Tetrahedron Letters 51 (2010) 6630–6634

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Ruthenium-catalyzed addition of carboxylic acids or cyclic 1,3-dicarbonyl compounds to propargyl alcohols

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ARTICLE INFO

Article history:
Received 3 August 2010
Revised 7 October 2010
Accepted 11 October 2010
Available online 16 October 2010

Keywords:
Addition
Homogeneous catalysis
Propargyl alcohols
Ruthenium
Vinylidene complexes

ABSTRACT

Monomeric ruthenium(0) complexes containing redox-coupled dienone ligands were found to catalyze the regio-selective addition of carboxylic acids or cyclic 1,3-dicarbonyl compounds to propargyl alcohols.

1. Introduction

Several ruthenium complexes catalyze the Markovnikov addition of carboxylic acids to alkynes.[1] The analogue addition to propargyl alcohols leads to β-oxopropyl esters by an addition *trans*-esterification sequence.[2] Ruthenium complexes that catalyze the anti-Markovnikov addition of acids to alkynes remains limited to a few electron rich examples.[3] Concerning the ruthenium-catalyzed anti-Markovnikov addition of carboxylic acids to propargyl alcohols Dixneuf and co-workers reported the addition of benzoic acid to terminal tertiary propargyl alcohols using Ru(η^3-methallyl)$_2$(dppe) as the precatalyst.[4] The latter reaction shows a stereo-selectivity favoring the formation of (*Z*)-hydroxy enolesters.

Ruthenium cyclopentadienone derivatives provide unique features toward catalytic transformations of bi-functional substrates due to the redox-coupling of the dienone ligand and its basic coordination site. We reported previously that complexes of type **1** catalyze the formation of α- or β-amino ketones, enamino ketones, aldehydes, ketones, imines, enynes, alkenes, and allenyl carbamates from propargyl alcohols.[5]

While extending our studies on new metal-catalyzed transformations of propargyl compounds we have now discovered that complexes of type **1** catalyze the anti-Markovnikov addition of carboxylic acids to propargyl alcohols. In contrast to the Dixneuf-system[4] only (*E*)-hydroxy enolesters are formed. With vinylogous carboxylic acids like cyclic 1,3-dicarbonyl compounds pyran structures are obtained. Two related ruthenium-catalyzed reactions have been described. Nishibayashi and co-workers reported the formation of pyran compounds from terminal secondary aromatic propargyl alcohols and cyclic 1,3-dicarbonyl compounds catalyzed by dimeric thiolate bridged complexes.[6] Gimeno and co-workers reported a ruthenium-catalyzed pyran ring formation from terminal or internal secondary aromatic propargyl alcohols with 1,3-cyclopentanedione while different 1,3-dicarbonyl compounds led to furan ring formation instead.[7]

2. Results and discussion

The ruthenium-catalyzed addition of carboxylic acids to terminal tertiary aromatic or aliphatic propargyl alcohols using **1a** (R = R′ = Ph) or **1b** (R = H, R′ = Me) as catalysts leads to high regio- and stereo-selectivity to (*E*)-hydoxy enolesters (**3**). Terminal secondary propargyl alcohols form β-oxopropyl esters (**4**) as well due to low regioselectivity (Scheme 1, Table 1). Internal propargyl alcohols remain unreactive under the same reaction conditions. The transformation does not occur in the absence of the ruthenium catalyst.

Cyclic 1,3-dicarbonyl compounds add to terminal propargyl alcohols in the presence of **1a** or **1b** (2 mol %) to form pyran compounds (**5**) in some cases accompanied by methylene dihydrofuran byproducts (**6**), other regioisomeric products were not detected. With 1,3-cyclopentanedione the reaction proceeds without an additive, otherwise CF_3COOH (TFA) was used as co-catalyst (2 mol %) (Scheme 2, Table 2).

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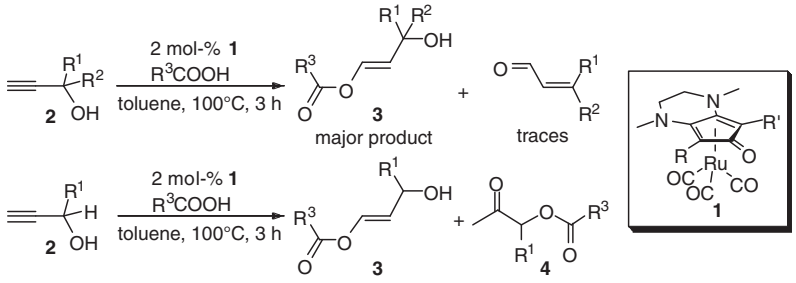
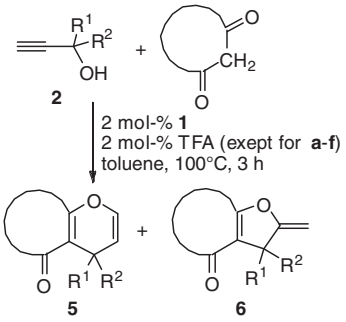
doi:10.1016/j.tetlet.2010.10.053



Scheme 1. Ruthenium-catalyzed addition of carboxylic acids to propargyl alcohols.

Table 1
Addition of carboxylic acids catalyzed by **1a**

Entry	R^1	R^2	R^3	Yield **3** (%)	Yield **4** (%)
a	Me	Me	Me	52	<1
b	Et	Me	Me	88	<1
c	C_5H_{10}		Me	85	<1
d	Ph	Me	Me	69	<1
e[10]	Me	H	Me	43	48
f	Ph	H	Me	30	59
g	Et	Me	CH=CH_2	53	<1
h	C_5H_{10}		CH=CH_2	48	<1
i	Et	Me	CH=CHPh	71	<1
j[10]	C_5H_{10}		CH=CHPh	64	<1



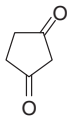
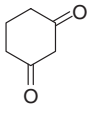
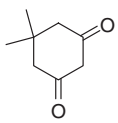
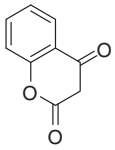
Scheme 2. Ruthenium-catalyzed addition of 1,3-dicarbonyl compounds to terminal propargyl alcohols.

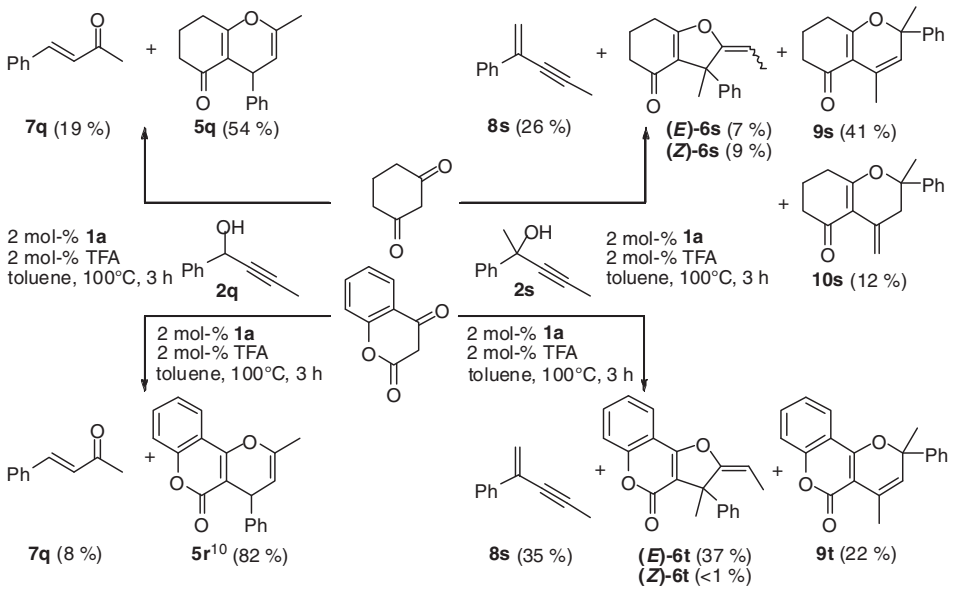
Secondary and tertiary aromatic or aliphatic terminal propargyl alcohols are suitable substrates while various internal aliphatic propargyl alcohols remain unreactive. Aliphatic propargyl alcohols are not transformed in the absence of the ruthenium complex. The reaction course of internal aromatic propargyl alcohols depends on the nature of the substrate. Secondary alcohols like **2q** lead to mixtures of enones (**7**) and pyran compounds (**5**), while tertiary alcohols like **2s** form enynes (**8**), dihydrofuran products (**6**), and the regioisomeric pyran compounds **9** accompanied by isomers like **10** in some cases (Scheme 3).

Aromatic propargyl alcohols undergo TFA-catalyzed benzylic substitution without the ruthenium catalyst to yield the propargylated compound **11**, as the sole product in case of secondary educt **2q** (Scheme 4). The acid catalyzed dehydration of **2s** to yield **8s** and the following cycloaddition of **8s** with phenols to yield 2-*H*-chromenes was reported previously by Sartori and co-workers and is closely related to the formation of compound **9**.[8]

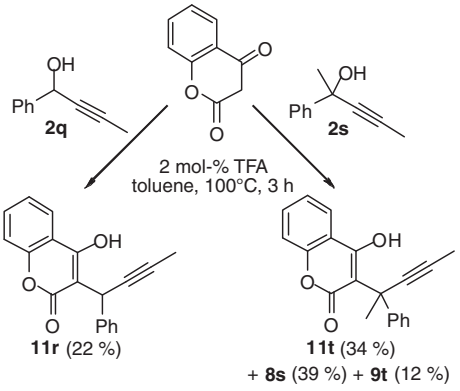
Pyran ring formation from acyclic 1,3-dicarbonyl compounds that form inner chelates in unpolar solvents was not observed. Terminal aliphatic propargyl alcohols like ethynylcyclohexanol (**2c**) form conjugated enynes **8** accompanied by terminal alkenes **12** in the absence of a suitable nucleophile instead (Scheme 5). This transformation does not occur without the ruthenium catalyst. Ruthenium-catalyzed formation of pyrans or furans from enyne **8c** and 1,3-dicarbonyl compounds in the presence of **1a** (2 mol %) and TFA (2 mol %) could not be detected.

Table 2
Addition of 1,3-dicarbonyl compounds to terminal propargyl alcohols catalyzed by **1a**

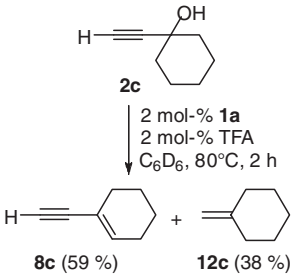
Entry	R^1	R^2	1,3-Dicarbonyl compound	Yield **5** (%)	Yield **6** (%)
a	Me	Me		48	<1
b[10]	Et	Me		86	<1
c	C_5H_{10}			84	<1
d[10]	Ph	Me		61	12
e	Me	H		45	<1
f[10]	Ph	H		71	<1
g	Me	Me		51	<1
h	Et	Me		86	<1
i[10]	C_5H_{10}			80	<1
j	Ph	Me		60	10
k	Me	H		44	<1
l	Ph	H		62	<1
m	Et	Me		55	10
n[10]	C_5H_{10}			49	13
o[10]	Et	Me		73	12
p	C_5H_{10}			67	16



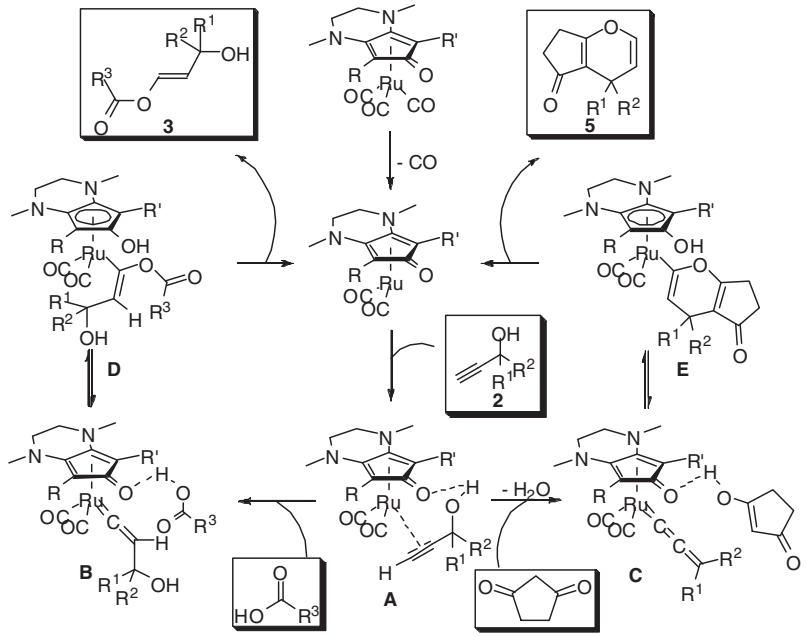
Scheme 3. Transformations of internal aromatic propargyl alcohols.



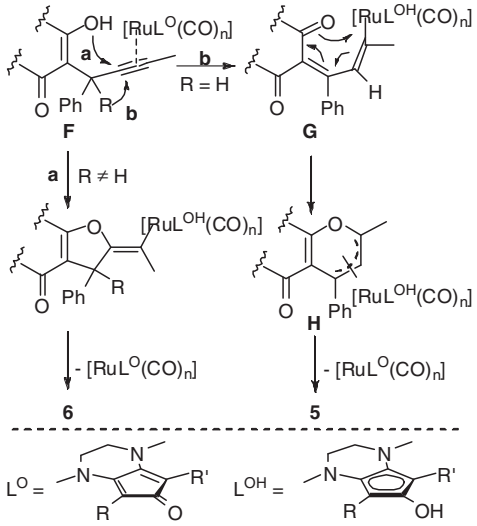
Scheme 4. TFA-catalyzed benzylic substitution.



Scheme 5. Formation of enyne **8c** and alkene **12c**.



Scheme 6. Postulated catalytic cycles for terminal substrates.



Scheme 7. Postulated transformation of internal aromatic substrates.

Due to the fact that internal aliphatic propargyl alcohols as well as aliphatic enynes like **8c** remain unreactive and in accordance with our previous results[5] we assume that the ruthenium-catalyzed-additions of carboxylic acids or cyclic 1,3-dicarbonyl compounds to terminal propargyl alcohols are initiated by chelating co-ordination of the propargyl alcohol to the 16-electron metal species (**A**) followed by the formation of ruthenium vinylidene complex **B** or allenylidene species **C**. Nucleophilic addition of a ligand-co-ordinated carboxylic acid at the C_α atom of vinylidene complex **B** should occur *trans*-selective from the less hindered site to give alkenyl complex **D** that liberates product **3**. Nucleophilic addition of a co-ordinated cyclic 1,3-dicarbonyl compound should occur at the C_γ atom of allenylidene complex **C** followed by cyclization of the resulting vinylidene species to give alkenyl complex **E** (Scheme 6).

The side products **4** and **6** could be driven from π-complexed terminal alkynes (analogues to **A**) that may be formed from vinylidene intermediates. The TFA needed as a co-catalyst in some cases may enhance the solubility of cyclic 1,3-diketones in toluene, promote the dehydration step of the allenylidene formation, and enhance the electrophilicity of the ruthenium center by protonation of the dienone ligand.

The transformation of internal aromatic propargyl alcohols may be initiated by TFA-catalyzed benzylic substitution. The following ruthenium-catalyzed cyclization could occur from the π-complexed alkyne **F** leading to methylene dihydrofuran compound **6** in case of quartary substrates like **11t** (Scheme 6, pathway **a**). Tertiary substrates like **11r** may undergo a 1,2-hydrogene shift prior to cyclization of the resulting unsaturated alkenyl complex **G** to give allyl complex **H** that liberates pyran compound **5** (Scheme 7, pathway **b**). A related hydrogene shift was reported previously.[5b,9] Competing hydrolysis of the alkenyl intermediate leads to Meyer-Schuster product **7**.

3. Conclusion

In summary, we have demonstrated that monomeric cyclopentadienone complexes of type **1** are suitable catalysts for regioselective additions of carboxylic acids or cyclic 1,3-dicarbonyl compounds to various terminal propargyl alcohols. The reaction mechanisms may involve the formation of neutral vinylidene or allenylidene species. The transformation of internal aromatic propargyl alcohols proceeds by different substrate-dependent pathways. Mechanistic details regarding intermediates of the catalytic cycles, stereochemical aspects, redox-coupling of the dienone ligand, and the role of its basic co-ordination site are currently under investigation.

4. General procedure

Compound **1a** (0.02 mmol) was dissolved in toluene (1 mL) mixed with a solution of TFA in toluene (20 μL, 1 M) if necessary and propargyl alcohol (1 mmol) as well as the nucleophilic component (1 mmol) were added. The mixture was stirred at 100 °C for 3 h under argon. Aqueous work-up and chromatography on silica furnished the purified products.

Acknowledgment

Constant support by the Fonds der Chemischen Industrie is gratefully acknowledged.

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10. *Data of selected compounds*
Compound **3e** ($C_6H_{10}O_3$): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35 (d, J = 7.1 Hz, 3H), 2.13 (s, 3H), 5.39 (dq, J = 7.6, 7.1 Hz, 1H), 5.46 (dd, J = 12.3, 7.6 Hz, 1H), 7.37 (d, J = 12.3 Hz, 1H) ppm. ^{13}C NMR (100 MHz, DEPT, $CDCl_3$): δ = 20.7 (CH_3), 21.3 (CH_3), 67.6 (CH), 114.1 (CH), 138.2 (CH), 167.7 (C) ppm. MS (EI): m/z 130 [M^+]. HRMS: calcd: 130.06299, found: 130.06276.
Compound **3j** ($C_{17}H_{20}O_3$): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26–1.70 (m, 10H), 5.71 (d, J = 12.5 Hz, 1H), 6.46 (d, J = 16.0, 1H), 7.40–7.42 (m, 3H), 7.51 (d, J = 12.5 Hz, 1H), 7.54–7.56 (m, 2H), 7.78 (d, J = 16.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, DEPT, $CDCl_3$): δ = 22.0 (CH_2), 25.4 (CH_2), 38.2 (CH_2), 70.4 (C), 117.3 (CH), 122.6 (CH), 128.2 (CH), 128.9 (CH), 130.7 (CH), 134.1 (C), 135.9 (CH), 146.9 (CH), 164.1 (C) ppm. MS (EI): m/z 272 [M^+]. HRMS: calcd: 272.14124, found: 272.14139.
Compound **5b** ($C_{11}H_{14}O_2$): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.74 (t, J = 7.6 Hz, 3H), 1.24 (dq, J = 13.6, 7.6 Hz, 1H), 1.31 (s, 3H), 2.02 (dq, J = 13.6, 7.6 Hz, 1H), 2.39–2.42 (m, 2H), 2.56–2.59 (m, 2H), 4.65 (d, J = 6.0 Hz, 1H), 6.48 (d, J = 6.2 Hz, 1H) ppm. ^{13}C NMR (100 MHz, DEPT, $CDCl_3$): δ = 10.3 (CH_3), 25.1 (CH_2), 28.2 (CH_3), 32.1 (CH_2), 33.3 (CH_2), 34.4 (C), 114.1 (CH), 119.5 (C), 138.7 (CH), 178.9 (C), 204.2 (C) ppm. MS (EI): m/z 178 [M^+]. HRMS: calcd: 178.09938, found: 178.09935.
Compound **5d** ($C_{15}H_{14}O_2$): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.77 (s, 3H), 2.35–2.40 (m, 2H), 2.60–2.64 (m, 2H), 4.98 (d, J = 6.1 Hz, 1H), 6.57 (d, J = 6.1 Hz, 1H), 7.10–7.51 (m, 5H) ppm. ^{13}C NMR (100 MHz, DEPT, $CDCl_3$): δ = 25.1 (CH_2), 26.2 (CH_3), 33.3 (CH_2), 36.7 (C), 114.9 (CH), 121.0 (C), 126.4 (CH), 127.0 (CH), 128.2 (CH), 137.4 (CH), 146.5 (C), 177.1 (C), 203.7 (C) ppm. MS (EI): m/z 226 [M^+]. HRMS: calcd: 226.09938, found: 226.09961.
Compound **5f** ($C_{14}H_{12}O_2$): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.36–2.40 (m, 2H),

2.59–2.68 (m, 2H), 4.30 (s br, 1H), 5.15 (dd, J = 6.4, 1.0 Hz, 1H), 6.63 (d, J = 6.4 Hz, 1H), 7.15–7.43 (m, 5H) ppm. ^{13}C NMR (100 MHz, DEPT, $CDCl_3$): δ = 25.4 (CH_2), 32.9 (CH_2), 34.5 (CH), 108.6 (CH), 117.3 (C), 126.4 (CH), 128.0 (CH), 128.4 (CH), 139.3 (CH), 142.8 (C), 178.1 (C), 203.0 (C) ppm. MS (EI): m/z 212 [M^+]. HRMS: calcd: 212.08373, found: 212.08379.

Compound **5i** ($C_{14}H_{18}O_2$): ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.27–1.35 (m, 1H), 1.42–1.49 (m, 5H), 1.60–1.64 (m, 2H), 1.92 (quint., J = 6.6 Hz, 2H), 2.34 (t, J = 6.6 Hz, 2H), 2.38 (t, J = 6.6 Hz, 2H), 2.53–2.58 (m, 2H), 5.43 (d, J = 6.3 Hz, 1H), 6.23 (d, J = 6.3 Hz, 1H) ppm. ^{13}C NMR (125 MHz, DEPT, $CDCl_3$): δ = 20.4 (CH_2), 20.8 (CH_2), 25.3 (CH_2), 28.5 (CH_2), 33.4 (C), 35.3 (CH_2), 39.5 (CH_2), 110.8 (CH), 117.6 (C), 135.0 (CH), 166.8 (C), 198.9 (C) ppm. MS (EI): m/z 218 [M^+]. HRMS: calcd: 218.13068, found: 218.13060.

Compound **5n** ($C_{16}H_{22}O_2$): ^{1}H NMR (600 MHz, CDCl3): δ = 1.04 (s, 6H), 1.27–1.33 (m, 1H), 1.42–1.49 (m, 5H), 1.61–1.64 (m, 2H), 2.20 (s, 2H), 2.24 (s, 2H), 2.53–2.58 (m, 2H), 5.43 (d, J = 6.6 Hz, 1H), 6.23 (d, J = 6.6 Hz, 1H) ppm. ^{13}C NMR (125 MHz, DEPT, $CDCl_3$): δ = 20.4 (CH_2), 20.7 (CH_2), 25.3 (CH_2), 27.9 (CH_3), 31.4 (C), 33.3 (C), 35.2 (CH_2), 42.0 (CH_2), 110.7 (CH), 116.3 (C), 135.1 (CH), 165.6 (C), 199.3 (C) ppm. MS (EI): m/z 246 [M^+]. HRMS: calcd: 246.16198, found: 246.16172.

Compound **5o** ($C_{15}H_{14}O_3$): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.82 (t, J = 7.6 Hz, 3H), 1.26 (dq, J = 13.6, 7.6 Hz, 1H), 1.52 (s, 3H), 2.44 (dq, J = 13.6, 7.6 Hz, 1H), 4.77 (d, J = 6.0 Hz, 1H), 6.63 (d, J = 6.0 Hz, 1H), 7.25–7.29 (m, 2H), 7.51 (t, J = 7.8 Hz, 1H), 7.74 (d, J = 8.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, DEPT, $CDCl_3$): δ = 10.6 (CH_3), 29.2 (CH_3), 32.4 (CH_2), 34.8 (C), 105.6 (C), 114.2 (CH), 114.3 (C), 116.3 (CH), 122.9 (CH), 123.8 (CH), 131.7 (CH), 137.1 (CH), 152.5 (C), 156.6 (C), 160.9 (C) ppm. MS (EI): m/z 242 [M^+]. HRMS: calcd: 242.09429, found: 242.09422.

Compound **5r** ($C_{19}H_{14}O_3$): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.01 (t, J = 1.2 Hz, 3H), 4.43 (dq, J = 4.5, 1.2 Hz, 1H), 5.00 (dq, J = 4.5, 1.1 Hz, 1H), 7.14 (t, J = 7.1 Hz, 1H), 7.21–7.29 (m, 6H), 7.46 (t, J = 7.4 Hz, 1H), 7.79 (d, J = 7.9 Hz, 1H) ppm. ^{13}C NMR (100 MHz, DEPT, $CDCl_3$): δ = 18.6 (CH_3), 36.5 (CH), 103.4 (C), 103.9 (CH), 114.5 (C), 116.7 (CH), 122.7 (CH), 124.0 (CH), 127.0 (CH), 128.2 (CH), 128.5 (CH), 131.8 (CH), 144.2 (C), 145.9 (C), 152.7 (C), 155.9 (C), 161.6 (C) ppm. MS (EI): m/z 290 [M^+]. HRMS: calcd: 290.09429, found: 290.09431.