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Palladium-catalyzed synthesis of 2*E*-[(methoxycarbonyl)methylene]tetrahydrofurans: oxidative cyclization–methoxycarbonylation of 4-yn-1-ols versus cycloisomerization–hydromethoxylation

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Dedicated to Professor Fausto Calderazzo in recognition of his outstanding contribution to organometallic chemistry.

Abstract

4-Yn-1-ols bearing a terminal triple bond undergo oxidative cyclization–alkoxycarbonylation in methanol at 70°C and 100 atm of a 9:1 mixture of carbon monoxide and air in the presence of catalytic amounts of $[PdI_4]^{2-}$ in conjunction with an excess of KI to give 2*E*-[(methoxycarbonyl)methylene]tetrahydrofurans in good yields. A competing reaction, cycloisomerization–hydromethoxylation leading to 2-methoxy-2-methyltetrahydrofurans, can be easily curtailed by increasing the KI excess. The latter products can be prepared from 4-yn-1-ols and methanol in high yields using the same catalytic system and without KI excess in the absence of carbon monoxide. © 2000 Elsevier Science S.A. All rights reserved.

Keywords: Carbonylation; 2*E*-[(Methoxycarbonyl)methylene]tetrahydrofurans; 2-Methoxy-2-methyltetrahydrofurans; Palladium; 4-Yn-1-ols

1. Introduction

Cyclization–alkoxycarbonylation of acetylenic substrates under the catalytic action of palladium complexes is a powerful methodology, which allows direct preparation of acetic acid derivatives containing an heterocyclic ring, otherwise difficult to obtain by classical approaches. In view of the successful utilization of the PdI_2/KI system in the oxidative cyclization–alkoxycarbonylation of prop-2-ynylamides [1], propynylureas [2], (*Z*)-2-en-4-yn-1-ols [3] and in the oxidative carboxylation–cyclization–alkoxycarbonylation of propynylamines [4], we wondered whether the application of our methodology to readily accessible 4-yn-1-ols (**1**) could lead to 2-[(alkoxycarbonyl)methylene]tetrahydrofurans (**2**). The 2-methylenetetrahydrofuran moiety is present in several biologically active natural products [5]. Moreover, compounds **2** are known to be useful starting materials for further transformations and so far have been prepared by several methods [6]. However, no synthesis of **2** by direct carbonylation of 4-yn-1-ols has been described to date.

We report here the preparation of 2*E*-[(alkoxycarbonyl)methylene]tetrahydrofurans (**2**) in good yields and catalytic efficiencies by Pd(II)-catalyzed oxidative cyclization–alkoxycarbonylation of 4-yn-1-ols (**1**).

2. Results and discussion

4-Yn-1-ols (**1**) were caused to react in methanol at 70°C and 100 atm of a 9:1 mixture of CO and air in the presence of catalytic amounts of PdI_2/KI (Eq. (1)).

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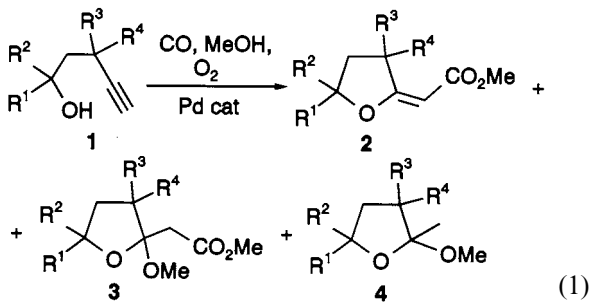
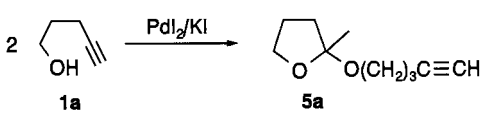
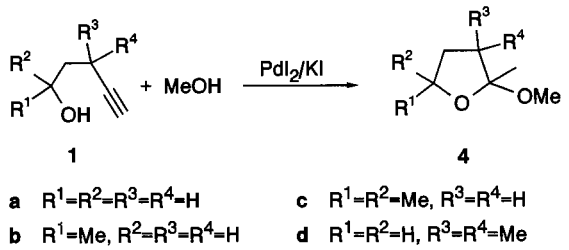
(*E*) - 2 - [(Methoxycarbonyl)methylene]tetrahydrofurans (**2**), together with products **3** deriving from methanol addition to the vinylethereal bond of **2**, were obtained as the main products. A competing reaction, however, corresponding to cycloisomerization [7] of **1** followed by alcohol addition, led to 2-methoxy-2-methyltetrahydrofurans (**4**). The latter reaction readily occurred in the absence of CO under nitrogen at room temperature. For example, when pent-4-yn-1-ol (**1a**) (100 equivalents) was allowed to react with PdI_2 (one equivalent) and KI (two equivalents) without a solvent at 25°C, cyclic acetal (**5a**) was obtained in 54% yield after 18 h (Eq. (2)). Using methanol as a coreagent (1:1 molar ratio with respect to **1**) under the same conditions compounds **4** were formed exclusively (Eq. (3)).



(1)

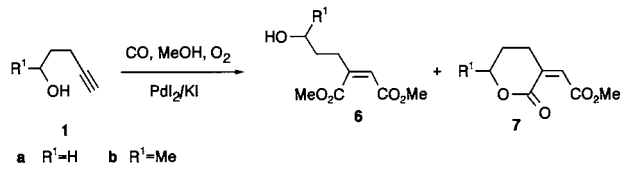


(2)



(3)

Minor amounts of maleates (**6**) and lactones (**7**) were also formed by carbonylation of substrates **1a** and **1b** (Eq. (4)), while **1d** also gave significant amounts of 3,3 - dimethyl - 2*Z* - [(methoxycarbonyl)methylene]tetrahydrofuran (**8d**).



(4)

The results obtained using different 4-yn-1-ols with and without carbon monoxide are collected in Tables 1 and 2, respectively. Under the same conditions used for **1a**–**d**, analogous 4-yn-1-ols bearing an internal triple bond reacted only to a very limited extent.

As shown in Table 1, the course of carbonylation reactions is strongly influenced by substituents. Formation of compounds **4**, resulting from methanol addition to cycloisomerization products (Eq. (3)), was effectively

Table 1
Reactions of 4-yn-1-ols **1** with CO–air (9:1) and MeOH in the presence of PdI_2 and KI at 70°C, initial pressure 100 atm at 20°C, substrate concentration: 0.22 mmol ml^{-1} MeOH)

Run	Substrate	KI: PdI_2	Mol **1**:mol PdI_2	*t* (h)	Conversion (%) [a]	Yields (%) [a]			Total yield (%) [a]
						2	**3**	**4**	
1	**1a**	10	1000	12	100	24	40	15	93 [b]
2	**1b**	10	1000	12	100	32	45 [c]	16 [d]	97 [e]
3	**1c**	10	2000	2	100	11	7	55	73
4	**1d**	10	2000	2	100	16	8	30	64 [f]
5	**1c**	50	2000	2	82	25	27	28	80
6	**1c**	100	2000	8	91	40	33	10	83
7	**1c**	100	3000	14	97	41	37	13	91
8	**1d**	100	1000	12	100	29	19	20	95 [g]
9 [h]	**1a**	10	2000	3	84	13	20	20	76 [i]

[a] Based on starting 4-yn-1-ol, by GLC.
[b] Including **6a** (5%) and **7a** (9%).
[c] Mixture of diastereomers (54:46).
[d] Mixture of diastereomers (68:32).
[e] Including **6b** (1%) and **7b** (3%).
[f] Including **8d** (10%).
[g] Including **8d** (27%).
[h] Reaction carried out at 20 atm pressure (CO:air = 3:1).
[i] Including **6a** (6%) and **7a** (17%).

Table 2
Reactions of 4-yn-ols **1** with methanol (1:1 molar ratio) in the presence of PdI_2+2KI at 25°C

Run	Substrate	Mol **1**:mol PdI_2	*t* (h)	Conversion (%) [a]	Yield of **4** (%) [b]
10	**1a**	100	16	100	84 (78)
11	**1b**	200	15	100	74 (68) [c]
12	**1c**	500	18	100	70 (62)
13	**1d**	500	18	100	70 (62)

[a] Based on starting (*Z*)-2-en-4-yn-1-ol, by GLC.
[b] GLC yields (isolated yields).
[c] Mixture of diastereomers (64:36).

promoted by geminal substitution on the carbon adjacent to the hydroxyl group or to the triple bond (runs 3, 4). This is also evident from the reactions carried out in the absence of CO (compare runs 12, 13 with runs 10, 11; Table 2). This rate enhancement must be due to the *gem*-dialkyl effect [8], which tends to favor a conformation in which the –OH is closer to the triple bond, so that even under a 90 atm pressure of CO, ring closure and proton uptake occurs faster than methoxycarbonylation (runs 3, 4). Carbonylation, however, turned out to be the main reaction pathway when a large excess of KI was used (runs 5–8). This can be due to a faster migration of the palladium-bonded vinyl group on the carbonyl group, probably as a consequence of the *trans* effect of the iodide ligands (Scheme 1; anionic iodide ligands are omitted for simplicity).

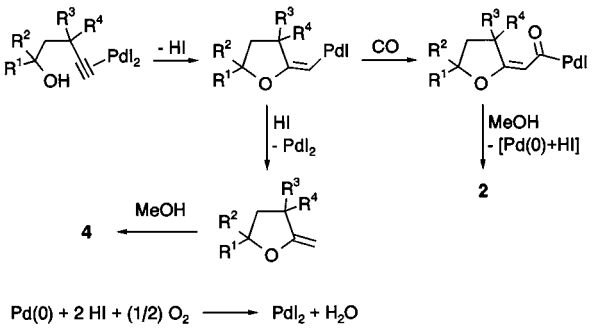
When the *gem*-dialkyl effect is not at work, the tendency to form either acyclic dialkoxycarbonylation [9] or cyclocarbonylation–alkoxycarbonylation [10] products (**6** and **7**, respectively) becomes evident (runs 1 and 2).

Interestingly, the use of a carbon monoxide partial pressure of 15 atm rather than 90 atm resulted in higher yields of dicarbonylated products **6** and **7** (run 9). It is conceivable that an excess of CO ligand slows down the insertion of the triple bond into the $Pd–CO_2R$ bond, which is a necessary step for the formation of dicarbonylated products [9,10]. On the other hand, a high carbon monoxide pressure not only does not hamper the intramolecular nucleophilic attack of the hydroxyl group on the coordinated triple bond but also tends to favor the carbon monoxide insertion at the vinylpalladium intermediate level (Scheme 1). As shown above, the use of KI in excess proved effective in reducing the amount of compound **4** thus increasing selectivity towards **2** + **3**.

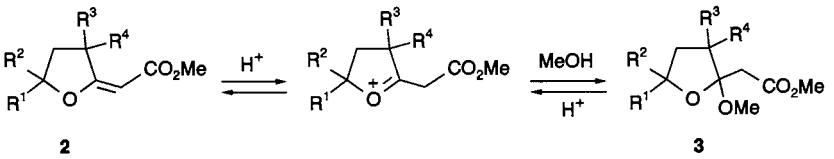
It has been ascertained that **2** partly convert into **3** when reacted under the reaction conditions, which is easily explained by acid-catalyzed addition of MeOH on the vinylethereal bond (Scheme 2). On the other hand, products **3** readily eliminate methanol to give the corresponding **2** when heated under reduced pressure (see Section 3), thus the reaction (Eq. (1)) allows us to obtain compounds **2** in a convenient overall yield. It is worth noting that a method reported some years ago for preparation of **2a** (in a ca. 5:1 mixture with its *Z* isomer) starting from **1a** required a sequence of four steps [6j].

We have still to comment briefly on stereochemical aspects. It is a well-established feature of reactions initiated by intramolecular nucleophilic attack on the triple bond coordinated to Pd(II) that the attack is *anti* with respect to palladium [11]. The exclusive occurrence of *E* stereochemistry in products **2** deriving from **1a**–**c** obtained in our reaction is clearly in agreement with this mechanistic hypothesis (Scheme 1). Another possibility could be that *Z* isomers are first formed by a different pathway and subsequently transform into the corresponding *E* isomers (the latter, in the absence of substituents at C-3, are known to be thermodynamically more stable [6b, 6i]). This does not seem likely, however, since no formation of the *Z* isomers from **1a**–**c** was observed even at low substrate conversion. It is noteworthy that the reaction of 3,3-dimethylpent-4-yn-1-ol (**1d**) afforded both isomers **2d** (*E*) and **8d** (*Z*). In this case, experiments carried out at different reaction times clearly showed that isomerization of **2d** into **8d** occurred. The higher stability of **8d** compared with **2d** is apparently due to the steric effect exerted by the geminal methyl groups on the methoxycarbonyl group. The isomerization process can be readily explained by methanol addition to **2d** to give **3d** and methanol elimination from **3d** (Scheme 3).

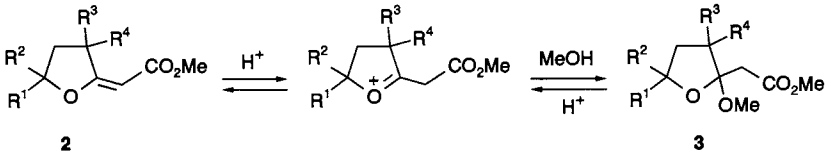
In conclusion, we have described a direct synthesis of 2-[(methoxycarbonyl)methylene]tetrahydrofurans by



Scheme 1.



Scheme 2.



Scheme 3.

carbonylation of readily available 4-yn-1-ols. A facile synthesis of 2-methoxy-2-methyltetrahydrofurans from the same substrates and methanol has also been achieved [12].

3. Experimental

3.1. General

m.p.s were determined on a Reichert Thermovar melting point apparatus and are uncorrected. Elemental analyses were carried out with a Carlo Erba Elemental Analyzer Mod. 1106. IR spectra were recorded on a Perkin-Elmer Paragon 1000 PC FT-IR spectrometer. Mass spectra were obtained using an HP 5972A spectrometer at 70 eV ionizing voltage. ^{1}H-NMR spectra were taken on a Bruker AC300 spectrometer and run on $CDCl_3$ solutions with Me_4Si as internal standard. Chemical shifts and coupling constants (J) are given as δ values (ppm) and in Hz, respectively.

The reaction mixtures were analyzed by TLC (SiO_2 or Al_2O_3) or by GLC using capillary columns with polymethylsilicone + 5% phenylsilicone (HP-5) or TPA-modified polyethyleneglycol (HP-FFAP) as the stationary phase. Products were separated by bulb-to-bulb distillation or chromatographic procedures on silica or alumina with suitable eluents. Merck silica gel 60 (60–230 mesh or 230–400 mesh) and neutral alumina 90 (70–230 mesh) were used for column chromatography. Analytical TLC plates and silica gel 60F254 for PTLC were purchased from Merck. Pent-4-yn-1-ol (**1a**) was commercially available (Aldrich, Fluka). Hex-5-yn-2-ol (**1b**) [13], 2-methylhex-5-yn-2-ol (**1c**) [13a, 13c] and 3,3-dimethylpent-4-yn-1-ol (**1d**) [14] were prepared according to literature procedures.

3.2. General procedure for catalytic oxidative carbonylation of 4-yn-1-ols

The carbonylation reactions were carried out in a 300 cm^3 stainless-steel autoclave (Parr) with magnetic stirring. In a typical experiment the autoclave was charged in the presence of air with PdI_2, KI and the appropriate substrate (10 mmol) dissolved in MeOH (45 ml). The autoclave was pressurized with air (10 atm) and CO (up to 100 atm of total pressure) and heated at 70°C with stirring for the required time. Reaction times, KI to PdI_2 and substrate to catalyst molar ratios used are indicated in Table 1.

3.3. General procedure for catalytic cycloisomerization–hydromethoxylation of 4-yn-1-ols

All reactions were carried out under nitrogen. Into a 25 ml Schlenk flask were introduced **1** (10 mmol), anhydrous MeOH (10 mmol) PdI_2 and KI (2 mol per mol of palladium) in this order (substrate to catalyst ratios used are indicated in Table 2). The reaction mixture was magnetically stirred at room temperature for the required time (Table 2). (Note: the reaction temperature must be controlled with the aid of a water bath owing to the exothermicity of the reaction).

3.4. Separation of products

2-Methoxy-2-methyltetrahydrofurans (**4**) deriving from the reaction carried out under nitrogen were easily isolated by transfer distillation, after elimination of any residual methanol in the reaction mixture by addition of small amounts of sodium. Cyclic acetal (**5a**) was purified by column chromatography on silica gel using pentane–acetone 98:2 as eluent. Products **4** were not isolated from the carbonylation reaction mixtures and were characterized by GC - MS comparison with pure

products obtained as above. Carbonylation products were separated by conventional chromatographic techniques, as described below. Products **2a**–**c** and **8d** were also readily isolated, after elimination of methanol and low - boiling products by rotary evaporation, by bulb-to-bulb distillation of the reaction crude under reduced pressure. In fact, under these conditions **3a**–**c** readily converted into **2a**–**c**, and both products **2d** and **3d** transformed into **8d**, as confirmed by the isolated yields of products **2a**–**c** and **8d** thus obtained.

Compounds **3a** + **2a**, **7a**, **6a** were eluted in this order by chromatography through a SiO_2 column, using a concentration gradient of hexane–ethyl acetate from 8:2 to 6:4. During the elution, partial transformation of **3a** into **2a** was observed. Products **2a** and **3a** were subsequently separated by PTLC (SiO_2) using hexane–ethyl acetate = 8:2 as eluent. Pure product **2b** was easily isolated by column chromatography or PTLC (SiO_2, hexane–ethyl acetate 8:2) carried out on the reaction crude deriving from **1b**. During the elution, partial transformation of **3b** into **2b** was observed, and product **3b** could only be obtained in a mixture with product **2b**. Products **6b** and **7b** were obtained from an experiment carried out at 70°C and 20 atm of a 3:1 mixture CO–air for 3 h using a molar ratio substrate:KI:PdI_2 = 2000:10:1. Chromatographic separation was effected on the crude reaction mixture by PTLC using hexane–ethyl acetate 1:1 as eluent; order of elution: **2b** + **3b**, **7b**, **6b**. Products **3c**, **2c** were separated by PTLC (SiO_2) using a mixture of hexane–ethyl acetate = 65:35 as eluent. During the elution, partial transformation of **3c** into **2c** was observed. Products **2d**, **3d**, **8d** were eluted in this order by chromatography through an alumina column, using a concentration gradient of hexane–chloroform from 90:10 to 0:100. During the elution, partial transformation of **2d** and **3d** into **8d** was observed. Note: once separated, pure products **3** did not show any tendency to release methanol to give **2a**–**c** or **8d**, and they could be recovered as such after several days. Therefore, formation of **2a**–**c** or **8d** from **3** resulting from distillation of the reaction crude or elution through column chromatography or PTLC, has to be due to the presence of traces of acidity [from HI or Pd(II)] in the crude. This was confirmed by the fact that, for example, partial transformation of pure **3d** into **8d** was observed on standing in chloroform solution in the presence of traces of added HI.

3.5. Characterization of products

Identification of known products **2a** [6j], **4a** [15] and **5** [16] was carried out by comparison with literature data. New products were characterized by elemental analysis and IR, ^{1}H-NMR and MS data. As described above 2-methoxy-2-[(methoxycarbonyl)methyl]-5-methyloxacyclopentane (**3b**) (mixture of diastereomers) could not be separated from **2b** and was characterized only by GC-MS; moreover, its easy transformation into **2b** (Section 3.4) was in agreement with the proposed structure.

3.5.1. 2E-[(Methoxycarbonyl)methylene]-5-methyltetrahydrofuran (2b)

Colorless oil. IR (film) ν 2977 m, 2949 m, 1707 s, 1644 s, 1436 m, 1362 m, 1116 s, 1053 m, 948 m, 875 w, 821 m, 726 w cm^{-1}; ^{1}H-NMR δ 1.37 (d, J = 5.9, 3 H, Me), 1.55–1.75 (m, 1 H, CHC*H*HCH$_2$), 2.18–2.30 (m, 1 H, CHCH*H*CH$_2$), 2.90–3.04 (m, 1 H, C*H*HC=), 3.27–3.40 (m, 1 H, CH*H*C=), 3.66 (s, 3 H, CO_2Me), 4.47–4.60 (m, 1 H, C*H*Me), 5.26 (distorted t, J = 1.5, 1 H, =CH); MS m/z 156 (M$^+$, 23%), 141 (< 0.5), 125 (35), 124 (15), 101 (22), 82 (9), 70 (5), 69 (100), 59 (7), 55 (11). Anal. Found: C, 61.45; H, 7.81; Anal. Calc. for $C_8H_{12}O_3$: C, 61.52; H 7.78%.

3.5.2. 5,5-Dimethyl-2E-[(methoxycarbonyl)methylene]-tetrahydrofuran (2c)

Colorless oil. IR (film) ν 2975 m, 1707 s, 1638 s, 1457 w, 1436 m, 1387 w, 1359 m, 1291 w, 1119 s, 1043 m, 955 m, 863 w, 821 w cm^{-1}; ^{1}H-NMR δ 1.37 (6 H, s, 2 Me), 1.91 (2 H, t, J = 7.9, C*H*$_2$CMe$_2$), 3.20 (2 H, td, J = 7.9, 1.7, CH$_2$C=), 3.65 (3 H, s, CO_2Me), 5.22 (1 H, t, J = 1.7, =CH); MS m/z 170 (M$^+$, 43%), 155 (1), 139 (34), 127 (25), 101 (89), 96 (14), 95 (9), 93 (16), 83 (7), 81 (10), 70 (23), 69 (100), 59 (11), 55 (34), 53 (12). Anal. Found: C, 63.64; H, 7.81; Anal. Calc. for $C_9H_{14}O_3$: C, 63.51; H 7.85%.

3.5.3. 3,3-Dimethyl-2E-[(methoxycarbonyl)methylene]-tetrahydrofuran (2d)

Colorless oil. IR (film) ν 2958 s, 2900 m, 1711 s, 1639 s, 1435 m, 1391 m, 1347 m, 1219 m, 1161 s, 1111 s, 1051 m, 922 m, 834 m, 711 w, 667 w cm^{-1}; ^{1}H-NMR δ 1.49 (6 H, s, 2 Me), 2.02 (2 H, t, J = 7.0, C*H*$_2$CMe$_2$), 3.64 (3H, s, CO_2Me), 4.17 (2 H, t, J = 7.0, CH$_2$O), 5.28 (1 H, s, CHC=); MS m/z 170 (M$^+$, 24%), 155 (24), 140 (10), 139 (100), 123 (15), 112 (7), 111 (10), 101 (6), 97 (8), 83 (5), 69 (77), 59 (6), 55 (15). Anal. Found: C, 63.46; H, 7.87; Anal. Calc. for $C_9H_{14}O_3$: C, 63.51; H 7.85%.

3.5.4. 2-Methoxy-2-[(methoxycarbonyl)methyl]-tetrahydrofuran (3a)

Colorless oil. IR (film) ν 2958 m, 1743 s, 1438 m, 1320 m, 1248 m, 1212 m, 1119 s, 1088 m, 1045 s cm^{-1}; ^{1}H-NMR δ 1.83–2.17 (4 H, m, C*H*$_2$C*H*$_2$CH$_2$O), 2.66 (1 H, distorted d, J = 14.2, C*H*HCO$_2$Me), 2.97 (1 H, distorted d, J = 14.2, CH*H*CO$_2$Me), 3.25 (3 H, s, OMe), 3.70 (3H, s, CO_2Me), 3.80–3.96 (2 H, m, CH$_2$O); MS m/z 174 (M$^+$, absent), 143 (46%), 133 (6), 129 (3), 101 (100), 83 (18), 69 (16), 59 (68), 57 (10), 55 (13). Anal. Found: C, 55.34; H, 8.16; Anal. Calc. for $C_8H_{14}O_4$: C, 55.16; H 8.10%.

3.5.5. 2-Methoxy-2-[(methoxycarbonyl)methyl]-5-methyltetrahydrofuran (3b) (mixture of diastereomers, A:B = 54:46)

MS m/z A: 188 (M$^+$, absent), 158 (10%), 157 (98), 141 (10), 133 (18), 129 (12), 125 (14), 115 (67), 101

(100), 97 (16), 84 (28), 83 (84), 81 (12), 73 (28), 69 (21), 59 (58), 57 (22), 56 (23), 55 (76), 53 (14); B: 188 (M^+, absent), 158 (8%), 157 (94), 141 (10), 133 (20), 131 (12), 125 (14), 115 (81), 101 (100), 97 (16), 85 (9), 84 (21), 83 (81), 81 (12), 73 (37), 71 (10), 69 (19), 59 (63), 57 (20), 56 (22), 55 (81), 53 (13).

*3.5.6. 5,5-Dimethyl-2-methoxy-2-[(methoxycarbonyl)-methyl]tetrahydrofuran (**3c**)*

Colorless oil. IR (film) ν 2972 m, 1743 s, 1437 m, 1318 m, 1249 w, 1121 s, 1044 m cm^{-1}; ^{1}H-NMR δ 1.37 (6 H, s, 2 Me), 1.72–2.37 (4 H, m, CH_2CH_2), 2.64 (distorted d, $J = 13.8$, C*H*HCO$_2$Me), 2.88 (1 H, distorted d, $J = 13.8$, CH*H*CO$_2$Me), 3.48 (3 H, s, OMe), 3.68 (3H, s, CO$_2$Me); MS m/z 202 (M^+, absent), 187 (6%), 171 (34), 170 (25), 155 (32), 139 (25), 129 (39), 127 (14), 101 (62), 97 (56), 96 (32), 95 (18), 84 (12), 81 (14), 70 (30), 69 (100), 59 (33), 55 (40). Anal. Found: C, 59.24; H, 9.03; Anal. Calc. for $C_{10}H_{18}O_4$: C, 59.39; H 8.97%.

*3.5.7. 3,3-Dimethyl-2-methoxy-2-[(methoxycarbonyl)-methyl]tetrahydrofuran (**3d**)*

Colorless oil. IR (film) ν 2952 s, 2891 m, 1743 s, 1437 m, 1309 m, 1263 m, 1109 m, 789 w cm^{-1}; ^{1}H-NMR δ 1.06 (3 H, s, Me), 1.12 (3 H, s, Me), 1.53–1.68 (1 H, m, C*H*HCMe$_2$), 2.03–2.17, (1 H, m, CH*H*CMe$_2$), 2.57 (1 H, distorted d, $J = 13.9$, C*H*HCO$_2$Me), 2.92 (1 H, distorted d, $J = 13.9$, CH*H*CO$_2$Me), 3.31 (3 H, s, OMe), 3.69 (3H, s, CO$_2$Me), 3.72–3.93 (2 H, m, CH$_2$O); MS m/z 202 (M^+, absent), 187 (< 0.5%), 171 (56), 157 (4), 133 (32), 129 (24), 101 (51), 97 (100), 73 (16), 70 (55), 69 (27), 59 (35), 57 (11), 55 (75). Anal. Found: C, 59.34; H, 8.91; Anal. Calc. for $C_{10}H_{18}O_4$: C, 59.39; H 8.97%.

*3.5.8. 2-Methoxy-2,5-dimethyltetrahydrofuran (**4b**) (mixture of diastereomers A:B = 64:36).*

Colorless oil. IR (film) ν 2972 s, 2903 m, 2827 w, 1457 m, 1375 m, 1325 w, 1213 m, 1123 m, 1067 s, 959 w, 860 m cm^{-1}; ^{1}H-NMR δ 1.24 [3 H, d, $J = 6.2$, C*H*$_3$CH (A)], 1.29 [3 H, d, $J = 6.1$, C*H*$_3$CH (B)], 1.42 [3 H, s, C*H*$_3$C(OMe) (B)], 1.44 [3 H, s, C*H*$_3$C(OMe) (A)], 1.38–1.53 [1 H, m, C*H*HCHMe (B)], 1.67–2.20 [7 H, m, CH*H*CHMe (B) + C*H*$_2$C(OMe), (A + B) + C*H*$_2$CHMe (A)], 3.23 [3 H, s, OMe (A)], 3.25 [3 H, s, OMe (B)], 4.10–4.28 [2 H, m, C*H*Me (A + B)]; MS m/z A: 130 (M^+, absent), 115 (31%), 99 (100), 86 (28), 83 (22), 75 (47), 73 (22), 71 (41), 56 (34), 55 (56); B: 130 (M^+, absent), 115 (30), 99 (100), 86 (24), 83 (27), 75 (58), 73 (30), 71 (36), 56 (39), 55 (67). Anal. Found: C, 64.65; H, 10.78; Anal. Calc. for $C_7H_{14}O_2$: C, 64.58; H 10.84%.

*3.5.9. 2-Methoxy-2,5,5-trimethyltetrahydrofuran (**4c**)*

Colorless oil. IR (film) ν 2971 s, 2825 w, 1458 m, 1377 m, 1137 m, 1073 s, 972 m, 885 m, 845 m cm^{-1}; ^{1}H-NMR δ 1.22 (3 H, s, C*H*$_3$CCH$_3$), 1.34 (3 H, s, CH$_3$CC*H*$_3$), 1.41 [3 H, s, C*H*$_3$C(OMe)], 1.70–2.08 (4 H, m, CH$_2$CH$_2$), 3.24 (3 H, s, OMe); MS m/z 144 (M^+, absent), 129 (75%), 113 (100), 97 (51), 86 (42), 75 (30), 71 (46), 70 (48), 69 (60), 55 (84). Anal. Found: C, 66.75; H, 11.24; Anal. Calc. for $C_8H_{16}O_2$: C, 66.63; H 11.18%.

*3.5.10. 2-Methoxy-2,3,3-trimethyltetrahydrofuran (**4d**)*

Colorless oil. IR (film) ν 2956 s, 2888 m, 2827 w, 1469 m, 1378 m, 1143 s, 1111 m, 1055 m, 1016 m, 993 w, 879 m cm^{-1}; ^{1}H-NMR δ 0.96 (3 H, s, C*H*$_3$CCH$_3$), 1.05 (3 H, s, CH$_3$CC*H*$_3$), 1.21 [3 H, s, C*H*$_3$C(OMe)], 1.54–1.63 (1 H, m, C*H*HCH$_2$O), 2.00–2.13 (1 H, m, CH*H*CH$_2$O), 3.20 (3 H, s, OMe), 3.71–3.89 (2 H, m, CH$_2$O); MS m/z 144 (M^+, absent), 129 (6%), 113 (100), 99 (24), 97 (8), 75 (35), 73 (11), 70 (57), 69 (15), 57 (9), 55 (88). Anal. Found: C, 66.55; H, 11.23; Anal. Calc. for $C_8H_{16}O_2$: C, 66.63; H 11.18%.

*3.5.11. Dimethyl 2-(3-hydroxy-1-propyl)but-2Z-ene-1,4-dioate (**6a**)*

Colorless oil. IR (film) ν 3437 m, br, 2953 m, 2882 w, 1727 s, 1651 m, 1437 m, 1373 w, 1271 m, 1201 m, 1171 m, 1121 w, 1060 m, 1018 w cm^{-1}; ^{1}H-NMR δ 1.70–1.82 (2 H, m, CH$_2$C*H*$_2$CH$_2$), 2.48 (2 H, td, $J = 7.6$, 1.4, CH$_2$C=), 3.67 (2 H, t, $J = 6.2$, C*H*$_2$OH), 3.73 (3 H, s, CO$_2$Me), 3.83 (3 H, s, CO$_2$Me), 5.88 (1 H, t, $J = 1.4$, =CH); MS m/z 202 (M^+, absent), 143 (100%), 142 (13), 140 (11), 139 (63), 138 (14), 112 (21), 111 (85), 101 (11), 83 (20), 82 (14), 81 (17), 69 (35), 67 (14), 59 (43), 55 (14), 53 (36). Anal. Found: C, 53.32; H, 7.04; Anal. Calc. for $C_9H_{14}O_5$: C, 53.46; H 6.98%.

*3.5.12. Dimethyl 2-(3-hydroxy-1-butyl)but-2Z-ene-1,4-dioate (**6b**)*

Colorless oil. IR (film) ν 3449 m, br, 2958 m, 2928 m, 2853 w, 1731 s, 1649 m, 1509 w, 1439 m, 1377 w, 1263 m, 1203 m, 1173 m cm^{-1}; ^{1}H-NMR δ 1.21 (3 H, d, $J = 6.0$, Me), 1.58–1.70 (1 H, m, C*H*$_2$CHOH), 2.37–2.61 (2 H, m, CH$_2$C=), 3.66–3.89 (1 H, m, C*H*OH), 3.72 (3 H, s, CO$_2$Me), 3.83 (3 H, s, CO$_2$Me), 5.87 (1 H, t, $J = 1.5$, =CH); MS m/z 216 (M^+, absent), 169 (11), 157 (100), 156 (14), 153 (35), 140 (25), 126 (12), 125 (45), 113 (12), 112 (51), 111 (11), 109 (14), 101 (17), 97 (16), 83 (20), 82 (19), 81 (34), 79 (25), 69 (22), 59 (42), 55 (16), 53 (37). Anal. Found: C, 55.46; H, 7.51; Anal. Calc. for $C_{10}H_{16}O_5$: C, 55.55; H 7.46%.

*3.5.13. 3Z-[(Methoxycarbonyl)methylene]oxacyclohexan-2-one (**7a**)*

White solid, m.p. 32–33°C. IR (film) ν 2954 m, 1730 s, 1645 m, 1435 m, 1402 m, 1354 m, 1254 s, 1225 s, 1181 s, 1147 s, 1071 m, 1014 m, 983 m, 909 w, 893 w, 763 w cm^{-1}; ^{1}H-NMR δ 1.98–2.07 (2 H, m, CH$_2$C*H*$_2$CH$_2$), 2.67–2.73 (2 H, m, CH$_2$C=), 3.80 (3 H,

s, CO_2Me), 4.33–4.38 (2 H, m, CH_2O), 6.19 (1 H, t, $J = 2.1$, =CH); MS m/z 170 (M^+, 2%), 155 (< 0.5), 142 (30), 140 (11), 139 (100), 112 (20), 111 (62), 110 (13), 97 (9), 84 (7), 83 (20), 82 (13), 81 (13), 69 (43), 68 (7), 67 (32), 66 (12), 65 (15), 59 (32), 55 (19), 54 (11), 53 (54), 52 (16). Anal. Found: C, 56.32; H, 5.99; Anal. Calc. for $C_8H_{10}O_4$: C, 56.47; H 5.92%.

3.5.14. 3Z-[(Methoxycarbonyl)methylene]-6-methyloxacyclohexan-2-one (**7b**)

Colorless oil; IR (film) ν 2980 m, 2952 m, 1721 s, 1647 m, 1435 m, 1364 m, 1257 s, 1221 s, 1197 s, 1129 m, 1056 m, 1022 w, 1003 w, 961 w, 946 w, 899 w, 763 w cm^{-1}; ^{1}H-NMR δ 1.41 (3 H, d, $J = 6.3$, Me), 1.67–1.83 (1 H, m CH_2CHHCH), 1.99–2.10 (1 H, m, CH_2CHHCH), 2.65–2.73 (2 H, m, CH_2C=), 3.79 (3 H, s, CO_2Me), 4.42–4.54 (1 H, m, C*H*Me), 6.19 (1 H, t, $J = 2.0$, =CH); MS m/z 184 (M^+, 3%), 169 (5), 156 (73), 154 (11), 153 (100), 140 (12), 135 (13), 125 (38), 124 (27), 112 (57), 109 (28), 101 (9), 97 (31), 83 (15), 82 (33), 81 (64), 80 (14), 79 (43), 77 (10), 69 (30), 67 (18), 59 (52), 53 (71). Anal. Found: C, 58.74; H, 6.61; Anal. Calc. for $C_9H_{12}O_4$: C, 58.69; H 6.57%.

3.5.15. 3,3-Dimethyl-2Z-[(methoxycarbonyl)-methylene]tetrahydrofuran (**8d**)

Colorless oil. IR (film) ν 2966 s, 2904 m, 1702 s, 1649 s, 1436 w, 1395 m, 1297 m, 1265 m, 1199 s, 1163 s, 1105 m, 1089 w, 1036 s, 997 w, 915 w, 900 w, 804 m cm^{-1}; ^{1}H-NMR δ 1.24 (6 H, s, 2 Me), 1.92 (2 H, t, $J = 6.9$, CH_2CMe_2), 3.68 (3H, s, CO_2Me), 4.42 (2 H, t, $J = 6.9$, CH_2O), 4.81 (1 H, s, CHC=); MS m/z 170 (M^+, 25%), 155 (19), 140 (9), 139 (100), 123 (11), 112 (6), 111 (12), 101 (4), 97 (8), 83 (6), 69 (74), 59 (6), 55 (18). Anal. Found: C, 63.58; H, 8.33; Anal. Calc. for $C_9H_{14}O_3$: C, 63.51; H 8.29%.

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