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Synthetic strategies towards the carbenoid reactions of α,β-acetylenic carbonyls

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Abstract: Catalytic reactions of α,β-conjugated carbonyl compounds have been a practical tool towards the synthesis of different useful heterocyclic compounds. Despite the numerous reactions with carbon-carbon double bond conjugated carbonyls, reactions of acetylenic carbonyls are limited. In this study, efficient dioxole synthesis was carried out via acetylenic aldehydes and butadiene formation was preferred over cyclopropene formation via acetylenic esters as different functional groups on these substrates change the product distribution. Both reaction conditions (such as solvent and temperature) and electrophilic structure of metal carbenoids alter the product distribution; acceptor (A), donor-acceptor (DA), and acceptor-acceptor (AA) functionalized diazo compounds yield different product types over different mechanisms.

Key words: Acetylenic carbonyl, carbenoid, diazo, butadiene, cyclopropene, $Rh_2(OAc)_4$, $Cu(acac)_2$

1. Introduction

Carbene transfer to appropriate substrates is a very practical tool for the construction of carbon frameworks with increased functional and structural complexity.[1–4] Among these methodologies the formal [2+1] annulations[5–11] of α,β-unsaturated carbonyl compounds have been widely applied in enantioselective construction of rings such as epoxides, aziridines, and cyclopropane and cyclopropene.[12–19] The other reaction probabilities are formations of dioxolane, dihydrofuran, furan, and dioxole derivatives.[15,16,20–27] Extending the conjugation to $\alpha,\beta,\gamma,\delta$-positions might allow the synthesis of dihydrobenzoxepines[28,29] and other large ring sizes (Scheme 1).

After Spencer's[25–27] pioneering work, several studies on the catalyzed reactions of ene/poly-ene-carbonyls with diazo compounds have been realized.[28–45] Despite this enormous amount of work, carbenoid reactions with conjugated acetylenic carbonyls are very limited[46–49] and the reaction of 1,3-diphenyl-2-yl-1-one with ethyl diazoacetate[50] is one of the unique examples related to our study. Generally, in these reactions, the relative nucleophilicity differences between carbon-carbon multiple bonds, which are related to the adjacent groups and electrophilicity of metal carbenoids, being acceptor (A), donor-acceptor (DA), or acceptor-acceptor (AA), may contribute to the distribution of the products.

As part of our ongoing research project on ylide reactions and their applications in organic synthesis,[30–36] we initially aimed to determine the structural influence of different acetylenic carbonyls on product distribution.

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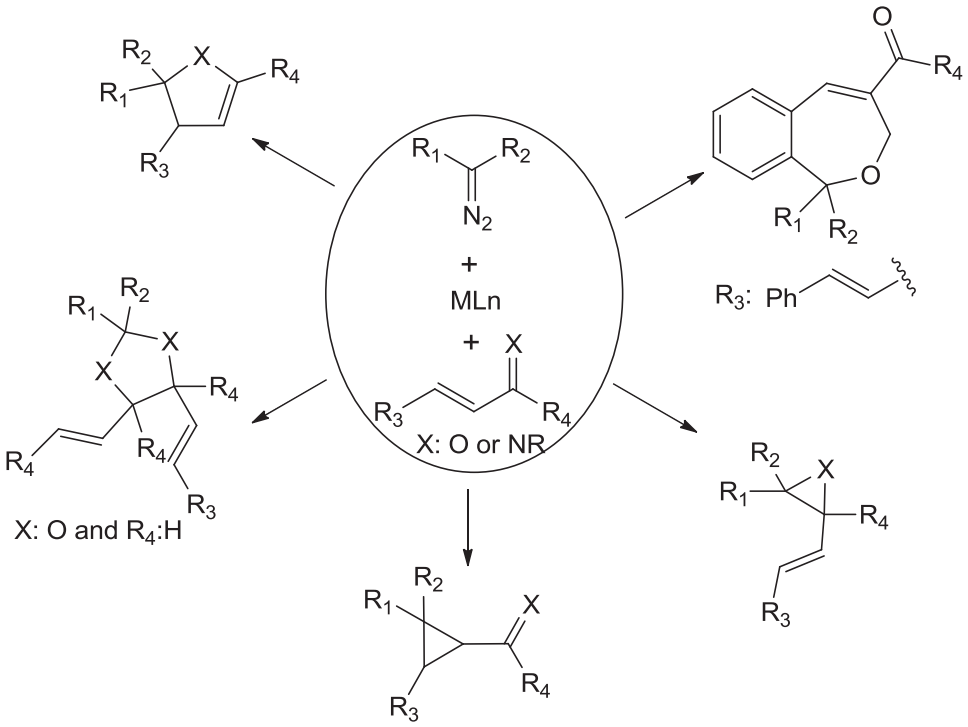


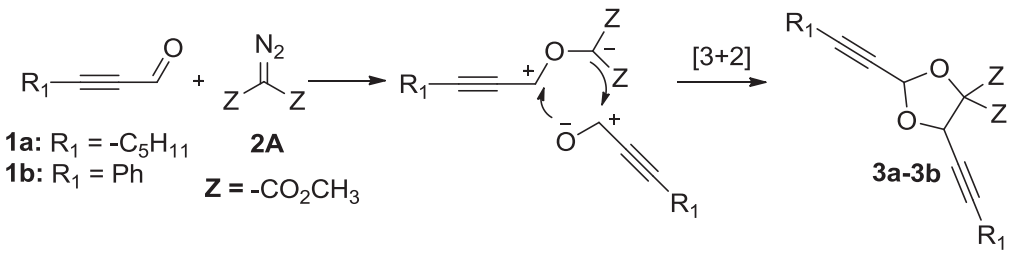
Scheme 1. Possible products from the reactions of α,β-conjugated carbonyl compounds with diazocarbonyls.

2. Results and discussion

In order to understand the effect of carbonyl functions on the substrates, we studied the reactions of four different conjugated yn-carbonyls, 2-octynal (**1a**), phenylpropargyl aldehyde (**1b**), ethyl 2-pentynoate (**1c**), and ethyl phenylpropiolate (**1d**), with dimethyl diazomalonate (**2A**). Copper dimethoxycarbonylcarbenoid reactions of these four α,β-acetylenic aldehyde/esters (**1a**–**1d**) with diazo compound **2A** gave the results summarized in Table 1.

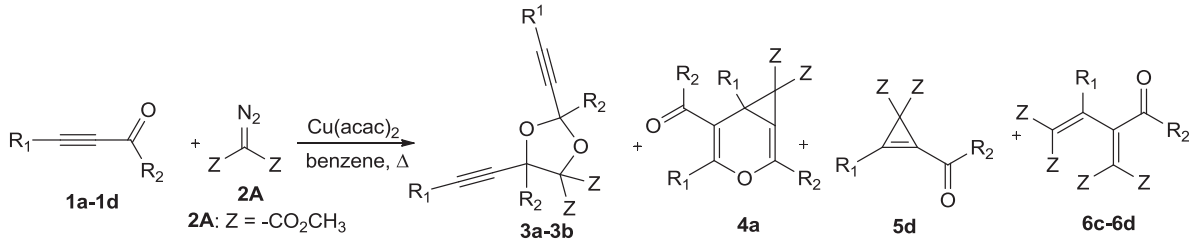
In the $Cu(acac)_2$ catalyzed reactions of dimethyl diazomalonate (**2A**) with acetylenic aldehydes (**1a**, **1b**), the major isolated products were 1,3-dioxolane derivatives (**3a**–**3b**), which were observed as *syn*/*anti* isomers in the crude mixture with ratio 1:1.2 for **3a** and 1:3 for **3b**. (Table 1, entries i and ii).

The plausible mechanism for the formation of **3a** and **3b** may involve intermolecular trapping of the carbonyl ylide intermediate (from aldehydes and **2A**) by another mole of **1a** via [3+2] cycloaddition reaction (Scheme 2).[15–17]



Scheme 2. Plausible mechanism for the formation of 1,3-dioxolane derivatives.

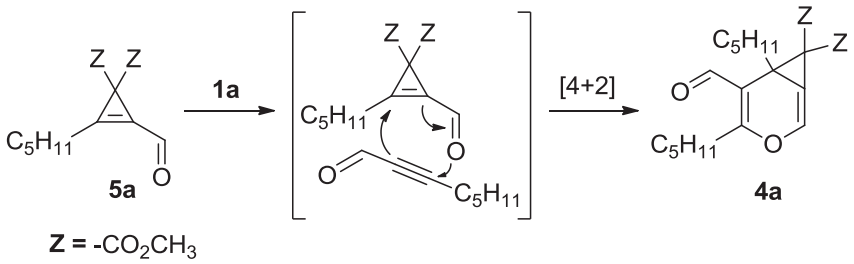
Table 1. Cu(acac)$_2$-catalyzed reactions of α,β-acetylenic aldehyde/esters (**1a**–**1d**).



Entry	1	R^1	R^2	3	4	5	6
				GC ratio, %[a]			
i	**a**	-C_5H_{11}	-H	80 (1:1.2)[b]	20	-	-
ii	**b**	-Ph	-H	85 (1:3)[b]	-	-	-
iii	**c**	-C_2H_5	-OC_2H_5	-	-	-	90
iv	**d**	-Ph	-OC_2H_5	-	-	20	75

[a] Relative product ratios were determined by gas chromatography (GC); there are also some minor undetermined products. [b] Obtained as two isomers (*syn/anti*).

Besides 1,3-dioxolane derivative (**3a**), an oxabicycloheptadiene derivative (**4a**) was also observed in the reaction of **1a**. The most appropriate mechanism for this compound is the cycloaddition of transient cyclopropene (**5a**) to another mole of **1a** (Scheme 3). This oxabicycloheptadiene derivative could not be observed in the reaction of **1b**, probably because of the steric hindrance caused by the phenyl group to prevent [4+2] cycloaddition.



Scheme 3. Formation of oxabicycloheptadiene derivative.

In the analogous reactions of acetylenic esters **1c** and **1d** with **2A** (Table 1, entries iii and iv), surprisingly, novel butadiene derivatives (**6c**, **6d**), containing five ester groups, were obtained clearly in good yields. Only from the reaction of ethyl phenylpropiolate (**1d**), cyclopropene derivative **5d** was also isolated and its structure was determined by single crystal X-ray analysis (Figure).

As observed clearly, changing the carbonyl functionality from aldehyde to ester totally changes the product distribution. In reactions of both **1c** and **1d**, butadiene derivative was obtained as a major product (90% yield for **6c** and 70% yield for **6d**). In these reactions, the cyclopropene derivative was one of the expected products, but it was isolated only from the reaction of **1d**. In this reaction, the phenyl substituent might cause an increased stability that postpones the conversion of cyclopropene into the butadiene derivative that was obtained as a

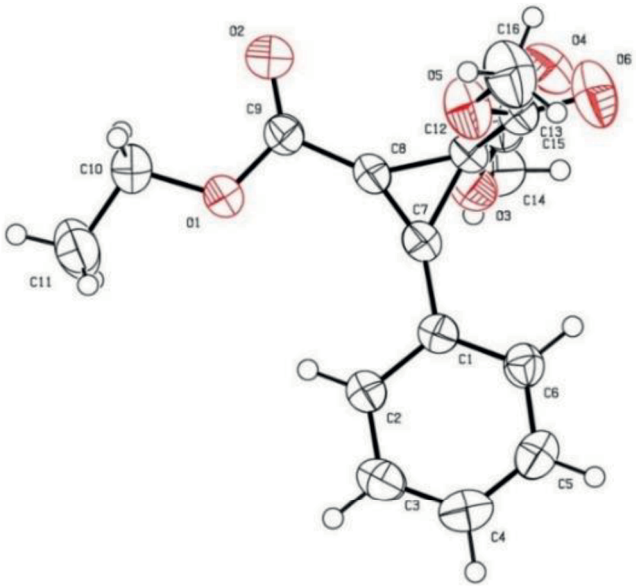


Figure. X-ray crystal structure of **5d**.

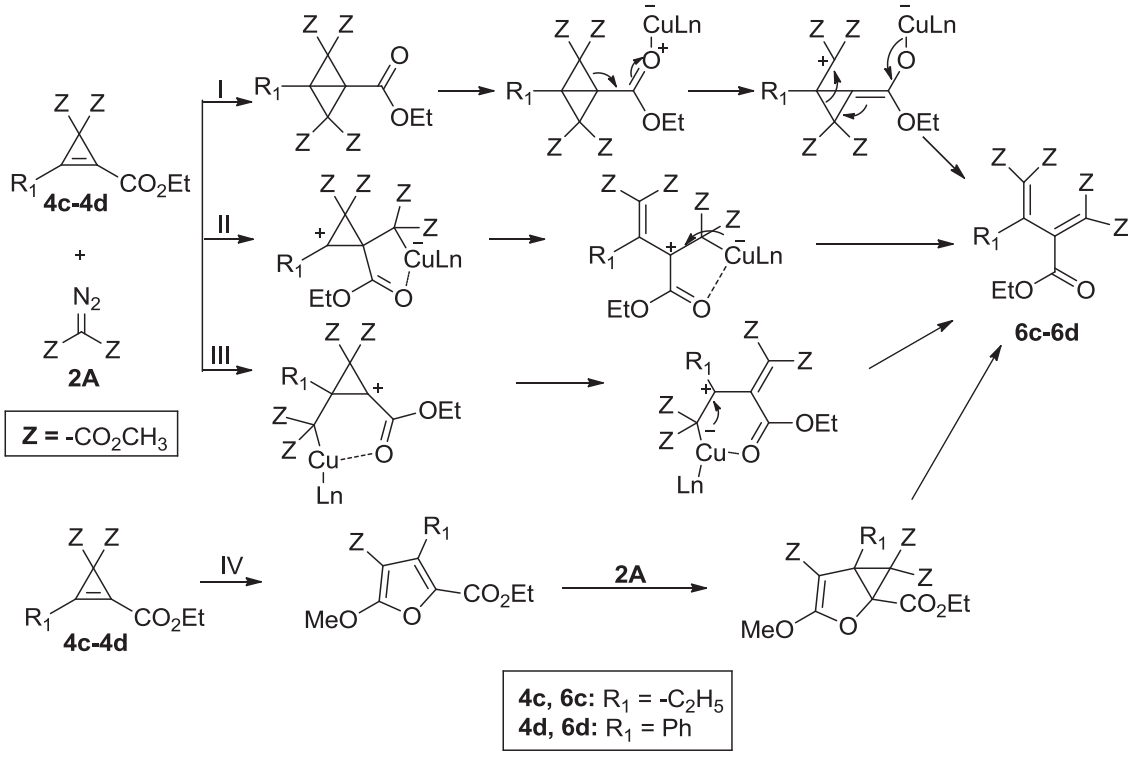
major product in reactions of both **1c** and **1d**. When the reaction of **1d** was performed with excess (three equivalents) diazo (**2A**) under longer reaction time, the only isolated product was butadiene derivative **6d**; no cyclopropene derivative was observed and the yield of **6d** was increased to 90%. From this point of view, the cyclopropene derivative helps to suggest a mechanism for the formation of butadiene derivatives based on the ring opening of a cyclopropene as depicted in Scheme 4.

For the formation of butadiene derivatives, route I is based on the catalytic ring opening of a bicyclo[1.1.0]butan derivative that may be formed from the reaction of transient cyclopropene with a new mole of **2A**. The other two mechanisms, II and III, were claimed to be realized via the ring opening of the intermediate cyclopropene via addition of a new mole of copper carbenoid. In route II, the carbenoid carbon attacked most probably the ester-substituted sp^2 carbon atom of the cyclopropenone to afford the intermediate, which leads to butadiene derivatives **6c** and **6d** via ring opening.

Another suggestion is route IV, which is represented by the rearrangement of cyclopropene to a furan derivative[51,52] and cyclopropanation with another mole of copper carbenoid[53] followed by ring opening. This mechanism was adapted from a $Cu(OTf)_2$-catalyzed isomerization of functionalized cyclopropenes to furan derivatives, which was reported in 2014.[51]

One of our recent studies[35] also showed the synthesis of an interesting disubstituted amide analogue of a butadiene derivative starting from α,β-conjugated amides. In that study, the cisoid structure of the butadiene derivative was confirmed with single-crystal X-ray analysis. On the basis of these initial results, a number of different catalysts, solvents, and operating procedures were tested to optimize the reaction conditions of metal carbenoids with acetylenic carbonyls. Thus, we realized a series of experiments for the reaction of **1a** with **2A** (Table 2). After these reactions, $Cu(acac)_2$ was seen as an effective catalyst in both benzene and dichloroethane solvents at 80 °C.

As expected, the diazo compound **2A** with $Rh_2(OAc)_4$ in CH_2Cl_2 at 45 °C (condition V) could not yield the corresponding carbenoid since dimethyl diazomalonate (**2A**) requires relatively elevated temperatures



Scheme 4. Formation mechanisms for the butadiene derivatives via cyclopropane derivative.

Table 2. Dimethyl diazomalonate (**2A**) and 2-octynal (**1a**) reaction under different conditions.

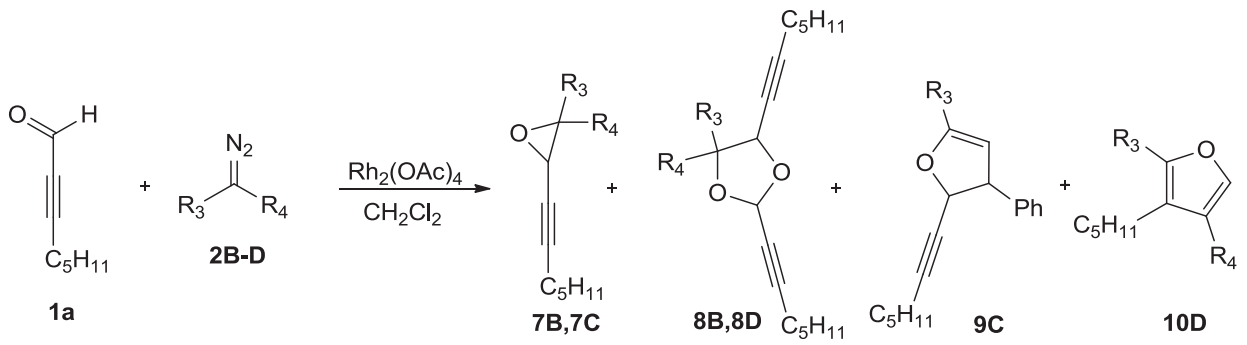
Condition	Catalyst	Solvent	Temp. (°C)	**3a** (*syn/anti*)	**4a**
			GC ratio (%)[a]		
I	$Cu(acac)_2$	Benzene	80	80 (1:1)	20
II	$Cu(acac)_2$	Dichloroethane	80	82 (1.2:1)	18
III	$Rh_2(OAc)_4$	Benzene	80	80 (1:1)	20
IV	$Rh_2(OAc)_4$	Dichloroethane	80	Very low	Very low
V	$Rh_2(OAc)_4$	Dichloromethane	40	No reaction product	

[a]Relative product ratios were determined by gas chromatography (GC).

to produce reactive carbene. Also in dichloroethane (condition IV), there was no satisfying yield although the temperature was 80 °C; however, the $Rh_2(OAc)_4$ catalyst worked well in benzene at 80 °C (condition III) and yielded the same results as $Cu(acac)_2$. From these results, it could be said that $Cu(acac)_2$ reactions are not affected by the solvent; dichloroethane and benzene both worked well since their working temperature is 80 °C. On the contrary, $Rh_2(OAc)_4$ reactions are affected more by the solvent type.

In order to check the effect of the substituents on the diazo compound, we studied the reactions of 2-octynal (**1a**) with different diazo carbonyl compounds: 1-diazo-1-phenylpropan-2-on (**2B**), (*E*)-methyl 2-diazo-4-phenyl-3-enoat (**2C**), and ethyl diazoacetate (**2D**). In these attempts dichloromethane was used as a solvent at 40 °C in order to prevent the probable decomposition of reactive diazo compounds at elevated temperatures. The results of performed reactions are summarized in Table 3.

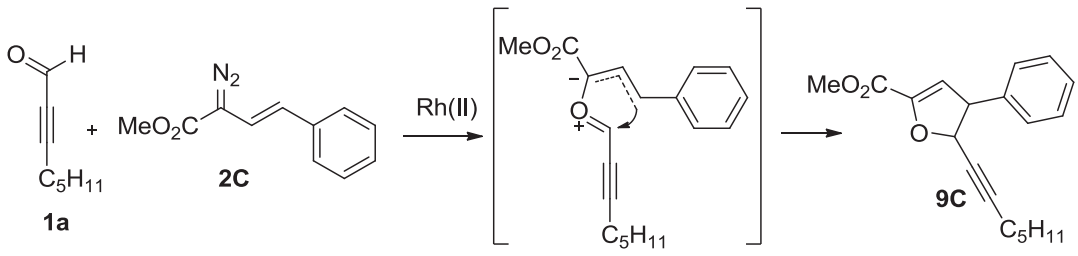
Table 3. $Rh_2(OAc)_4$-catalyzed reactions of 2-octynal with diazocarbonyls (**2A**–**2D**).



Diazo **(2)**	$\mathbf{R^3}$	$\mathbf{R^4}$	**7**	**8**	**9**	**10**
			GC ratio, %[a]			
B	-$COCH_3$	Ph	76 (4:3)[b]	24 (4:3:2:2)[b]	-	-
C	-CO_2CH_3	-CH=CHPh	23	-	75 (3:1)[b]	-
D	-$CO_2C_2H_5$	-H	-	62 (2:2:1:1)[b]	-	33

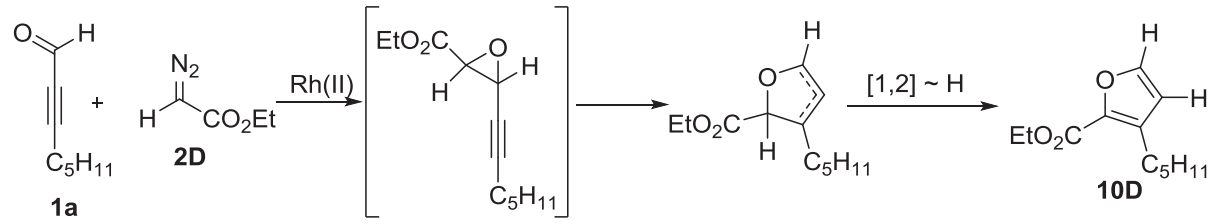
[a] Relative product ratios were determined by gas chromatography (GC); there are also some minor undetermined products. [b] Obtained as isomer mixtures.

Despite the undesirable result with diazo carbonyl **2A** due to its very stable character, other diazo carbonyls (**2B**–**2D**) resulted in satisfactory yields when the $Rh_2(OAc)_4$ catalyst was used in dichloromethane at 40 °C. Since the reactions of donor-acceptor (DA) diazo compounds give better results with Rh(II) catalyst in dichloromethane,[34] $Rh_2(OAc)_4$ was preferred over $Cu(acac)_2$ for the following reactions. The reaction of 2-octynal (**1a**) and donor-acceptor (DA) 1-diazo-1-phenylpropan-2-one (**2B**) resulted in the formation of epoxide (**7B**) and 1,3-dioxolane isomers (**8B**). When the reaction was performed with another DA, diazo carbonyl (*E*)-methyl 2-diazo-4-phenylbut-3-enoate (**2C**), dihydrofuran derivative **9C** was observed as the major product along with epoxide derivative **7C**. Because of the presence of a vinyl group in diazocarbonyl **2C**, the intermediate carbonyl ylide could realize a [1,5]-electrocylization reaction to produce dihydrofuran derivative **9C** (Scheme 5).



Scheme 5. Formation mechanism for the dihydrofuran derivative **9C**.

The reaction of 2-octynal (**1a**) and ethyl diazoacetate (**2D**), which yielded furan derivative **10D** near dioxolane isomers **8D**, was highly surprising. The plausible mechanism for the formation of this furan derivative (**10D**) may involve epoxide ring formation of the corresponding carbonyl ylide followed by rearrangement to a five-membered ring and 1,2-hydride shift (Scheme 6).



Scheme 6. Formation mechanism for the furan derivative **10D**.

In the present literature, there is only one report about the copper(I) iodide-catalyzed [4+1] cycloaddition reaction of α,β-acetylenic ketones with diazoacetates producing 2,3,5-trisubstituted furans in fair to good yields.[50] It is thus reported herein for the first time that polysubstituted furan **10D** could also be obtained from the reactions of α,β-acetylenic aldehyde with ethyl diazoacetate using rhodium catalyst, albeit with modest yield. In spite of the used catalyst, $Rh_2(OAc)_2$, which was claimed to be an inefficient one in the previous report,[50] formation of these furan derivatives was highly surprising. Another interesting point was the preferential migration of ethoxycarbonyl function being different from the previous report.

It is noteworthy that two acetylenic esters, **1b** and **1c**, did not realize any product over carbonyl-ylide formation but easily gave polysubstituted butadienes (**6**) in good yields over cyclopropene derivatives.

In conclusion, the catalytic reactions between acetylenic carbonyl compounds and diazocarbonyls have been presented. Aldehyde and ester functionalities on the acetylenic carbonyl had a drastic impact on the product distribution; for example, acetylenic esters preferred to form a cyclopropane ring and/or derivatives under the studied conditions. Thus, novel butadiene derivatives **6c** and **6d** were obtained efficiently by the approach used. Moreover, oxirane (**7B**, **7C**) and dihydrofuran (**9C**) derivatives could be synthesized in relatively high yields with a similar method.

Furthermore, subsequent derivatives of the synthesized compounds may be used as valuable intermediates, especially in the synthesis of natural products and their analogues. The recent literature shows that alkyne functionalized dioxoles give diketone derivatives to be further used for the synthesis of novel naphthalene derivatives with pharmaceutical activity.[54,55] Penta-ester substituted butadienes might also allow the synthesis of different polymer materials after the hydrolysis of ester groups.[56]

3. Experimental

3.1. General

Dimethyl diazomalonate was prepared according to the literature.[57] All other reagents and solvents were supplied commercially as reagent grade. Flash column chromatography was carried out on silica gel 60 (70–230 mesh). NMR spectra were recorded in $CDCl_3$ at ambient temperature on a Bruker AC (^{1}H: 250 MHz; ^{13}C: 60 MHz) and Varian Unity Inova (^{1}H: 500 MHz; ^{13}C: 125 MHz). TMS was always applied as the internal standard. Data are reported as follows: chemical shift, multiplicity (s: singlet, brs: broad singlet, d: doublet, dd: doublet of doublets, t: triplet, q: quartet, m: multiplet), coupling constants (J in Hz), and integration. GC/MS: Hewlett-Packard instrument, with HP-1 capillary column (24 m) packed with cross-linked (phenylmethyl)siloxane. Column temperature program: Isothermal at 100 °C for 5 min, heated to 290 °C at 20 °C/min and kept isothermal for 10 min. Retention times (t_R) of the synthesized compounds were given in minutes. IR spectra: PerkinElmer Spectrum One. Reported melting points are uncorrected.

3.2. General procedure for the catalytic reactions of dimethyl diazomalonate (2A) with α,β-acetylenic carbonyls

To a solution of α,β-acetylenic carbonyl (**1a-1d**, 6.6 mmol) in benzene (10 mL) was added $Cu(acac)_2$ (0.02 mmol) and the mixture was heated at reflux. A solution of dimethyl diazomalonate (3.3 mmol) in benzene (5 mL) was added dropwise over 3 h. When the IR spectrum indicated total consumption of dimethyl diazomalonate (absence of characteristic diazo band at 2130 cm^{-1}), the reaction mixture was concentrated under reduced pressure and subjected to flash silica gel chromatography. Different types of products (**3**–**6**) were obtained from each reaction.

3.2.1. Dimethyl 2,5-di(hept-1-yn-1-yl)-1,3-dioxolane-4,4-dicarboxylate (3a)

Obtained as two isomers with the ratio of 1:1.2 (totally 80% GC ratio). Minor isomer was isolated alone with 33% yield and major isomer was observed with compound **4a**. However, they could not be identified as *E* or *Z*.

3.2.1.1. Major isomer of 3a

^{1}H NMR (500 MHz, $CDCl_3$): 5.68 (t, J = 1.5 Hz, 1H), 5.34 (t, J = 2.0 Hz, 1H), 3.85 (bs, 6H), 2.26 (td, J = 7.4 and 1.5 Hz, 2H), 2.21 (td, J = 7.3 and 1.2 Hz, 2H), 1.56–1.47 (m, 4H), 1.39–1.29 (m, 8H), 0.90 (t, J= 7.3 Hz, 6H). ^{13}C NMR (125 MHz $CDCl_3$): 167.1, 166.0, 95.0, 90.9, 90.0, 89.2, 86.4, 75.7, 71.9, 53.5, 53.1, 31.0, 30.9, 27.9, 27.6, 22.1 (2C), 18.8 (2C), 13.9 (2C). t_R (min): 13.85; EI-MS (m/z) 377 (4, M^+), 319 (33), 307 (1), 286 (3), 254 (43), 222 (21), 195 (18), 139 (100), 135 (34), 59 (22).

3.2.1.2. Minor isomer of 3a

^{1}H NMR (500 MHz, $CDCl_3$): 6.00 (t, J = 1.3 Hz, 1H), 5.64 (t, J = 1.9 Hz, 1H), 3.84 (s, 3H), 3.81 (s, 3H), 2.21 (td, J = 7.2 and 1.4 Hz, 2H), 2.19 (td, J = 7.3 and 2.2 Hz, 2H), 1.52–1.45 (m, 4H), 1.35–1.28 (m, 8H), 0.89 (t, J= 7.3 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): 165.7, 165.3, 94.2, 90.0, 88.8, 85.9, 72.5, 71.3, 70.5, 52.4, 52.0, 29.9 (2C), 26.9, 26.6, 21.1 (2C), 17.7, 17.6, 12.9 (2C). t_R (min): 13.95; EI-MS (m/z) 377 (4, M^+), 319 (33), 307 (1), 286 (3), 254 (43), 222 (21), 195 (18), 139 (100), 135 (34), 59 (22). HRMS 379.2108 [$C_{21}H_{30}O_6$ + H], calcd. 379.2121.

3.2.2. Dimethyl 5-formyl-4,6-dipentyl-3-oxabicyclo[4.1.0]hepta-1,4-diene-7,7-dicarboxylate (4a)

Obtained in a mixture with the minor isomer of **3a** (GC ratio of **4a** was observed as 20% in the mixture). ^{1}H NMR (500 MHz, $CDCl_3$): 9.99 (s, 1H), 5.80 (brs, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 2.20 (td, J= 7.9 and 2.0 Hz, 2H), 1.56–1.47 (m, 6H), 1.39–1.27 (m, 8H), 0.88 (t, J = 7.3 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): 185.2, 167.1, 166.8, 154.3, 137.4, 94.2, 77.3, 73.4, 72.1, 53.4, 53.3, 32.0, 30.9, 30.2, 29.7, 28.0, 25.8, 22.2, 18.8, 13.9 (2C). t_R (min): 14.55; EI-MS (m/z) 319 (65, M^+), 291 (100), 259 (25), 231 (15), 119 (26), 105 (15), 91 (30), 59 (20).

3.2.3. Dimethyl 2,5-bis(phenylethynyl)-1,3-dioxolane-4,4-dicarboxylate (3b)

Obtained as dark orange oil with 79% yield (with 85% GC ratio) as two isomers with the ratio of 1:3.

3.2.3.1. Major isomer of 3b

^{1}H NMR (500 MHz, $CDCl_3$): 7.41–7.44 (m, 4H), 7.40–7.33 (m, 6H), 6.35 (s, 1H), 5.98 (s, 1H), 3.89 (s, 3H), 3.85 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): 166.4, 166.1, 132.0 (2C), 131.9 (2C), 129.4, 129.3, 128.5, 128.4 (3C), 121.2, 121.0, 95.7, 89.6, 88.0, 87.1, 80.9, 71.8, 53.7, 53.4. t_R (min): 19.20; EI-MS (m/z) 390 (2, M^+), 331 (5), 244 (35), 129 (30), 114 (100), 59 (10). HRMS 391.1190 [$C_{23}H_{18}O_6$ + H], calcd. 391.1182.

3.2.3.2. Minor isomer of 3b

^{1}H NMR (500 MHz, $CDCl_3$): 7.49–7.44 (m, 4H), 7.40–7.33 (m, 6H), 6.10 (s, 1H), 5.77 (s, 1H), 3.90 (s, 3H), 3.87 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): 166.5, 165.7, 132.1, 131.9 (2C), 131.8, 129.4, 129.2, 129.1, 128.3, 128.2 (2C), 121.4, 121.3, 95.9, 89.5, 88.0, 87.4, 82.4, 81.7, 72.1, 53.6, 53.4. t_R (min): 19.20; EI-MS (m/z) 390 (2, M^+), 331 (5), 244 (35), 129 (30), 114 (100), 59 (10). HRMS 391.1190 [$C_{23}H_{18}O_6$ + H], calcd 391.1182.

3.2.4. 2-Ethyl 1,1,4,4-tetramethyl 3-ethylbuta-1,3-diene-1,1,2,4,4-pentacarboxylate (6c)

Obtained as orange oil with 81% yield (with 90% GC ratio). ^{1}H NMR (250 MHz, $CDCl_3$): 4.20 (q, J = 7.0 Hz, 2H), 3.84 (s, 3H), 3.81 (s, 3H), 3.72 (s, 3H), 3.66 (s, 3H), 2.55–2.30 (m, 2H), 1.22 (t, J = 6.9 Hz, 3H), 1.02 (t, J = 7.4 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): 164.4, 164.1, 162.9 (2C), 162.0, 161.4, 153.3, 130.7, 124.8, 61.4, 52.0 (2C), 51.5, 51.4, 28.1, 12.8, 11.0. t_R (min): 13.17; EI-MS (m/z) 386 (1, M^+), 327 (100), 323 (10), 313 (12), 249 (10), 221 (10), 191 (7), 163 (5), 105 (4), 77 (5), 59 (7). HRMS 387.1284 [$C_{17}H_{22}O_{10}$ + H], calcd 387.1291.

3.2.5. 2-Ethyl 1,1-dimethyl 3-phenylcycloprop-2-ene-1,1,2-tricarboxylate (5d)

Obtained as light yellow oil with 16% yield (with 20% GC ratio). ^{1}H NMR (250 MHz, $CDCl_3$): 7.79 (d, J = 5.8 Hz, 2H), 7.50 (d, J = 6.7 Hz, 3H), 4.38 (q, J = 7.1 Hz, 2H), 3.74 (s, 6H), 1.38, (t, J = 7.0 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ 165.9, 165.0 (2C), 142.2, 131.4, 128.9, 127.7, 126.4, 113.0, 59.2, 58.2, 51.5, 51.4, 14.1 ppm. t_R (min): 12.95, EI-MS (m/z) 304 (65, M^+), 289 (62), 259 (13), 245 (41), 229 (77), 227 (16), 203 (31), 173 (25), 129 (74), 105 (100), 59 (5). HRMS 305.1031 [$C_{16}H_{16}O_6$ + H], calcd. 305.1025.

3.2.6. 2-Ethyl 1,1,4,4-tetramethyl 3-phenylbuta-1,3-diene-1,1,2,4,4-pentacarboxylate (6d)

Obtained as dark orange oil with 67 % yield (with 75% GC ratio). ^{1}H NMR (250 MHz, $CDCl_3$): 7.43–7.34 (m, 5H), 4.20 (q, J = 7.1 Hz, 2H), 3.88 (s, 3H), 3.78 (s, 3H), 3.69 (s, 3H), 3.60 (s, 3H), 1.17 (t, J = 7.1 Hz, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): 166.2, 164.9, 164.0, 163.3, 162.8, 149.4, 142.0, 136.1, 133.0, 130.0, 128.8 (2C), 128.6 (2C), 127.6, 62.7, 53.2 (2C), 52.9, 52.7, 13.9 ppm. t_R (min): 14.71; EI-MS (m/z) 434 (1, M^+), 389 (14), 375 (100), 329 (46), 255 (17), 203 (8), 153 (8), 129 (8), 59 (5). HRMS 435.1272 [$C_{21}H_{23}O_{10}$ + H], calcd. 435.1291.

3.3. General procedure for the catalytic reactions of 2-octynal (1a) with different diazo carbonyls

To a solution of 2-octynal (6.6 mmol) (**1a**) in dichloromethane (10 mL) was added $Rh_2(OAc)_4$ (0.02 mmol) and the mixture was heated at reflux. A solution of the corresponding diazo carbonyl (3.3 mmol) in dichloromethane (5 mL) was added dropwise over 3 h. When the IR spectrum indicated total consumption of the characteristic

diazo band, the reaction mixture was concentrated under reduced pressure and subjected to flash silica gel chromatography. Different types of products (**7**–**10**) were obtained from each reaction.

3.3.1. 1-(3-(Hept-1-yn-1-yl)-2-phenyloxiran-2-yl)ethanone (7B)

Obtained as yellow oil with 76% GC ratio as two isomers with the ratio of 1.5:2. Only the isomer major isomer was isolated alone from the mixture but it could not be identified as E or Z.

3.3.1.1. Major isomer of 7B

^{1}H NMR (500 MHz, $CDCl_3$): 7.51–7.49 (m, 2H), 7.40–7.34 (m, 3H), 3.85 (t, J = 1.3 Hz, 1H), 2.18 (s, 3H), 1.99 (td, J = 6.7 and 1.3 Hz, 2H), 1.23–1.11 (m, 4H), 1.05–1.00 (m, 2H), 0.81 (t, J = 7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): 203.7, 132.1, 128.5 (2C), 127.9 (2C), 127.8, 89.4, 73.4, 68.6, 51.5, 30.5, 27.3, 22.0, 18.5, 13.8. t_R: 11.33; EI-MS (m/z): 256 (M^+, 57), 213 (13), 185 (7), 129 (13), 105 (100), 77 (53).

3.3.1.2. Minor isomer of 7B

t_R (min): 11.71; EI-MS (m/z): 256 (M^+, 57), 213 (13), 185 (7), 129 (13), 105 (100), 77 (53).

3.3.2. 1-(2,5-Di(hept-1-yn-1-yl)-4-phenyl-1,3-dioxolan-4-yl)ethanone (8B)

Obtained as yellow oil with 18% yield (with 24% GC ratio) as four isomers with the ratio of 1:1:1.5:2. All isomers were isolated together in one fraction and the structures were tentatively identified.

3.3.2.1. Major isomer of 8B

^{1}H NMR (500 MHz, $CDCl_3$): 7.61–7.32 (m, 5H), 5.49 (brs, 1H), 4.63–4.59 (m, 1H), 2.23 (s, 3H), 1.74–1.53 (m, 8H), 1.52–1.48 (m, 4H), 1.38–1.19 (m, 4H), 0.89 (t, J = 7.3 Hz, 6H). t_R (min): 15.95; EI-MS (m/z): 337 (20), 256 (3), 213 (8), 171 (1), 157 (7), 105 (100), 93 (8), 77 (19).

3.3.2.2. Other major isomer of 8B

^{1}H NMR (500 MHz, $CDCl_3$): 7.61–7.32 (m, 5H), 6.39 (t, J = 2.0 Hz, 1H), 5.04 (s, 1H), 2.20 (s, 3H), 1.74–1.53 (m, 8H), 1.52–1.48 (m, 4H), 1.38–1.19 (m, 4H), 0.92–0.81 (m, 6H). t_R (min): 15.75; EI-MS (m/z): 337 (20), 256 (3), 213 (8), 171 (1), 157 (7), 105 (100), 93 (8), 77 (19).

3.3.2.3. Minor isomer of 8B

^{1}H NMR (500 MHz, $CDCl_3$): 7.61–7.32 (m, 5H), 5.69 (t, J = 2.0 Hz, 1H), 4.25 (s, 1H), 2.43 (s, 3H), 1.74–1.53 (m, 8H), 1.52–1.48 (m, 4H), 1.38–1.19 (m, 4H), 0.92–0.81 (m, 6H). t_R (min): 15.38; EI-MS (m/z): 337 (20), 256 (3), 213 (8), 171 (1), 157 (7), 105 (100), 93 (8), 77 (19).

3.3.2.4. Minor isomer of 8B

^{1}H NMR (500 MHz, $CDCl_3$): 7.61–7.32 (m, 5H), 5.68 (t, J = 1.9 Hz, 1H), 4.71 (s, 1H), 2.31 (s, 3H), 1.74–1.53 (m, 8H), 1.52–1.48 (m, 4H), 1.38–1.19 (m, 4H), 0.92–0.81 (m, 6H). t_R (min): 15.40; EI-MS (m/z): 337 (20), 256 (3), 213 (8), 171 (1), 157 (7), 105 (100), 93 (8), 77 (19).

3.3.3. (*E*)-Methyl 3-(hept-1-yn-1-yl)-2-styryloxirane-2-carboxylate (7C)

The product (with 23% GC ratio) was isolated with the starting compound 2-octynal. ^{1}H NMR (500 MHz, $CDCl_3$): 7.37–7.15 (m, 5H), 6.67 (d, J = 16.3 Hz, 1H), 6.58 (d, J = 16.3 Hz, 1H), 3.84 (s, 3 H), 3.43 (t, J = 1.7 Hz, 1H), 2.19 (td, J = 7.3 and 1.7 Hz, 2H), 1.39–1.25 (m, 6 H), 0.78 (t, J = 7.2 Hz, 3H). t_R (min): 13.09; EI-MS (m/z): 298 (M^+, 15), 283 (12), 241 (7), 152 (10), 131 (11), 115 (22), 105 (100), 77 (24), 55 (10).

3.3.4. Methyl 5-(hept-1-yn-1-yl)-4-phenyl-4,5-dihydrofuran-2-carboxylate (9C)

9C was obtained as two isomers with the ratio of 3:1 (75% GC ratio for both isomers). The major isomer was isolated as yellow oil with 42% yield and the minor one was obtained in a mixture with its water adduct. The isomers could not be identified as E or Z.

3.3.4.1. Major isomer of 9C

^{1}H NMR (500 MHz, $CDCl_3$): 7.36–7.18 (m, 5H), 6.07 (d, J = 3.4 Hz, 1H), 5.55 (dt, J = 10.3 and 1.7 Hz, 1H), 4.30 (dd, J = 9.9 and 3.0 Hz, 1H), 3.90 (s, 3H), 2.26 (td, J = 6.9 and 2.2 Hz, 2H), 1.50–1.00 (m, 6H), 0.80 (t, J = 7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.3, 138.2, 131.4, 131.3 (2C), 130.5 (2C), 129.2, 103.7, 87.8, 82.4, 67.7, 51.9, 48.0, 30.3, 29.7, 24.7, 21.2, 16.5. t_R (min): 13.09. EI-MS (m/z): 298 (M^+, 12), 239 (8), 211 (25), 155 (29), 141 (42), 131 (100), 91 (57), 77 (49), 55 (31).

3.3.4.2. Minor isomer of 9C

^{1}H NMR (500 MHz, $CDCl_3$): 7.36–7.18 (m, 5 H), 5.68 (d, J = 9.0 Hz, 1H), 5.00 (dt, J = 6.9 and 2.2 Hz, 1H), 4.32 (dd, J = 11.2 and 7.3 Hz, 1H), 3.92 (s, 3H), 2.00 (td, J = 6.9 and 1.6 Hz, 2H), 1.50–100 (m, 6H), 0.84 (t, J = 7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): 172.0, 144.1, 138.2, 131.1 (2C), 130.5 (2C), 129.2, 103.7, 87.8, 82.4, 77.8, 52.0, 48.0, 30.5, 29.7, 24.8, 21.4, 16.5. t_R (min): 13.22.

3.3.5. Methyl 5-(hept-1-yn-1-yl)-3-hydroxy-4-phenyltetrahydrofuran-2-carboxylate (water adduct of 9C)

The product was not observed in the crude mixture and was obtained as two isomers after column chromatography. It could not be identified as E or Z.

3.3.5.1. Isomer of 9Cw

^{1}H NMR (500 MHz, $CDCl_3$): 7.36–7.18 (m, 5H), 5.46 (dt, J = 7.7 and 2.2 Hz, 1H), 4.61 (s, 1H), 3.95 (s, 3H), 3.74 (d, J = 6.5 Hz, 1H), 3.72 (d, J = 7.3 Hz, 2H), 2.03 (td, J = 6.9 and 1.6 Hz, 2H), 1.54–1.08 (m, 6H), 0.88–8.83 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): 167.1, 139.0, 131.3 (2C), 130.5 (2C), 129.3, 93.6, 85.4, 79.4, 75.8, 64.9, 54.3, 44.4, 33.2, 29.7, 24.7, 21.6, 16.5.

3.3.5.2. Isomer of 9Cw

^{1}H NMR (500 MHz, $CDCl_3$): 7.36–7.18 (m, 5H), 5.23 (dt, J = 8.2 and 2.1 Hz, 1H), 4.61 (s, 1H), 3.75 (s, 1H), 3.74 (d, J = 6.5 Hz, 1H), 3.72 (d, J = 7.3 Hz, 2H), 2.04 (td, J = 6.9 and 1.6 Hz, 2H), 1.08–1.54 (m, 6H), 0.88–0.83 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): 167.1, 139.2, 131.1 (2C), 130.8 (2C), 129.4, 94.0, 83.9, 79.9, 75.9, 66.2, 54.2, 42.6, 33.0, 29.7, 24.8, 21.7, 16.6.

3.3.6. Ethyl 2,5-di(hept-1-yn-1-yl)-1,3-dioxolane-4-carboxylate (8D)

Obtained as yellow oil with 24% yield (with 62% GC ratio) as four isomers with the ratio of 2:2:1:1. All isomers were isolated together in one fraction and the structures were tentatively identified.

t_R (min): 13.37, 13.29, 13.59 and 13.26 (ratio 2:2:1:1 respectively). EI-MS (m/z): 333 (M^+, 1), 261 (15), 210 (47), 153 (100), 123 (22), 91 (39), 81 (40), 55 (40).

3.3.6.1. Minor isomer of 8D

^{1}H NMR (500 MHz, $CDCl_3$): 5.96 (s, 1H), 5.15 (dt, J = 6.9 and 1.9 Hz, 1H), 4.72 (d, J = 6.9 Hz, 1H), 4.24 (qd, J = 7.3 and 3.0 Hz, 2H), 2.23 (td, J = 6.9 and 1.2 Hz, 2 H), 2.17 (td, J = 6.9 and 1.8 Hz, 2H), 1.50 (pentet, J = 7.3 Hz, 2H), 1.47 (pentet, J = 7.3 Hz, 2H), 1.37–1.25 (m, 8H), 1.30 (t, J = 7.3 Hz, 3H), 0.88 (t, J = 7.7 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): 168.2, 94.2, 90.2, 88.9, 88.7, 79.4, 77.2, 68.5, 61.4, 30.9 (2C), 27.9, 27.7, 22.1 (2C), 18.6 (2C), 14.2, 13.9. t_R (min): 13.59.

3.3.6.2. Minor isomer 8D

Isolated as a yellow oil with 8% yield. ^{1}H NMR (500 MHz, $CDCl_3$): 5.64 (t, J = 1.8 Hz, 1H), 4.93 (dt, J = 7.0 and 1.7 Hz, 1H), 4.56 (d, J = 6.9 Hz, 1H), 4.26 (qd, J = 7.3 and 0.5 Hz, 2H), 2.25 (td, J = 7.3 and 1.7 Hz, 2H), 2.18 (td, J = 7.3 and 1.7 Hz, 2H), 1.56 (pentet, J = 7.3 Hz, 2H), 1.49 (pentet, J = 7.3 Hz, 2H), 1.37–1.25 (m, 8H), 1.32 (t, J = 7.3 Hz, 3H), 0.89 (t, J = 7.7 Hz, 6H) ppm. t_R (min): 13.26. HRMS 335.4592 [$C_{20}H_{30}O_4$ + H], calcd. 335.4577.

3.3.7. Ethyl 3-pentylfuran-2-carboxylate (10D)

Obtained as an orange oil with 27% yield (with 33% GC ratio). ^{1}H NMR (500 MHz, $CDCl_3$): 7.43 (d, J = 1.7 Hz, 1H), 6.38 (d, J = 1.7 Hz, 1H), 4.35 (q, J = 7.3 Hz, 2H), 2.78 (t, J = 7.7 Hz, 2H), 1.58 (pentet, J = 7.3 Hz, 2H), 1.38 (t, J = 7.3 Hz, 3H), 1.34–1.29 (m, 4H), 0.88 (t, J = 7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): 159.5, 144.8, 139.8, 119.0, 113.8, 60.5, 31.5, 29.5, 25.5, 22.4, 14.4, 14.0. t_R (min): 9.09; EI-MS: 210 (M^+, 37), 167 (30), 154 (100), 138 (36), 125 (89), 81 (89), 41(25), 29 (29). HRMS 211.2799 [$C_{12}H_{18}O_3$ + H], calcd. 211.2775.

CCDC-1472527 contains the supplementary crystallographic data for this work. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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