NMR analysis of the crude reaction mixture. The *E*- and *Z*-isomers of **3da** were separated using a preparative HPLC. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.5. 1-Bromo-2-(4-acetylphenyl)-1,4-pentadiene (**3ea**).*[8] Obtained as an *E*/*Z* isomeric mixture in a 27/73 ratio (249 mg, 94%), as determined by ^{1}H NMR analysis of the crude reaction mixture. The *E*- and *Z*-isomers of **3ea** were separated using a preparative HPLC. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.6. 1-Bromo-2-(4-nitrophenyl)-1,4-pentadiene (**3fa**).* Obtained as an *E*/*Z* isomeric mixture in a 4/96 ratio (161 mg, 60%), as determined by ^{1}H NMR analysis of the crude reaction mixture. The *E*- and *Z*-isomers of **3fa** were separated using a preparative HPLC. ***Z* isomer**; Light yellow oil; R_f=0.23 (Hexane:Et$_2$O=30:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.19 (dd, *J*=6.9, 1.0 Hz, 2H), 5.04–5.14 (m, 2H), 5.73 (ddt, *J*=16.9, 10.1, 6.9 Hz, 1H), 6.40 (s, 1H), 7.42–7.46 (m, 2H), 8.22–8.26 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 42.53, 105.57, 118.35, 123.55, 129.21, 133.33, 142.69, 146.11, 147.15; IR (neat): 3077, 1640, 1518 cm^{-1}; EIMS *m*/*z* (relative intensity) 267 ([M]$^+$, 39), 252 (7), 250 (7), 222 (6), 220 (6), 188 (49), 171 (12), 142 (100), 141 (98), 115 (51); HRMS (EI) *m*/*z* calcd for $C_{11}H_{10}NO_2{}^{79}Br$ [M]$^+$: 266.9895,

found: 266.9891. ***E* isomer**; Light yellow oil; R_f=0.23 (Hexane:Et_2O=30:1); ^1H NMR (500 MHz, $CDCl_3$) δ 3.47 (d, J=6.0 Hz, 2H), 5.08–5.15 (m, 2H), 5.80 (ddt, J=17.0, 10.1, 6.5 Hz, 1H), 6.71 (s, 1H), 7.48–7.52 (m, 2H), 8.17–8.22 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 37.39, 110.07, 117.24, 123.85, 127.17, 132.75, 141.80, 146.28, 147.27; IR (neat): 3079, 1638, 1520 cm^{-1}; EIMS m/z (relative intensity) 267 ($[M]^+$, 41), 252 (8), 250 (8), 222 (6), 220 (6), 188 (53), 171 (13), 142 (100), 141 (94), 115 (48); HRMS (EI) m/z calcd for $C_{11}H_{10}NO_2{}^{79}Br$ $[M]^+$: 266.9895, found: 266.9901. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.7. 1-Bromo-4-methyl-2-phenyl-1,4-pentadiene (**3ac**).*[8] Obtained as an *E*/*Z* isomeric mixture in a 10/90 ratio (225 mg, 95%), as determined by ^1H NMR analysis of the crude reaction mixture. The *E*- and *Z*-isomers of **3ac** were separated using a preparative HPLC.

*4.3.8. 1-Bromo-2-(2-chlorophenyl)-1,4-pentadiene (**3ga**).*[8] Obtained as an *E*/*Z* isomeric mixture in a 6/94 ratio (250 mg, 97%), as determined by ^1H NMR analysis of the crude reaction mixture. The *E*- and *Z*-isomers of **3ga** were separated using a preparative HPLC. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.9. 1-Bromo-2-(3-chlorophenyl)-1,4-pentadiene (**3ha**).*[8] Obtained as an *E*/*Z* isomeric mixture in a 14/86 ratio (219 mg, 85%), as determined by ^1H NMR analysis of the crude reaction mixture. The *E*- and *Z*-isomers of **3ha** were separated using a preparative HPLC. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.10. 1-Bromo-2-(4-chlorophenyl)-1,4-pentadiene (**3ia**).*[8] Obtained as an *E*/*Z* isomeric mixture in a 18/82 ratio (207 mg, 81%), as determined by ^1H NMR analysis of the crude reaction mixture. The *E*- and *Z*-isomers of **3ia** were separated using a preparative HPLC. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.11. 1-Bromo-2-(2,5-dimethoxyphenyl)-1,4-pentadiene (**3ja**).*[8] Obtained as an *E*/*Z* isomeric mixture in a 6/94 ratio (254 mg, 90%), as determined by ^1H NMR analysis of the crude reaction mixture. The *E*- and *Z*-isomers of **3ja** were separated using a preparative HPLC. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.12. (E)-1-Bromo-2-(1-naphthyl)-1,4-pentadiene (**3ka**).*[8] Obtained as only *E* isomer (227 mg, 83%). *E* configuration was determined by NOESY analysis.

*4.3.13. 1-Bromo-2-(2-naphthyl)-1,4-pentadiene (**3la**).*[8] Obtained as an *E*/*Z* isomeric mixture in a 26/74 ratio (238 mg, 87%), as determined by ^1H NMR analysis of the crude reaction mixture. The *E*- and *Z*-isomers of **3la** were separated using a preparative HPLC. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.14. 1-Bromo-2-thiophen-3-yl-1,4-pentadiene (**3ma**).*[8] Obtained as an *E*/*Z* isomeric mixture in a 58/42 ratio (176 mg, 77%), as determined by ^1H NMR analysis of the crude reaction mixture. The *E*- and *Z*-isomers of **3ma** were separated using a preparative HPLC. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.15. 1-Bromo-2-ethoxycarbonyl-1,4-pentadiene (**3na**).*[8] Obtained as an *E*/*Z* isomeric mixture in a 26/74 ratio (188 mg, 86%), as determined by ^1H NMR analysis of the crude reaction mixture.

*4.3.16. Dimethyl 2-allyl-3-bromofumarate (**3oa**).*[8] Obtained as an *E*/*Z* isomeric mixture in a 34/66 ratio (132 mg, 49%), as determined by ^1H NMR analysis of the crude reaction mixture. The *E*- and *Z*-isomers of **3oa** were separated by a flash column chromatography on silica gel (Hexane:Et_2O=10:1). *E*/*Z* configuration was determined by NOESY analysis.

*4.3.17. Ethyl 5-bromo-2-methylene-4-phenyl-4-pentenoate (**3ab**).* Obtained as an *E*/*Z* isomeric mixture in a 22/78 ratio (245 mg, 83%), as determined by ^1H NMR analysis of the crude reaction mixture. Colorless oil; R_f=0.43 (Hexane:EtOAc=10:1); ***Z* isomer**; ^1H NMR (400 MHz, $CDCl_3$) δ 1.28 (t, J=6.8 Hz, 3H), 3.45 (s, 2H), 4.19 (q, J=6.8 Hz, 2H), 5.50 (d, J=1.2 Hz, 1H), 6.20 (s, 1H), 6.32 (s, 1H), 7.26–7.32 (m, 3H), 7.35–7.38 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.09, 40.45, 60.78, 104.73, 127.31, 127.64, 128.07, 128.12, 136.85, 138.79, 142.91, 166.30. ***E* isomer**; ^1H NMR (400 MHz, $CDCl_3$) δ 1.30 (t, J=6.8 Hz, 3H), 3.71 (s, 2H), 4.21 (q, J=6.8 Hz, 2H), 5.50–5.51 (m, 1H), 6.21 (s, 1H), 6.67 (s, 1H), 7.26–7.32 (m, 3H), 7.35–7.38 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.09, 34.87, 60.78, 108.16, 125.47, 126.21, 127.98, 128.52, 135.67, 139.28, 142.43, 166.65; IR (neat): 1716, 1443, 1142 cm^{-1}; EIMS m/z (relative intensity) 249 ($[M-OEt]^+$, 7), 215 (100), 187 (63), 169 (25), 141 (89), 115 (32), 102 (22), 91 (6), 71 (6); HRMS (EI) m/z calcd for $C_{12}H_{10}O^{81}Br$ $[M-OEt]^+$: 250.9895, found: 250.9893. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.18. Ethyl 5-bromo-4-(4-methoxyphenyl)-2-methylene-4-pentenoate (**3cb**).* Obtained as an *E*/*Z* isomeric mixture in a 10/90 ratio (231 mg, 71%), as determined by ^1H NMR analysis of the crude reaction mixture. Colorless oil; R_f=0.30 (Hexane:EtOAc=10:1); ***Z* isomer**; ^1H NMR (400 MHz, $CDCl_3$) δ 1.28 (t, J=6.8 Hz, 3H), 3.43 (s, 2H), 3.81 (s, 3H), 4.19 (q, J=6.8 Hz, 2H), 5.49 (s, 1H), 6.19 (s, 1H), 6.28 (s, 1H), 6.88–6.90 (m, 2H), 7.23–7.28 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.09, 40.36, 55.06, 60.76, 104.22, 113.40, 127.15, 129.43, 130.78, 137.03, 142.25, 158.89, 166.36. ***E* isomer**; ^1H NMR (400 MHz, $CDCl_3$) δ 1.30 (m, 3H), 3.68 (s, 2H), 3.80 (s, 3H), 4.20 (q, J=6.8 Hz, 2H), 5.49 (s, 1H), 6.21 (s, 1H), 6.59 (s, 1H), 6.83–6.85 (m, 2H), 7.23–7.28 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.09, 34.78, 55.16, 60.81, 106.48, 113.85, 125.36, 127.36, 131.65, 135.75, 141.74, 159.38, 166.69; IR (neat): 3073, 2981, 1715, 1509, 1249 cm^{-1}; EIMS m/z (relative intensity) 324 ($[M]^+$, 6), 245 (100), 217 (18), 171 (40), 128 (19), 89 (10), 63 (3); HRMS (EI) m/z calcd for $C_{15}H_{17}O_3{}^{79}Br$ $[M]^+$: 324.0361, found: 324.0352. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.19. Ethyl 5-bromo-4-(4-ethoxycarbonylphenyl)-2-methylene-4-pentenoate (**3db**).* Obtained as an *E*/*Z* isomeric mixture in a 20/80 ratio (268 mg, 73%), as determined by ^1H NMR analysis of the crude reaction mixture. Colorless oil; R_f=0.40 (Hexane:EtOAc=10:1); ***Z* isomer**; ^1H NMR (400 MHz, $CDCl_3$) δ 1.28 (t, J=6.8 Hz, 3H), 1.39 (t, J=6.8 Hz, 3H), 3.45 (s, 2H), 4.19 (q, J=6.8 Hz, 2H), 4.38 (q, J=6.8, 2H), 5.48–5.49 (m, 1H), 6.19–6.20 (m, 1H), 6.37–6.38 (m, 1H), 7.33–7.35 (m, 2H), 8.04–8.06 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.11, 14.28, 40.33, 60.91, 60.94, 105.69, 127.59, 128.27, 129.44, 129.71, 136.56, 142.31, 143.48, 166.19. ***E* isomer**; ^1H NMR (400 MHz, $CDCl_3$) δ 1.30 (t, J=7.2 Hz, 3H), 1.39 (t, J=7.2 Hz, 3H), 3.73 (m, 2H), 4.22 (q, J=7.2 Hz, 2H), 4.37 (q, J=7.2 Hz, 2H), 5.48–5.49 (m, 1H), 6.21–6.22 (m, 1H), 6.78 (s, 1H), 7.36–7.38 (m, 2H), 7.98–8.00 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.11, 14.28, 34.74, 60.91, 60.94, 110.09, 125.71, 126.17, 129.82, 135.52, 141.85, 143.48, 166.05, 166.53; IR (neat): 3417, 3074, 2981, 1714, 1275 cm^{-1}; EIMS m/z (relative intensity) 321 ($[M-OEt]^+$, 8), 287 (100), 259 (39), 213 (21), 169 (13), 141 (26), 115 (12); HRMS (EI) m/z calcd for $C_{15}H_{14}O_3{}^{79}Br$ $[M-OEt]^+$: 321.0126, found: 321.0125. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.20. Ethyl 5-bromo-4-(2-chlorophenyl)-2-methylene-4-pentenoate (**3gb**).* Obtained as an *E*/*Z* isomeric mixture in a 7/93 ratio (273 mg, 83%), as determined by ^1H NMR analysis of the

crude reaction mixture. Colorless oil; R_f=0.53 (Hexane: EtOAc=10:1); ***Z* isomer**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (t, J=7.2 Hz, 3H), 3.43 (s, 2H), 4.19 (q, J=7.2 Hz, 2H), 5.46 (d, J=0.8 Hz, 1H), 6.19 (d, J=0.8 Hz, 1H), 6.42 (t, J=1.6 Hz, 1H), 7.04–7.09 (m, 1H), 7.18–7.28 (m, 2H), 7.39–7.43 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.04, 39.62, 60.71, 107.13, 126.49, 127.83, 128.90, 129.39, 130.24, 132.03, 136.21, 137.82, 141.72, 166.10. ***E* isomer**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (t, J=7.2 Hz, 3H), 3.71 (s, 2H), 4.10 (q, J=7.2 Hz, 2H), 5.62 (d, J=0.8 Hz, 1H), 6.14–6.16 (m, 1H), 6.36–6.37 (m, 1H), 7.04–7.09 (m, 1H), 7.18–7.28 (m, 2H), 7.39–7.43 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.97, 35.74, 60.62, 109.57, 126.69, 129.01, 129.60, 130.63, 132.31, 135.67, 138.39, 141.66, 166.34 (One carbon signal superposed that of *Z* isomer); IR (neat): 3070, 2981, 1717, 1630, 1143 cm^{-1}; EIMS *m*/*z* (relative intensity) 283 ([M−OEt]$^+$, 3), 251 (33), 249 (100), 221 (29), 175 (27), 141 (22), 139 (13), 115 (11), 83 (7), 75 (3); HRMS (EI) *m*/*z* calcd for $C_{12}H_9O^{79}Br^{35}Cl$ [M−OEt]$^+$: 282.9525, found: 282.9529. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.21. Ethyl 5-bromo-4-(3-chlorophenyl)-2-methylene-4-pentenoate (**3hb**).* Obtained as an *E*/*Z* isomeric mixture in a 13/87 ratio (264 mg, 80%), as determined by ^{1}H NMR analysis of the crude reaction mixture. Colorless oil; R_f=0.47 (Hexane:EtOAc=10:1); ***Z* isomer**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (t, J=6.8 Hz, 3H), 3.42 (s, 2H), 4.20 (q, J=6.8 Hz, 2H), 5.51 (d, J=1.6 Hz, 1H), 6.22 (s, 1H), 6.34 (s, 1H), 7.11–7.22 (m, 1H), 7.24–7.32 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.10, 40.34, 60.90, 105.70, 126.47, 127.58, 127.82, 128.23, 129.46, 133.95, 136.58, 140.62, 141.78, 166.16. ***E* isomer**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (t, J=7.2 Hz, 3H), 3.68 (s, 2H), 4.22 (q, J=7.2 Hz, 2H), 5.49 (d, J=1.2 Hz, 1H), 6.22 (s, 1H), 6.70 (s, 1H), 7.11–7.22 (m, 1H), 7.24–7.32 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.10, 34.80, 60.90, 109.43, 124.44, 125.68, 126.39, 128.05, 129.78, 134.45, 135.44, 141.09, 141.39, 166.50; IR (neat): 3070, 2981, 1714, 1142 cm^{-1}; EIMS *m*/*z* (relative intensity) 283 ([M−OEt]$^+$, 3), 251 (35), 249 (100), 221 (42), 175 (25), 141 (17), 115 (7), 70 (4); HRMS (EI) *m*/*z* calcd for $C_{12}H_9O^{79}Br^{35}Cl$ [M−OEt]$^+$: 282.9525, found: 282.9527. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.22. Ethyl 5-bromo-4-(4-chlorophenyl)-2-methylene-4-pentenoate (**3ib**).* Obtained as an *E*/*Z* isomeric mixture in a 13/87 ratio (270 mg, 82%), as determined by ^{1}H NMR analysis of the crude reaction mixture. Colorless oil; R_f=0.53 (Hexane:EtOAc=10:1); ***Z* isomer**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (t, J=6.8 Hz, 3H), 3.42 (s, 2H), 4.19 (q, J=6.8 Hz, 2H), 5.48–5.49 (m, 1H), 6.20–6.21 (m, 1H), 6.33–6.34 (m, 1H), 7.20–7.23 (m, 2H), 7.32–7.35 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.99, 40.21, 60.73, 105.30, 127.33, 128.25, 129.51, 133.36, 136.56, 137.03, 141.75, 166.00. ***E* isomer**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (t, J=7.2 Hz, 3H), 3.67–3.68 (m, 2H), 4.21 (q, J=7.2 Hz, 2H), 5.48–5.49 (m, 1H), 6.20–6.21 (m, 1H), 6.67 (s, 1H), 7.20–7.24 (m, 2H), 7.29–7.35 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.99, 34.65, 60.78, 108.61, 125.48, 127.42, 128.57, 133.74, 135.43, 137.54, 141.29, 166.34; IR (neat): 3073, 2981, 1714, 1141 cm^{-1}; EIMS *m*/*z* (relative intensity) 283 ([M−OEt]$^+$, 9), 251 (82), 249 (100), 221 (79), 203 (22), 175 (66), 141 (41), 115 (19), 70 (8); HRMS (EI) *m*/*z* calcd for $C_{12}H_9O^{79}Br^{35}Cl$ [M−OEt]$^+$: 282.9525, found: 282.9522. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.23. Ethyl 5-bromo-2-methylene-4-(3-thiophenyl)-4-pentenoate (**3mb**).* Obtained as an *E*/*Z* isomeric mixture in a 24/76 ratio (220 mg, 73%), as determined by ^{1}H NMR analysis of the crude reaction mixture. Colorless oil; R_f=0.43 (Hexane:EtOAc=10:1); ***Z* isomer**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (t, J=6.8 Hz, 3H), 3.46–3.47 (m, 2H), 4.20 (q, J=6.8, 2H), 5.52–5.53 (m, 1H), 6.22 (s, 1H), 6.30 (s, 1H), 7.27–7.31 (m, 2H), 7.48 (dd, J=2.8, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.10, 40.01, 60.85, 104.41, 124.43, 124.70, 126.93, 127.52, 136.85, 137.27, 138.12, 166.42. ***E* isomer**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (t, J=6.8 Hz, 3H), 3.66–3.67 (m, 2H), 4.25 (q, J=6.8, 2H), 5.49–5.50 (m, 1H), 6.22 (s, 1H), 6.80 (s, 1H), 7.13–7.14 (m, 1H), 7.17–7.18 (m, 1H), 7.27–7.31 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.10, 34.51, 60.91, 107.69, 121.47, 124.97, 125.21, 126.08, 135.62, 137.17, 139.75, 166.76; IR (neat): 3106, 2980, 1714, 1140 cm^{-1}; EIMS *m*/*z* (relative intensity) 255 ([M−OEt]$^+$, 4), 221 (100), 193 (27), 147 (48), 108 (11), 103 (3); HRMS (EI) *m*/*z* calcd for $C_{10}H_8O^{79}BrS$ [M−OEt]$^+$: 254.9479, found: 254.9476. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.24. Ethyl 5-bromo-2-methylene-4-phenyl-4-hexenoate (**3pb**).* Obtained as an *E*/*Z* isomeric mixture in a 18/82 ratio (176 mg, 57%), as determined by ^{1}H NMR analysis of the crude reaction mixture. Colorless oil; R_f=0.43 (Hexane:EtOAc=10:1); ***Z* isomer**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27 (t, J=7.2 Hz, 3H), 2.48 (s, 3H), 3.45 (s, 2H), 4.17 (q, J=7.2 Hz, 2H), 5.46–5.47 (m, 1H), 6.17 (s, 1H), 7.11–7.15 (m, 2H), 7.22–7.33 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.12, 25.86, 37.07, 60.80, 120.71, 126.12, 127.01, 127.89, 128.45, 136.31, 136.37, 142.70, 166.58. ***E* isomer**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (t, J=7.2 Hz, 3H), 2.26 (s, 3H), 3.63 (s, 2H), 4.12 (q, J=7.2 Hz, 2H), 5.57–5.59 (m, 1H), 6.18–6.19 (m, 1H), 7.11–7.15 (m, 2H), 7.22–7.33 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.09, 26.74, 40.81, 60.67, 122.81, 125.55, 127.17, 128.20, 128.41, 136.27, 136.95, 139.74, 166.79; IR (neat): 2981, 1714, 1140 cm^{-1}; EIMS *m*/*z* (relative intensity) 263 ([M−OEt]$^+$, 2), 229 (100), 183 (18), 155 (49), 115 (22), 77 (4); HRMS (EI) *m*/*z* calcd for $C_{13}H_{12}O^{79}Br$ [M−OEt]$^+$: 263.0072, found: 263.0069. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.25. Ethyl 4-bromomethylene-2-methylene-decanoate (**3qb**).* Obtained as an *E*/*Z* isomeric mixture in a 93/7 ratio (252 mg, 83%), as determined by ^{1}H NMR analysis of the crude reaction mixture. Colorless oil; R_f=0.47 (Hexane:EtOAc=10:1); ***Z* isomer**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, J=6.8 Hz, 3H), 1.38–1.44 (m, 11H), 2.05–2.08 (m, 2H), 3.24 (s, 2H), 4.23 (q, J=6.8 Hz, 2H), 5.53 (d, J=1.2 Hz, 1H), 6.09 (s, 1H), 6.23–6.24 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.54, 28.79, 34.33, 35.89, 60.76, 103.78, 125.31, 136.07, 142.66, 166.86 (Some carbon signals superposed that of *E* isomer). ***E* isomer**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, J=6.4 Hz, 3H), 1.25–1.33 (m, 11H), 2.16–2.20 (m, 2H), 3.10 (s, 2H), 4.20 (q, J=6.4 Hz, 2H), 5.55 (d, J=1.2 Hz, 1H), 5.94 (s, 1H), 6.25 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.99, 14.09, 22.52, 26.83, 29.03, 31.55, 32.49, 37.69, 60.76, 103.66, 126.63, 137.58, 142.66, 166.46; IR (neat): 3076, 2928, 2858, 1719, 1142 cm^{-1}; EIMS *m*/*z* (relative intensity) 257 ([M−OEt]$^+$, 1), 223 (100), 195 (92), 177 (18), 149 (39), 93 (25), 79 (23), 67 (13); HRMS (EI) *m*/*z* calcd for $C_{12}H_{18}O^{79}Br$ [M−OEt]$^+$: 257.0541, found: 257.0543. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.26. Ethyl 4-bromomethylene-6-(tert-butyldimethylsilyl)oxy-2-methylene-hexanoate (**3rb**).* Obtained as an *E*/*Z* isomeric mixture in a 91/9 ratio (283 mg, 75%), as determined by ^{1}H NMR analysis of the crude reaction mixture. Colorless oil; R_f=0.50 (Hexane:EtOAc=10:1); ***Z* isomer**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.03 (s, 6H), 0.87 (s, 9H), 1.30 (m, 3H), 2.29 (t, J=6.4 Hz, 2H), 3.26 (s, 2H), 3.66 (t, J=6.4 Hz, 2H), 4.20 (m, 2H), 5.56 (s, 1H), 6.17 (s, 1H), 6.26 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.42, 25.83, 34.71, 38.95, 61.09, 105.65, 125.52, 135.92, 139.54, 166.87 (One carbon signal superposed that of *E* isomer). ***E* isomer**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.06 (s, 6H), 0.89 (s, 9H), 1.30 (t, J=6.8 Hz, 3H), 2.44 (t, J=6.8 Hz, 2H), 3.16 (s, 2H), 3.71 (t, J=6.8 Hz, 2H), 4.20 (q, J=6.8 Hz, 2H), 5.56 (s, 1H), 6.03 (s, 1H), 6.26 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.37, 14.14, 18.25, 25.90, 35.98, 38.81, 60.71, 60.82, 105.36, 126.81, 137.45, 139.95, 166.47; IR (neat): 2955, 2929, 1720, 1255, 1096 cm^{-1}; EIMS *m*/*z* (relative intensity) 319 ([M−^{t}Bu]$^+$, 96), 275 (19), 273 (19), 139 (11),

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137 (11), 91 (10), 75 (12), 73 (11); HRMS (EI) *m*/*z* calcd for $C_{12}H_{20}{}^{81}BrO_3Si$ $[M-{}^tBu]^+$: 321.0345, found: 321.0342. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.27. Ethyl 4-bromomethylene-6-hydroxy-2-methylene-hexanoate (**3rb′**).* Obtained as an *E*/*Z* isomeric mixture in a 96/4 ratio (50 mg, 19%), as determined by ^{1}H NMR analysis of the crude reaction mixture. Colorless oil; R_f=0.18 (Hexane:EtOAc=5:1); ***Z* isomer**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32–1.33 (m, 3H), 1.69 (br s, 1H), 2.36 (t, *J*=6.4 Hz, 2H), 3.29 (s, 2H), 3.70 (t, *J*=6.4 Hz, 2H), 4.24–4.28 (m, 2H), 5.59–5.60 (m, 1H), 6.22 (s, 1H), 6.27 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.10, 34.39, 38.87, 60.13, 61.01, 105.94, 125.90, 135.92, 139.25, 166.91. ***E* isomer**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (t, *J*=6.8 Hz, 3H), 1.69 (br s, 1H), 2.52 (t, *J*=6.4 Hz, 2H), 3.16 (s, 2H), 3.80 (t, *J*=6.4 Hz, 2H), 4.21 (q, *J*=6.8 Hz, 2H), 5.62–5.63 (m, 1H), 6.06 (s, 1H), 6.29 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.10, 36.21, 38.49, 60.36, 61.12, 105.65, 127.51, 137.20, 139.90, 166.65; IR (neat): 3418, 2980, 1714, 1147 cm^{-1}; EIMS *m*/*z* (relative intensity) 217 ($[M-OEt]^+$, 3), 183 (100), 153 (54), 137 (43), 125 (34), 79 (32), 77 (28); HRMS (EI) *m*/*z* calcd for $C_8H_{10}{}^{79}BrO_2$ $[M-OEt]^+$: 216.9864, found: 216.9862. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.28. Ethyl 5-bromo-4-(1-cyclohexenyl)-2-methylene-4-pentenoate (**3sb**).* Obtained as an *E*/*Z* isomeric mixture in a 24/76 ratio (102 mg, 34%), as determined by ^{1}H NMR analysis of the crude reaction mixture. Colorless oil; R_f=0.48 (Hexane:EtOAc=10:1); ***Z* isomer**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (t, *J*=6.8 Hz, 3H), 1.52–1.68 (m, 4H), 2.01–2.09 (m, 4H), 3.15 (s, 2H), 4.20 (q, *J*=6.8 Hz, 2H), 5.52–5.56 (m, 2H), 5.96 (s, 1H), 6.21–6.22 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.14, 21.89, 22.53, 24.96, 26.83, 38.64, 60.74, 102.30, 126.83, 127.03, 135.69, 137.30, 145.35, 166.55; ***E* isomer**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (t, *J*=6.8 Hz, 3H), 1.52–1.68 (m, 4H), 2.12–2.14 (m, 4H), 3.30–3.45 (m, 2H), 4.24 (q, *J*=6.8 Hz, 2H), 5.38–5.40 (m, 1H), 5.79–5.81 (m, 1H), 6.18–6.20 (m, 1H), 6.43 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.14, 21.84, 22.60, 25.80, 25.97, 32.43, 60.80, 106.37, 124.64, 134.30, 136.24, 143.13, 166.94 (One carbon signal superposed that of *Z* isomer); IR (neat): 3031, 2930, 1715, 1138 cm^{-1}; EIMS *m*/*z* (relative intensity) 253 ($[M-OEt]^+$, 3), 219 (100), 191 (9), 145 (25), 91 (9), 83 (5), 67 (3); HRMS (EI) *m*/*z* calcd for $C_{12}H_{14}{}^{79}BrO$ $[M-OEt]^+$: 253.0228, found: 253.0225. *E*/*Z* configuration was determined by NOESY analysis.

*4.3.29. Ethyl 5-bromo-4-cyclopropyl-2-methylene-4-pentenoate (**3tb**).* Obtained as an *E*/*Z* isomeric mixture in a 12/88 ratio (220 mg, 85%), as determined by ^{1}H NMR analysis of the crude reaction mixture. Colorless oil; R_f=0.50 (Hexane:EtOAc=10:1); ***Z* isomer**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.56–0.60 (m, 2H), 0.74–0.79 (m, 2H), 1.30 (t, *J*=6.8 Hz, 3H), 1.93–1.99 (m, 1H), 2.72–2.74 (m, 2H), 4.20 (q, *J*=6.8 Hz, 2H), 5.57–5.58 (m, 1H), 5.94–5.95 (m, 1H), 6.25–6.26 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 5.20, 14.07, 14.31, 33.23, 60.79, 104.23, 126.57, 137.64, 141.74, 166.41. ***E* isomer**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.43–0.47 (m, 2H), 0.62–0.67 (m, 2H), 1.32 (t, *J*=6.8 Hz, 3H), 1.36–1.48 (m, 1H), 3.18–3.20 (m, 2H), 4.23 (q, *J*=6.8 Hz, 2H), 5.57–5.58 (m, 1H), 6.09 (s, 1H), 6.25–6.26 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 5.30, 14.10, 16.45, 34.13, 60.76, 103.19, 125.29, 136.18, 143.28, 166.81; IR (neat): 3086, 2982, 1715, 1145 cm^{-1}; EIMS *m*/*z* (relative intensity) 213 ($[M-OEt]^+$, 1), 179 (100), 151 (31), 105 (52), 79 (19), 77 (14), 63 (2); HRMS (EI) *m*/*z* calcd for $C_9H_{10}{}^{79}BrO$ $[M-OEt]^+$: 212.9915, found: 212.9916. *E*/*Z* configuration was determined by NOESY analysis.

4.4. Experimental procedure for radical cascade reaction of enyne malonate (4) with 2b

To a 4 mL screw capped test tube made by Pyrex glass, enyne malonate **4** (126 mg, 0.5 mmol), ethyl 2-(bromomethyl)acrylate **2b** (193 mg, 1.0 mmol) and benzene (1.0 mL) were added. Then, this test tube was purged with argon and sealed. The mixture was irradiated by Solarbox equipped 1500 W xenon lamp (350 W/m^2) with stirring for 12 h. The reaction mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography on SiO_2 and preparative HPLC (chloroform) to give the corresponding product **5** (173 mg, 76%, *E* isomer only).

*4.4.1. (E)-Diethyl 3-(bromomethylene)-4-(4-(ethoxycarbonyl)-2-methyl-4-penten-2-yl)cyclopentane-1,1-dicarboxylate (**5**).* Colorless oil; R_f=0.21 (Hexane:EtOAc=10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82 (s, 3H), 0.83 (s, 3H), 1.22–1.33 (m, 9H), 2.08 (dd, *J*=12.4, 8.4 Hz, 1H), 2.29 (d, *J*=13.2 Hz, 1H), 2.37 (d, *J*=12.4 Hz, 1H), 2.58–2.74 (m, 3H), 3.28–3.36 (m, 1H), 4.12–4.28 (m, 6H), 5.47–5.50 (m, 1H), 6.09 (m, 1H), 6.21–6.24 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.97, 14.09, 23.64, 24.09, 36.00, 37.17, 39.62, 42.34, 52.42, 57.92, 60.73, 61.55, 61.63, 101.46, 127.76, 137.94, 145.71, 167.92, 170.90, 170.97; IR (neat): 2979, 2938, 2906, 2874, 1732, 1627, 1302, 1249 cm^{-1}; EIMS *m*/*z* (relative intensity) 458 ($[M]^+$, 1), 413 ($[M-OEt]^+$, 3), 379 (33), 347 (17), 345 (17), 333 (50), 305 (25), 273 (37), 271 (38), 259 (53), 155 (100), 109 (77), 81 (50); HRMS (EI) *m*/*z* calcd for $C_{19}H_{26}BrO_5$ $[M-OEt]^+$: 413.0964, found: 413.0976.

4.5. Experimental procedure for the formation of ethyl 2-(2,2,6,6-tetramethyl-1-piperidinyloxymethyl)acrylate (7)

To a 4 mL screw capped test tube made by Pyrex glass, 1-octyne **1q** (0.5 mmol, 55 mg), ethyl 2-(bromomethyl)acrylate **2b** (2.0 mmol, 386 mg), TEMPO (0.05 mmol, 8 mg) and benzene (0.5 mL) were added. Then, this test tube was purged with argon and sealed. The mixture was irradiated by Solarbox equipped 1500 W xenon lamp (350 W/m^2) with stirring for 12 h. The reaction mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography on SiO_2 (Hexane/EtOAc=1:0 to 100:1) and preparative HPLC (chloroform) to give ethyl 2-(2,2,6,6-tetramethyl-1-piperidinyloxymethyl)acrylate (**7**).

*4.5.1. Ethyl 2-(2,2,6,6-tetramethyl-1-piperidinyloxymethyl)acrylate (**7**).* Colorless oil; R_f=0.50 (Hexane:EtOAc=10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12 (s, 6H), 1.17 (s, 6H), 1.30 (t, *J*=7.2 Hz, 3H), 1.30–1.35 (m, 1H), 1.43–1.66 (m, 5H), 4.21 (q, *J*=7.2 Hz, 2H), 4.49 (s, 2H), 5.88–5.90 (m, 1H), 6.26–6.29 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.18, 17.06, 20.22, 32.74, 39.62, 59.91, 60.60, 74.58, 125.06, 137.15, 165.95; IR (neat): 2977, 2932, 1727, 1472, 1060 cm^{-1}; EIMS *m*/*z* (relative intensity) 269 ($[M]^+$, 3), 156 (100), 123 (14), 114 (4), 83 (6), 69 (9); HRMS (EI) *m*/*z* calcd for $C_{14}H_{24}NO_3$ $[M-Me]^+$: 254.1756, found: 254.1765.

4.6. Experimental procedure for Pd-catalyzed carbonylation reaction leading to α,β-unsaturated ester 8[19]

Ethyl 5-bromo-2-methylene-4-phenyl-4-pentenoate **3ab** (87 mg, *E*/*Z*=2/98, 0.30 mmol), $PdCl_2(PPh_3)_2$ (6.3 mg, 0.009 mmol, 3.0 mol %), PPh_3 (4.7 mg, 0.018 mmol, 6.0 mol %), diisopropylethylamine (49 mg, 0.36 mmol, 1.2 equiv), dry THF (0.6 mL) and dry MeOH (0.6 mL) were placed in a 30 mL stainless steel autoclave. The autoclave was closed, purged three times with 10 atm of carbon monoxide, pressured with 10 atm of carbon monoxide, and then heated at 100 °C for 3.5 h. After the reaction excess carbon monoxide was discharged at room temperature. The reaction mixture poured into NH_4Cl aq solution. The aqueous phase was extracted with Et_2O, and the combined organic layers were washed with brine, dried over anhydrous magnesium sulfate, and filtered. The filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography on SiO_2

(Hexane:EtOAc=25:1) to give 6-ethyl 1-methyl-5-methylene-3-phenyl-2-hexenedioate **8** (77 mg, 93%, *E*/*Z*=1/99).

*4.6.1. (Z)-6-Ethyl 1-methyl-5-methylene-3-phenyl-2-hexenedioate (**8**).* Light yellow oil; R_f=0.19 (Hexane:EtOAc=10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (t, *J*=6.8 Hz, 3H), 3.44 (t, *J*=0.8 Hz, 2H), 3.54 (s, 3H), 4.20 (q, *J*=6.8 Hz, 2H), 5.55 (q, *J*=1.6 Hz, 1H), 5.88 (t, *J*=1.2 Hz, 1H), 6.28 (d, *J*=0.8 Hz, 1H), 7.16–7.22 (m, 2H), 7.27–7.38 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.06, 42.07, 50.98, 60.87, 118.01, 127.16, 127.78, 128.20, 136.56, 139.45, 156.59, 166.06, 166.18; IR (neat): 2984, 2950, 1716, 1633, 1223, 1166 cm^{-1}; EIMS *m*/*z* (relative intensity); 274 ([M]$^+$, 8), 242 (22), 228 (58), 201 (22), 185 (25), 170 (18), 169 (72), 168 (19), 142 (28), 141 (100), 115 (27); HRMS (EI) *m*/*z* calcd for $C_{16}H_{18}O_4$ [M]$^+$: 274.1205, found: 274.1206. *Z* configuration was determined by NOESY analysis.

4.7. Experimental procedure for Pd-catalyzed carbonylation reaction leading to α,β-unsaturated ketone 9[20]

To a 20 mL test tube, ethyl 5-bromo-2-methylene-4-phenyl-4-pentenoate **3ab** (59 mg, 0.2 mmol), $Pd(PPh_3)_4$ (12 mg, 0.01 mmol, 5 mol%), $NaBPh_4$ (69 mg, 0.2 mmol), dry toluene (2 mL) were added. The test tube was purged three times with 1 atm of carbon monoxide then heated at 90 °C for 24 h. The reaction mixture poured into NH_4Cl aq solution. The aqueous phase was extracted with EtOAc, and the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and filtered. The filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hexane:EtOAc=25:1) to give ethyl 2-methylene-6-oxo-4,6-diphenyl-4-hexenoate **9** (53 mg, 83%).

*4.7.1. Ethyl 2-methylene-6-oxo-4,6-diphenyl-4-hexenoate (**9**).* Obtained as an *E*/*Z* isomeric mixture in a 17/83 ratio, as determined by ^{1}H NMR analysis of the crude reaction mixture. Colorless oil; R_f=0.40 (Hexane:EtOAc=10:1); ***Z* isomer**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (t, *J*=7.2 Hz, 3H), 3.58 (s, 2H), 4.25 (q, *J*=7.2 Hz, 2H), 5.65 (q, *J*=1.2 Hz, 1H), 6.33 (d, *J*=0.8 Hz, 1H), 6.60 (t, *J*=1.6 Hz, 1H), 7.15–7.25 (m, 4H), 7.29–7.60 (m, 4H), 7.75–7.82 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.14, 41.44, 61.02, 125.31, 127.89, 128.03, 128.20, 128.78, 132.58, 137.17, 137.56, 137.76, 139.48, 152.52, 166.53, 193.71. ***E* isomer**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27 (t, *J*=7.2 Hz, 3H), 4.12 (m, 2H), 4.19 (q, *J*=7.2 Hz, 2H), 5.50 (q, *J*=1.2 Hz, 1H), 6.19 (q, *J*=1.6 Hz, 1H), 7.15–7.25 (m, 4H), 7.29–7.60 (m, 5H), 7.98–8.02 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.21, 33.02, 60.86, 124.10, 126.84, 154.74, 166.81, 190.88 (Some carbon signals superposed that of *Z* isomer); IR (neat): 3060, 2980, 1715, 1666, 1237 cm^{-1}; EIMS *m*/*z* (relative intensity); 320 ([M]$^+$, 7), 319 (7), 274 (93), 247 (25), 215 (38), 169 (100), 141 (38), 105 (89), 77 (37); HRMS (EI) *m*/*z* calcd for $C_{21}H_{20}O_3$ [M]$^+$: 320.1412 found: 320.1418.

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Supplementary data

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