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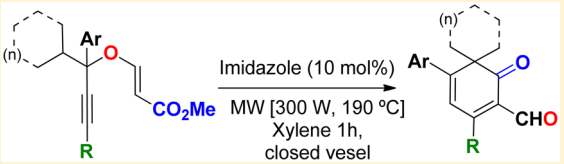
Synthesis of α-Quaternized 2,4-Cyclohexadienones from Propargyl Vinyl Ethers

David Tejedor,* Samuel Delgado-Hernández, Mariana Ingold,† and Fernando García-Tellado*

Instituto de Productos Naturales y Agrobiología, Consejo Superior de Investigaciones Científicas, Avda. Astrofísico Francisco Sánchez 3, 38 206 La Laguna, Tenerife, Islas Canarias, Spain

Supporting Information

ABSTRACT: A microwave-assisted and base-catalyzed domino manifold to construct 2,4-cyclohexadienone derivatives has been implemented. The domino manifold uses easily accessible tertiary propargyl vinyl ethers bearing a methine group at the homopropargylic position and imidazole as the catalyst to deliver 2,4-cyclohexadienones featuring a key formyl group and a quaternized carbon atom in good yields.



The α-quaternized 2,4-cyclohexadienone moiety constitutes an important structural motif of many bioactive natural products.[1] Some examples include trigoflavidone A,[1a] lepidotol A,[1b] garciniacowone A,[1c] fimbricalyx A,[1d] trigonostemone,[1e] and *ent*-3β-hydroxypimara-8(14),9,15-trien-12-one[1f] (Figure 1), which has been recently isolated and proven to be the biogenetic precursor of spruceanol, a cleistanthane diterpene with antitumor activity.[2] This biogenetic connection was proven by chemical means making use of the known propensity of this structural motif to host single bond migrations to generate the corresponding phenol derivatives.[3] This property converts these structural motifs in versatile and well-studied templates for the synthesis of substituted phenols.[3a] We envisioned that these scaffolds could be directly accessed in a diversity-oriented fashion through our recently described base-catalyzed rearrangement of readily available propargyl vinyl ethers **1** (PVEs) (Scheme 1A).[4]

The idea is outlined in Scheme 1B. When the starting tertiary PVE[5] bears a methine at the homopropargylic position, upon the formation of the 1-oxatriene intermediate via a sequential [3,3]-sigmatropic/imidazole-assisted [1,3]H-shift pair of reactions, two different reaction pathways could take place. We have previously demonstrated that the methylene-biased enolization pathway affords salicylaldehydes **5** via a tandem electrocyclization/imidazole-assisted aromatization reaction.[4a] On the other hand, we envisioned that the methine-biased enolization route would afford the cyclohexadiene hemiketal **IV** which would deliver the 2,4-cyclohexadione scaffold through elimination of methanol. We have also shown that the substitution grade of the terminal double bond of the enol-diene intermediate plays a pivotal role in determining the outcome of the domino manifold.[4a] Accordingly, we hypothesized that the formation of the enol-diene **II** should be favored over the formation of enol-diene **I**, and consequently, the whole process should be biased toward the formation of the 2,4-cyclohexadienone product **6**. Because the precursor PVEs can be accessed with a wide functional/structural diversity (Figure 2), the manifold should deliver the cyclohexadiene scaffolds hosting a high topological, structural, and functional diversity. With this idea in mind, we undertook the implementation of this domino strategy as a convenient and instrumentally simple preparative method for the diversity-oriented synthesis of these scaffolds.

We began this study exploring the reactivity of tertiary PVE **3a**, which presents a methine at the homopropargylic position to launch the methine-based enol route and a phenyl ring at the propargylic position to block the alternative methylene-biased enol pathway. According to Scheme 1B, **3a** should uniquely deliver the cyclohexadienone derivative **6a**. As expected, the microwave irradiation (300 W, 190 °C) of a solution of **3a** in xylene and in the presence of a catalytic amount of imidazole (10 mol %) generated the cyclohexadienone **6a** in 78% yield (Table 1). Once the chemical cartography of the domino process was established, we next studied the scope of this reaction by submitting PVEs **3b**–**h**[6] to the same reaction conditions (Table 1).[7] Gratifyingly, the reaction accommodated a convenient variety of functionalities on the structure of the tertiary PVEs. Thus, PVEs armed with a methine/aryl pair at the propargylic position and bearing a phenyl, *tert*-butyl, trimethylsilyl, or methoxycarbonyl substituent at the terminal alkyne position were consistently transformed into the corresponding 2,4-cyclohexadienone derivatives **6a**–**h** in good yields (59–87% yield). It should be pointed out that although the reaction of PVE **3g** delivered the corresponding cyclohexadienone **6g** (59% yield by NMR) accompanied by a minor amount of the rearranged product **6g-lac** (6%),[8] **6g** decomposed during chromatographic purification and could not be conveniently isolated. With the goal of increasing the yield of isolable **6g-lac**, in a different experiment crude **6g** was directly treated with methanol (190 °C, 10 min) to generate the **6g-lac** derivative (39% isolated yield). Although the overall yield of this transformation is considerably lower than the other

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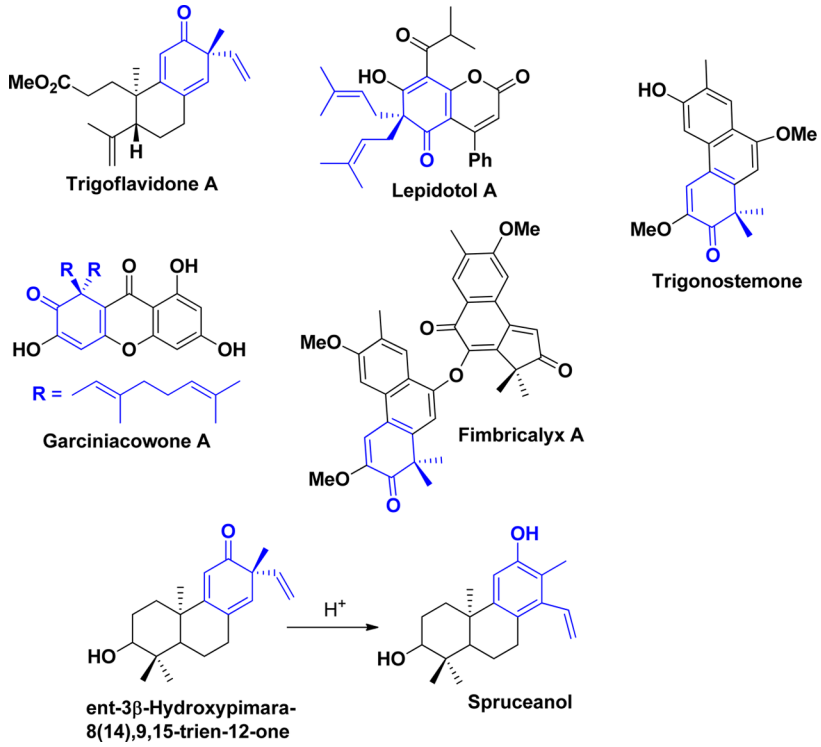

Figure 1. Selected natural products containing α-quaternized 2,4-cyclohexadienone motifs.

examples (yield range: 63−87%), it is still of preparative value for the access of this functionalized cyclohexadienone derivative which presents a functional complexity not easily accessible from other direct and metal-free methods.[9] From the point of view of complexity generation, cyclohexadienones derivatives **6e** and **6g** incorporate in their structures a chemical handle (Me_3Si, masked ester group) for further elaboration. Hence, the reaction manifold proved to be tolerant with a varied set of substituents to deliver the corresponding 2,4-cyclohexadienones bearing a formyl group at C-2, an all-carbon-quaternized center at C-6, and two differentiated substituents at C-3 and C-5.[10]

The microwave irradiation of PVE **3j**, able to react through the two pathways outlined in the Scheme 1B, followed the expected chemical cartography affording the corresponding cyclohexadienone **6j** (50% yield by NMR) as the major reaction product (Scheme 2) accompanied by the corresponding salicylaldehyde **5j** (25%). All attempts to isolate **6j** were unsuccessful, as it decomposed during the column chromatography separation.

We finally turned our attention to the rearrangement of PVEs **3k**−**3m** derived from naturally occurring nopinone, menthone, and isomenthone, which all contain both a methine and a methylene at the homopropargylic positions. For the case of (+)-nopinane, due to the presence of a bridgehead methine, it was anticipated that only the hydrogens bounded to the methylene carbon would participate in the enolization step to avoid the formation of a hypothetical anti-Bredt intermediate (Scheme 3). Indeed, when PVE **3k** was submitted to microwave irradiation under the standard reaction conditions, the expected polysubstituted salicylaldehyde **10** was obtained as the major product (73% yield) accompanied by a minor amount of benzoate **11** (17% yield), formed through the reaction pathway launched by the hydroxyl-triene **I**.[11]

Lastly, racemic PVEs **3l** and **3m** were synthesized from a commercially available mixture of DL-isomenthone and DL-menthone (Scheme 4) and were studied.[12] Interestingly, when both PVEs[13] were independently submitted to microwave irradiation under the standard reaction conditions a similar result was obtained: salicylaldehyde **12** as the major product (64%−65%) and an inseparable mixture of two salicylaldehyde **13** (26%−30%; 4:1 mixture of diastereomers) as minor products. These results were expected for a domino reaction following both chemical pathways outlined in Scheme 1B. Due to the increased stability of the triene intermediate **I** (the terminal double bond in triene **I** is more substituted than in triene **II**), the main reaction pathway affords salicylaldehyde **12** via a tandem electrocyclization/double elimination reaction. It should be pointed out that the facile elimination of the isopropyl group as propene from hemiketal intermediate **III** avoids the formation of the corresponding 2,4-cyclohexadienone derivative **6l**. This example demonstrates that the reaction manifold allows for a significant level of selectivity toward the methine-biased pathway when both possibilities are present.

In summary, we have implemented a microwave-assisted and base-catalyzed domino platform to construct 2,4-cyclohexadienone structural motifs from easily accessible tertiary propargyl vinyl ethers containing a methine group at the homopropargylic position. These 2,4-cyclohexadienones contain a key formyl group at C-2, an aryl substituent at C-3, different substituents at C-5, and a quaternized carbon at C-6.[10] On the other hand, PVEs derived from nopinone, menthone, or isomenthone deliver polysubstituted salicylaldehydes via a methylene-biased pathway or a methine-biased pathway followed by a more favored elimination of propene.

EXPERIMENTAL SECTION

General Information. ^{1}H NMR and ^{13}C NMR spectra of $CDCl_3$ solutions were recorded either at 400 and 100 MHz or at 500 and 125

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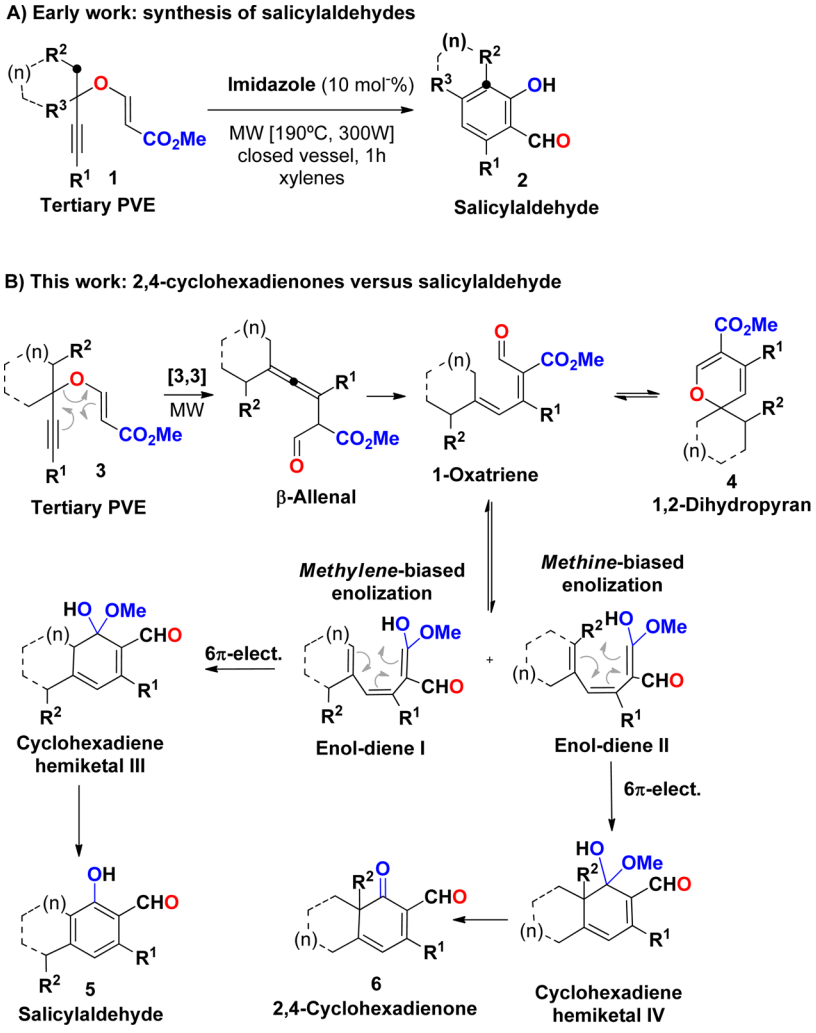
Scheme 1. Methine-Biased versus Methylene-Biased Enolization in the Microwave Assisted-Rearrangement of Tertiary Propargyl Vinyl Ethers



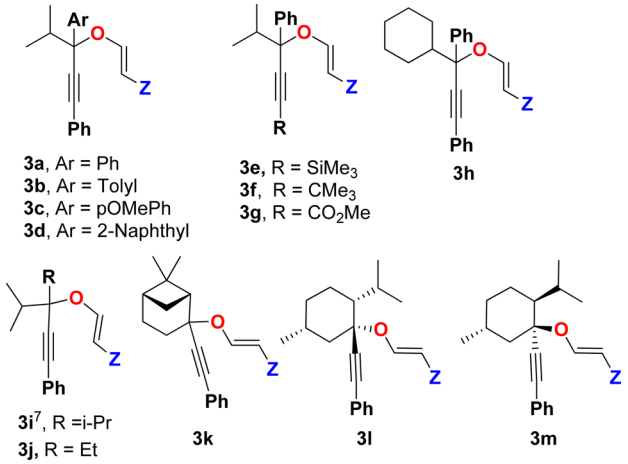
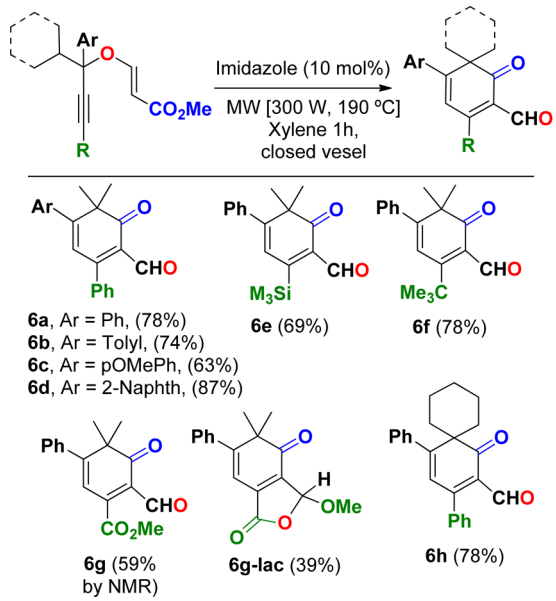


Figure 2. Structure of PVEs used in this study. Z = CO_2Me.

MHz, respectively. Microwave reactions were conducted in sealed glass vessels (capacity 10 mL) using a CEM Discover microwave reactor equipped with a surface sensor for temperature measuring of the reaction mixture. FT-IR spectra were measured in chloroform solutions using an FT-IR spectrophotometer. Mass spectra (low resolution) (EI/CI) and HRMS (EI/TOF) were obtained with a gas chromatograph/mass spectrometer. Analytical thin-layer chromatog-

Table 1. Synthesis of α-Quaternized 2,4-cyclohexadienones 6 from PVEs 3



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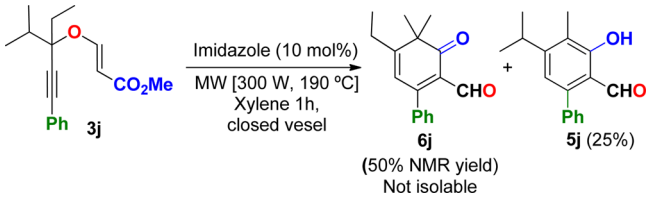
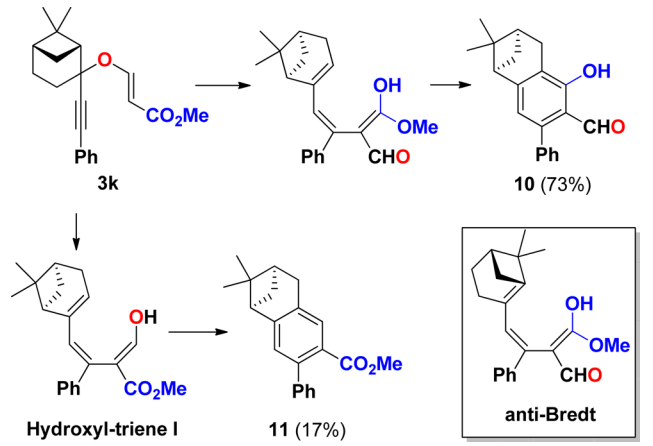
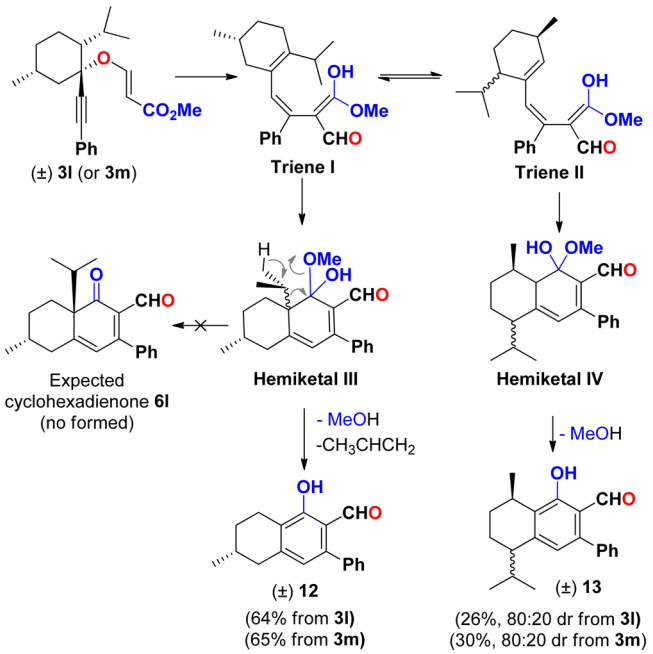
Scheme 2. Microwave-Assisted Rearrangement of PVE 3j



Scheme 3. Microwave-Assisted Rearrangement of Bicyclic PVE 3k



Scheme 4. Microwave-Assisted Rearrangement of PVEs 3l–m



raphy plates used UV-active silica on aluminum. Flash column chromatography was carried out with silica gel of particle size less than 0.020 mm, using appropriate mixtures of ethyl acetate and hexanes as eluents. All reactions were performed in oven-dried glassware. All materials were obtained from commercial suppliers and used as received unless otherwise noted. The propargyl alcohols were prepared by addition of the lithium acetylides onto the appropriate aldehydes or ketones following standard procedures. Propargyl vinyl ethers were prepared according to our previous experimental procedure (see below for a general procedure).[6] Note: PVEs **3a**, **3b**, **3c**, and **3h**, start to suffer the propargyl Claisen rearrangement at room temperature, what makes difficult their isolation and characterization as pure products. Nevertheless, they are isolated as pure 2*H*-pyrans **4** or mixtures of PVEs and 2*H*-pyrans, and they are subsequently used for the preparation of 2,4-cyclohexadienone products **6**.

Representative Procedure for the Synthesis of Propargyl Vinyl Ethers (3). Methyl propiolate (up to 4.0 mmol) was added dropwise (time of addition 10 min; more if needed, until completion) to a solution of 3-ethyl-4-methyl-1-phenylpent-1-yn-3-ol (2.0 mmol) and DABCO (0.20 mmol) in a 1:5 mixture of dry CH_2Cl_2 and hexane (10 mL). The reaction mixture was stirred for 5 min (TLC control). The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (silica gel; *n*-hexane/EtOAc, 90:10) to give **3j** (90%).

Representative Procedure for the Microwave-Assisted Reaction of Propargyl Vinyl Ethers. PVE **3d** (0.50 mmol) and imidazole (0.05 mmol) in dry xylene (1 mL) were placed in a microwave-special closed vial, and the solution was irradiated for 1 h in a single-mode microwave oven (300 W, 190 °C). After removing the solvent at reduced pressure the products were purified by flash column chromatography (silica gel, *n*-hexane/EtOAc 95/5) to yield **6d** (87%).

*(E)-Methyl 3-(3-(4-Methoxyphenyl)-4-methyl-1-phenylpent-1-yn-3-yloxy)acrylate (**3c**).* After its synthesis and purification **3c** partially rearranges to **4c**. The isolated material (sticky oil) is a 1:1 mixture that can be used as it is for the microwave-assisted reaction.

*(E)-Methyl 3-((4-Methyl-3-(naphthalen-1-yl)-1-phenylpent-1-yn-3-yl)oxy)acrylate (**3d**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.74 (d, 3H, ^3J(H,H) = 6.8 Hz), 1.36 (d, 3H, ^3J(H,H) = 6.8 Hz), 2.99–3.06 (m, 1H), 3.54 (s, 3H), 5.50 (d, 1H, ^3J(H,H) = 12.1 Hz), 7.36–7.41 (m, 3H), 7.44–7.53 (m, 3H), 7.59–7.61 (m, 2H), 7.74 (d, 1H, ^3J(H,H) = 12.1 Hz), 7.85–7.89 (m, 2H), 8.09 (d, 1H, ^3J(H,H) = 7.3 Hz), 8.52–8.55 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.9, 18.8, 37.3, 50.8, 85.8, 91.0, 91.4, 99.9, 121.9, 124.4, 125.6, 125.8, 126.2, 128.4 (2C), 128.5, 129.0, 129.2, 129.6, 130.4, 132.0 (2C), 134.6, 134.9, 159.0, 167.9 ppm; MS (70 eV): *m*/*z* (%): 384 (M^+, 92), 341 (91), 337 (100), 309 (67), 283 (91), 252 (63), 252 (46), 239 (33), 165 (36). Elemental analysis calcd (%) for $C_{26}H_{24}O_3$: C, 81.22; H, 6.29. Found: C, 81.28; H, 6.45. Pale yellow oil.

*(E)-Methyl 3-(4-Methyl-3-phenyl-1-(trimethylsilyl)pent-1-yn-3-yloxy)acrylate (**3e**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.25 (s, 9H), 0.72 (d, 3H, ^3J(H,H) = 6.8 Hz), 1.11 (d, 3H, ^3J(H,H) = 6.8 Hz), 2.16–2.22 (m, 1H), 3.61 (s, 3H), 5.39 (d, 1H, ^3J(H,H) = 12.1 Hz), 7.29–7.36 (m, 3H), 7.43–7.46 (m, 2H), 7.61 (d, 1H, ^3J(H,H) = 12.1 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ −0.24 (3C), 17.6, 17.7, 40.1, 50.9, 87.9, 96.8, 99.5, 101.3, 127.0 (2C), 128.2 (2C), 128.3, 139.9, 159.7, 168.0 ppm; MS (70 eV): *m*/*z* (%): 330 (M^+, 0.5), 287 (30), 230 (24), 229 (96), 199 (11), 73 (100); HRMS calculated for $C_{19}H_{26}O_3Si$: 330.1651, found 330.1658. Colorless oil.

*(E)-Methyl 3-(2,6,6-Trimethyl-3-phenylhept-4-yn-3-yloxy)acrylate (**3f**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.69 (d, 3H, ^3J(H,H) = 6.8 Hz), 1.10 (d, 3H, ^3J(H,H) = 6.6 Hz), 1.32 (s, 9H), 2.14–2.20 (m, 1H), 3.60 (s, 3H), 5.37 (d, 1H, ^3J(H,H) = 12.1 Hz), 7.26–7.35 (m, 3H), 7.42–7.45 (m, 2H), 7.64 (d, 1H, ^3J(H,H) = 12.1 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.7, 17.8, 27.8, 30.8 (3C), 40.2, 50.8, 74.8, 88.0, 99.0, 100.8, 127.0 (2C), 128.08 (2C), 128.14, 140.8, 160.0, 168.2 ppm; MS (70 eV): *m*/*z* (%): 314 (M^+, 0.2), 271 (24), 213 (100), 157 (42), 105 (39), 57 (66); HRMS calculated for $C_{20}H_{26}O_3$: 314.1882, found 314.1875. Colorless oil.

*(E)-Methyl 4-(3-Methoxy-3-oxoprop-1-enyloxy)-5-methyl-4-phenylhex-2-ynoate (**3g**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.78 (d, 3H, ^3J(H,H) = 6.9 Hz), 1.14 (d, 3H, ^3J(H,H) = 6.9 Hz), 2.24–2.32 (m, 1H), 3.61 (s, 3H), 3.82 (s, 3H), 5.43 (d, 1H, ^3J(H,H) = 12.1 Hz), 7.31–7.42 (m, 5H), 7.41 (d, 1H, ^3J(H,H) = 12.1 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.5, 17.6, 40.5, 51.0, 53.0, 81.4, 83.2, 87.0, 101.0, 126.8 (2C), 128.6 (2C), 128.9, 138.1, 153.1, 158.6, 167.6 ppm; MS (70 eV): *m*/*z* (%): 316 (M^+, 2.0), 273 (100), 215 (95), 187 (29), 172 (22), 155 (44); HRMS calculated for $C_{18}H_{20}O_5$: 316.1311, found 316.1308. Colorless oil.

*(E)-Methyl 3-(1-Cyclohexyl-1,3-diphenylprop-2-ynyloxy)acrylate (**3h–4h**).* After its synthesis and purification **3h** partially rearranges

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to **4h**. The isolated material (sticky oil) is a 2:1 mixture that can be used as it is for the microwave-assisted reaction. Characteristic data for **3h**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.61 (s, 3H), 5.45 (d, 1H, ^3J(H,H) = 12.1 Hz), 7.69 (d, 1H, ^3J(H,H) = 12.1 Hz) ppm; Characteristic data for **4h**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.48 (s, 3H), 5.61 (s, 1H), 7.71 (s, 1H) ppm.

*(E)-Methyl 3-(3-Ethyl-4-methyl-1-phenylpent-1-yn-3-yloxy)-acrylate (**3j**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.00−1.07 (m, 9H), 1.89 (q, 2H, ^3J(H,H) = 7.1 Hz), 2.07−2.14 (m, 1H), 3.68 (s, 3H), 5.40 (d, 1H, ^3J(H,H) = 12.1 Hz), 7.28−7.36 (m, 3H), 7.46−7.49 (m, 2H), 8.10 (d, 1H, ^3J(H,H) = 12.1 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 8.00, 17.3, 17.4, 30.5, 36.2, 50.8, 85.7, 86.8, 90.7, 97.9, 121.9, 128.3 (2C), 128.8, 131.8 (2C), 159.8, 168.5 ppm; MS (70 eV): m/z (%): 286 (M^+, 2.2), 243 (72), 185 (100), 157 (29), 143 (36), 141 (31), 129 (32), 128 (28), 115 (35), 91 (25); HRMS calculated for $C_{18}H_{22}O_3$: 286.1569, found 286.1568. Colorless oil.

*(E)-Methyl 3-((1R,5S)-6,6-Dimethyl-2-(phenylethynyl)bicyclo-[3.1.1]heptan-2-yloxy) Acrylate (**3k**).* $[\alpha]_D^{20}$ = −0.335 (c = 0.17, $CHCl_3$);^{1}H NMR (400 MHz, $CDCl_3$): δ 1.00 (s, 3H), 1.24 (s, 3H), 1.41 (d, 1H, ^3J(H,H) = 10.4 Hz), 1.88−1.96 (m, 1H), 1.98−2.05 (m, 2H), 2.24−2.31 (m, 1H), 2.37−2.46 (m, 2H), 2.51−2.59 (m, 1H), 3.69 (s, 3H), 5.39 (d, 1H, ^3J(H,H) = 12.1 Hz), 7.28−7.32 (m, 3H), 7.40−7.43 (m, 2H), 7.92 (d, 1H, ^3J(H,H) = 12.1 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.6, 24.1, 27.2, 27.9, 31.1, 38.2, 40.4, 51.0, 51.1, 83.7, 85.1, 90.6, 99.4, 122.1, 128.3 (2C), 128.6, 131.8 (2C), 158.9, 168.3 ppm. Elemental analysis calcd (%) for $C_{21}H_{24}O_3$: C, 77.75; H, 7.46. Found: C, 77.52; H, 7.76. Pale yellow oil.

*(E)-Methyl 3-((1R,2R,5R)-2-Isopropyl-5-methyl-1-(phenylethynyl)-cyclohexyloxy)acrylate (**3l**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.85−0.90 (m, 1H), 0.94 (d, 3H, ^3J(H,H) = 6.3 Hz), 0.97 (d, 3H, ^3J(H,H) = 6.8 Hz), 1.00 (d, 3H, ^3J(H,H) = 6.8 Hz), 1.29 (m, 1H), 1.42−1.52 (m, 2H), 1.73−1.86 (m, 3H), 2.10−2.18 (m, 2H), 3.68 (s, 3H), 5.39 (d, 1H, ^3J(H,H) = 12.1 Hz), 7.32−7.34 (m, 3H), 7.44−7.46 (m, 2H), 8.12 (d, 1H, ^3J(H,H) = 12.1 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.4, 21.7, 23.6, 24.5, 26.8, 30.5, 34.4, 48.8, 50.9, 51.8, 83.3, 86.4, 91.5, 98.5, 122.1, 128.4 (2C), 128.9, 131.7 (2C), 159.0, 168.5 ppm; MS (70 eV): m/z (%): 340 (M^+, 3.8), 240 (25), 239 (100), 183 (30), 157 (21), 141 (22), 129 (30), 105 (23), 91 (34). Elemental analysis calcd (%) for $C_{22}H_{28}O_3$: C, 77.62; H, 8.29. Found: C, 77.89; H, 8.08. Colorless oil.

*(E)-Methyl 3-((1S,2S,5R)-2-Isopropyl-5-methyl-1-(phenylethynyl)-cyclohexyloxy)acrylate (**3m**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (d, 3H, ^3J(H,H) = 6.6 Hz), 0.90 (d, 3H, ^3J(H,H) = 6.9 Hz), 0.93−1.04 (m, 1H), 0.99 (d, 3H, ^3J(H,H) = 7.0 Hz), 1.40−1.64 (m, 5H), 1.76−1.81 (m, 1H), 2.16−2.21 (m, 1H), 2.42−2.49 (m, 1H), 3.68 (s, 3H), 5.42 (d, 1H, ^3J(H,H) = 12.1 Hz), 7.26−7.31 (m, 3H), 7.43−7.46 (m, 2H), 8.03 (d, 1H, ^3J(H,H) = 12.1 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.1, 20.4, 21.6, 23.6, 26.8, 28.4, 34.3, 47.3, 50.77, 50.82, 82.2, 88.3, 88.5, 98.9, 121.9, 128.2 (2C), 128.6, 131.7 (2C), 158.5, 168.2 ppm; MS (70 eV): m/z (%): 340 (M^+, 2.2), 240 (20), 239 (100), 183 (30), 157 (19), 141 (21), 129 (29), 105 (18), 91 (31). Elemental analysis calcd (%) for $C_{22}H_{28}O_3$: C, 77.62; H, 8.29. Found: C, 77.75; H, 8.01. Colorless oil.

*Methyl 2-Isopropyl-2,4-diphenyl-2H-pyran-5-carboxylate (**4a**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.89 (d, 3H, ^3J(H,H) = 7.1 Hz), 0.94 (d, 3H, ^3J(H,H) = 6.8 Hz), 2.26−2.32 (m, 1H), 3.49 (s, 3H), 5.61 (s, 1H), 7.25−7.38 (m, 8H), 7.45−7.47 (m, 2H), 7.73 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.3, 17.4, 38.5, 50.9, 87.0, 109.4, 119.4, 125.7 (2C), 127.2 (2C), 127.3, 127.5, 127.7 (2C), 127.9 (2C), 134.6, 139.7, 143.4, 156.5, 165.6 ppm; MS (70 eV): m/z (%): 334 (M^+, 1.1), 292 (23), 291 (100), 202 (10); HRMS calculated for $C_{22}H_{22}O_3$: 334.1569, found 334.1561. Pale yellow oil.

*Methyl 2-Isopropyl-4-phenyl-2-p-tolyl-2H-pyran-5-carboxylate (**4b**).* After its synthesis and purification **3b** partially rearranges to **4b**. The isolated material (sticky oil) is a 1:11 mixture that can be used as it is for the microwave-assisted reaction. Characteristic data for **4b**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.89 (d, 3H, ^3J(H,H) = 7.1 Hz), 0.96 (d, 3H, ^3J(H,H) = 6.8 Hz), 2.26−2.35 (m, 1H), 2.37 (s, 3H), 3.50 (s, 3H), 5.60 (s, 1H), 7.18 (d, 2H, ^3J(H,H) = 8.1 Hz), 7.26 (d, 2H, ^3J(H,H) = 8.1 Hz), 7.31−7.37 (m, 5H), 7.72 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.2, 17.4, 21.0, 38.4, 50.8, 87.0, 109.3, 119.3, 125.7 (2C), 127.18, 127.21 (2C), 127.7 (2C), 128.5 (2C), 134.5, 137.2, 139.8, 140.3, 156.5, 165.6 ppm; MS (70 eV): m/z (%): 348 (M^+, 5.6), 306 (82), 305 (100), 202 (21); HRMS calculated for $C_{23}H_{24}O_3$: 348.1725, found 348.1722. Pale yellow oil.

*3-Hydroxy-5-isopropyl-4-methylbiphenyl-2-carbaldehyde (**5j**).* Yield: 31.8 mg, 25%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.25 (d, 6H, ^3J(H,H) = 7.1 Hz), 2.28 (s, 3H), 3.22−3.32 (m, 1H), 6.80 (s, 1H), 7.35−7.38 (m, 2H), 7.42−7.47 (m, 3H), 9.78 (s, 1H), 12.35 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 9.9, 22.6 (2C), 30.2, 115.6, 118.1, 123.0, 127.9, 128.3 (2C), 130.1 (2C), 138.2, 144.6, 156.4, 161.2, 196.6 ppm; MS (70 eV): m/z (%): 254 (M^+, 100), 253 (35), 239 (25), 221 (13), 211 (28), 165 (11); HRMS calculated for $C_{17}H_{18}O_2$: 254.1307, found 254.1312. Pale yellow oil.

*5,5-Dimethyl-6-oxo-2,4-diphenylcyclohexa-1,3-diene-carbaldehyde (**6a**).* Yield: 117.8 mg, 78%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42 (s, 6H), 6.33 (s, 1H), 7.25−7.27 (m, 2H), 7.36−7.44 (m, 8H), 9,88 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.5 (2C), 51.1, 123.9, 125.3, 127.8 (2C), 128.0 (2C), 128.37, 128.39 (2C), 128.5 (2C), 130.1, 136.2, 139.0, 159.8, 164.4, 190.4, 201.7 ppm; MS (70 eV): m/z (%): 302 (M^+, 28), 288 (25), 287 (100), 246 (14), 215 (14), 105 (34). Elemental analysis calcd (%) for $C_{21}H_{18}O_2$: C, 83.42; H, 6.00. Found: C, 83.58; H, 6.14. Orange oil.

*5,5-Dimethyl-6-oxo-2-phenyl-4-p-tolylcyclohexa-1,3-diene-carbaldehyde (**6b**).* Yield: 116.9 mg, 74%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.43 (s, 6H), 2.37 (s, 3H), 6.34 (s, 1H), 7.18 (s, 4H), 7.38−7.45 (m, 5H), 9.89 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.1, 24.6 (2C), 51.3, 123.8, 125.2, 127.8 (2C), 128.5 (2C), 128.6 (2C), 128.8 (2C), 130.1, 136.3, 136.4, 138.5, 160.0, 164.7, 190.5, 202.0 ppm; MS (70 eV): m/z (%): 316 (M^+, 66), 302 (36), 301 (100), 260 (16), 229 (11), 215 (11); HRMS calculated for $C_{22}H_{20}O_2$: 316.1463, found 316.1452. Orange-red oil.

*4-(4-Methoxyphenyl)-5,5-dimethyl-6-oxo-2-phenylcyclohexa-1,3-dienecarbaldehyde (**6c**).* Yield: 104.6 mg, 63%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.44 (s, 6H), 3.22 (s, 3H), 6.34 (s, 1H), 6.88−6.92 (m, 2H), 7.22−7.26 (m, 2H), 7.38−7.47 (m, 5H), 9.88 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.8 (2C), 51.5, 55.3, 113.7 (2C), 123.7, 125.2, 128.5 (2C), 128.6 (2C), 129.4 (2C), 130.2, 131.7, 136.6, 160.0, 160.2, 164.6, 190.6, 200.2 ppm; MS (70 eV): m/z (%): 332 (M^+, 97), 318 (68), 317 (100), 276 (38), 261 (21), 215 (19); HRMS calculated for $C_{22}H_{20}O_3$: 332.1412, found 332.1428. Orange-red oil.

*4,4-Dimethyl-5-(naphthalen-1-yl)-3-oxo-3,4-dihydro-[1,1′-biphenyl]-2-carbaldehyde (**6d**).* Yield: 153.1 mg, 87%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.21 (s, 3H), 1.58 (s, 3H), 6.46 (s, 1H), 7.31 (dd, 1H, ^3J(H,H) = 7.1 and 1.0 Hz), 7.41−7.52 (m, 8H), 7.79−7.82 (m, 1H), 7.86−7.89 (m, 2H), 9,96 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.3, 26.5, 52.3, 124.5, 124.6, 125.6, 125.7, 126.1, 126.5, 127.4, 128.5, 128.6 (2C), 128.7, 128.8 (2C), 130.4, 131.9, 133.7, 136.0, 136.2, 159.3, 162.6, 190.7, 202.3 ppm; MS (70 eV): m/z (%): 352 (M^+, 51), 337 (100), 296 (8.0), 265 (10), 86 (11), 84 (17). Elemental analysis calcd (%) for $C_{25}H_{20}O_2$: C, 85.20; H, 5.72. Found: C, 84.91; H, 6.10. Amorphous orange solid.

*5,5-Dimethyl-6-oxo-4-phenyl-2-(trimethylsilyl)cyclohexa-1,3-dienecarbaldehyde (**6e**).* Yield: 102.8 mg, 69%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.27 (s, 9H), 1.35 (s, 6H), 6.49 (s, 1H), 7.23−7.25 (m, 2H), 7.37−7.40 (m, 3H), 10.3 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ −0.6 (3C), 24.6 (2C), 51.0, 125.4, 128.0 (2C), 128.1 (2C), 128.3, 132.6, 139.8, 163.7, 164.9, 192.7, 204.5 ppm; MS (70 eV): m/z (%): 298 (M^+, 4.9), 284 (31), 283 (100), 255 (7.0), 165 (8.7), 73 (25); HRMS calculated for $C_{18}H_{22}O_2Si$: 298.1389, found 298.1381. Orange-red oil.

*2-tert-Butyl-5,5-dimethyl-6-oxo-4-phenylcyclohexa-1,3-diene-carbaldehyde (**6f**).* Yield: 110 mg, 78%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.28 (s, 9H), 1.30 (s, 6H), 6.33 (s, 1H), 7.20−7.24 (m, 2H), 7.35−7.39 (m, 3H), 10.34 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.7 (2C), 30.4 (3C), 37.4, 49.2, 122.2, 128.07, 128.10 (2C), 128.3 (2C), 128.5, 139.7, 159.7, 162.9, 197.3, 205.4 ppm; MS (70 eV): m/z (%): 282 (M^+, 13), 268 (64), 267 (100), 211 (25), 171 (29), 165 (21), 128 (19), 115 (21), 91 (27), 57 (41); HRMS calculated for $C_{19}H_{22}O_2$: 282.1620, found 282.1615. Light yellow solid.

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J. Org. Chem. 2016, 81, 10099−10105

*3-Methoxy-5,5-dimethyl-6-phenylisobenzofuran-1,4(3H,5H)-dione (**6g-lac**).* Yield: 55.4 mg, 39%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.33 (s, 3H), 1.37 (s, 3H), 3.66 (s, 3H), 6.14 (s, 1H), 6.42 (s, 1H), 7.19−7.21 (m, 2H), 7.36−7.39 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.9, 25.4, 54.0, 57.7, 102.5, 113.1, 128.1 (2C), 128.2 (2C), 128.5, 138.9, 139.7, 141.1, 166.6, 168.1, 199.8 ppm; MS (70 eV): *m*/*z* (%): 284 (M^+, 100), 253 (27), 252 (72), 223 (13), 210 (14), 197 (13), 181 (18), 167 (20), 165 (21), 153 (29), 152 (29); HRMS calculated for $C_{17}H_{16}O_4$: 284.1049, found 284.1043. Orange oil.

*1-Oxo-3,5-diphenylspiro[5.5]undeca-2,4-diene-2-carbaldehyde (**6h**).* Yield: 133.4 mg, 78%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.99−1.07 (m, 1H), 1.50−1.59 (m, 2H), 1.64−1.81 (m, 5H), 2.13−2.18 (m, 2H), 6.20 (s, 1H), 7.20−7.25 (m, 2H), 7.36−7.46 (m, 8H), 9.76 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.5 (2C), 25.2, 31.5 (2C), 55.4, 125.6, 126.6, 128.09 (2C), 128.10 (2C), 128.3, 128.5 (2C), 128.7 (2C), 130.2, 135.4, 139.0, 158.3, 164.0, 189.6, 204.1 ppm; MS (70 eV): *m*/*z* (%): 342 (M^+, 100), 325 (15), 299 (36), 285 (33), 259 (15), 215 (15); HRMS calculated for $C_{24}H_{22}O_2$: 342.1620, found 342.1632. Orange-red oil.

*(1R,3R)-5-Hydroxy-2,2-dimethyl-7-phenyl-1,2,3,4-tetrahydro-1,3-methanonaphthalene-6-carbaldehyde (**10**).* $[\alpha]_D^{20}$ = −71.0 (*c* = 1, $CHCl_3$); Yield: 106.6 mg, 73%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.72 (s, 3H), 1.29 (d, 1H, ^3J(H,H) = 9.4 Hz), 1.40 (s, 3H), 2.35−2.40 (m, 1H), 2.63−2.68 (m, 1H), 2.77 (t, 1H, ^3J(H,H) = 5.5 Hz), 2.88 (dd, 1H, ^3J(H,H) = 17.3 and 2.3 Hz), 2.96 (dd, 1H, ^3J(H,H) = 17.3 and 2.8 Hz), 6.53 (s, 1H), 7.35−7.43 (m, 5H), 9.76 (s, 1H), 12.05 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.3, 26.1, 28.0, 31.5, 39.2, 39.8, 48.6, 116.5, 120.1, 121.5, 127.9, 128.2 (2C), 130.2 (2C), 137.9, 145.2, 157.3, 160.1, 196.7 ppm; MS (70 eV): *m*/*z* (%): 292 (M^+, 56), 249 (100), 248 (43), 221 (75), 203 (21), 202 (16); HRMS calculated for $C_{20}H_{20}O_2$: 292.1463, found 292.1460. Pale yellow oil.

*(1R,3R)-Methyl 2,2-dimethyl-7-phenyl-1,2,3,4-tetrahydro-1,3-methanonaphthalene-6-carboxylate (**11**).* $[\alpha]_D^{20}$ = −32.8 (*c* = 1, $CHCl_3$); Yield: 26 mg, 17%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.67 (s, 3H), 1.27 (d, 1H, ^3J(H,H) = 9.4 Hz), 1.39 (s, 3H), 2.30−2.33 (m, 1H), 2.63−2.69 (m, 1H), 2.78 (t, 1H, ^3J(H,H) = 5.3 Hz), 3.03 (m, 2H), 3.61 (s, 3H), 6.92 (s, 1H), 7.29−7.38 (m, 5H), 7.60 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.4, 26.1, 31.7, 32.6, 39.2, 40.4, 47.8, 51.7, 126.9, 127.9 (2C), 128.1, 128.38, 128.40 (2C), 129.3, 134.1, 139.8, 141.8, 150.8, 169.4 ppm; MS (70 eV): *m*/*z* (%): 306 (M^+, 53), 263 (100), 262 (41), 231 (69), 219 (68), 204 (68); HRMS calculated for $C_{21}H_{22}O_2$: 306.1620, found 306.1614. Pale yellow solid.

*(±)-1-Hydroxy-6-methyl-3-phenyl-5,6,7,8-tetrahydronaphthalene-2-carbaldehyde (**12**).* Yield: 86.45 mg, 65%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.08 (d, 3H, ^3J(H,H) = 6.6 Hz), 1.33−1.43 (m, 1H), 1.82−1.90 (m, 1H), 1.95−2.00 (m, 1H), 2.42 (dd, 1H, ^3J(H,H) = 17.4 and 10.2 Hz), 2.55−2.62 (m, 1H), 2.83 (dd, 1H, ^3J(H,H) = 17.4 and 4.3 Hz), 2.91−2.98 (m, 1H), 6.60 (s, 1H), 7.33−7.35 (m, 2H), 7.38−7.45 (m, 3H), 9,75 (s, 1H), 12.35 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 22.1, 28.5, 30.5, 38.9, 115.4, 122.0, 124.9, 127.9, 128.3 (2C), 130.0 (2C), 137.9, 143.8, 147.1, 161.2, 196.6 ppm; MS (70 eV): *m*/*z* (%): 266 (M^+, 100), 265 (47), 233 (17), 224 (15), 165 (18), 152 (12). Elemental analysis calcd (%) for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.07; H, 6.60. White solid. Melting point 123−124 °C.

*(±)-1-Hydroxy-5-isopropyl-8-methyl-3-phenyl-5,6,7,8-tetrahydronaphthalene-2-carbaldehyde (**13**).* Yield: 46.2 mg, 30%; Mixture of isomers (4:1) tentatively assigned (syn:anti). Characteristic data for major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (d, 3H, ^3J(H,H) = 6.9 Hz), 1.02 (d, 3H, ^3J(H,H) = 6.9 Hz), 1.27 (d, 3H, ^3J(H,H) = 6.9 Hz), 2.54−2.57 (m, 1H), 3.27−3.33 (m, 1H), 6.71 (s, 1H), 9.78 (s, 1H), 12.45 (s, 1H) ppm; Characteristic data for minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.73 (d, 3H, ^3J(H,H) = 6.9 Hz), 1.07 (d, 3H, ^3J(H,H) = 6.9 Hz), 1.29 (d, 3H, ^3J(H,H) = 6.9 Hz), 6.82 (s, 1H), 9,76 (s, 1H), 12.40 (s, 1H) ppm.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02137.

Copies of ^{1}H and ^{13}C NMR spectra of all new compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: fgarcia@ipna.csic.es.

*E-mail: dtejedor@ipna.csic.es.

Present Address

†On leave from the Departamento de Química Orgánica, Facultad de Química, Universidad de la República, Montevideo, Uruguay.

Notes

The authors declare no competing financial interest.

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(8) Some precedents for this rearrangement have been described under different reaction conditions: (a) Copper-catalyzed: Matsuda, T.; Suzuki, K.; Abe, S.; Kirikae, H.; Okada, N. *Tetrahedron* **2015**, *71*, 9264−9270. (b) Photochemical: Jung, M.; Blum, R. *J. Chem. Soc., Chem. Commun.* **1981**, 962−963.
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