Synthesis of Highly Functionalized γ-Lactones *via* 1,5-Electrocyclic Ring Closure

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We have investigated 1,5-electrocyclic ring-closure reactions of conjugated esters with dimethyl diazomalonate in the presence of $[Cu(acac)_2]$ as catalyst. Our new protocol offers an easy entry to various polyfunctionalized γ-lactones in high yields. Their subsequent derivatives may be used as valuable intermediates, especially in the synthesis of natural products and their analogues.

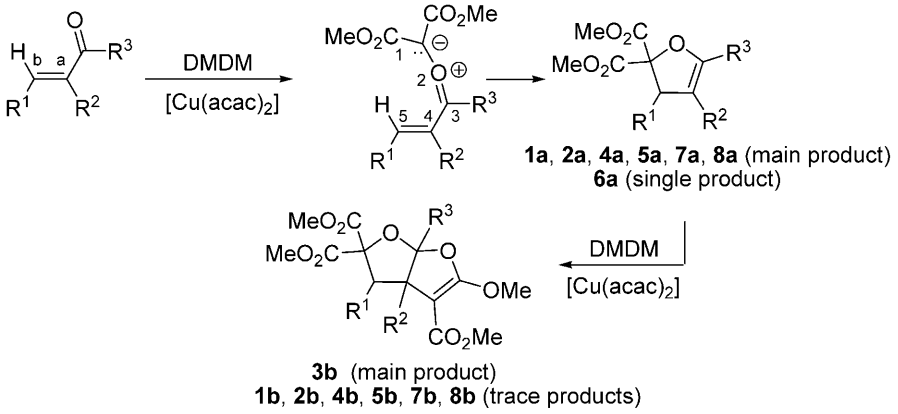
Introduction. – Furan and 1,3-dioxole derivatives are among the most-significant heterocycles in natural products. Consequently, a wide range of methods for their synthesis have been developed [1–9]. We previously reported the reactions of several (*Z*)- and (*E*)-configured enones and of (*E*)-enals with ethyl acetodiazoacetate and dimethyl diazomalonate (DMDM) in the presence of (acetylacetonato)copper(II) ($[Cu(acac)_2]$) [1][2][10][11]. In these reports, we noted that, under mild conditions, dihydrofuran derivatives such as **1**–**8** should be formed by 1,5-electrocyclic ring closure of the related carbonyl ylides derived from properly chosen β-monosubstituted (*E*)-enones, which are present mainly as the s-*cis* conformers (*Scheme 1*).

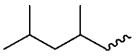
Substituents of both the enone and the diazo carbonyl compound, stabilizing the concerted transition state of the initially formed enone ylide, were found to have a beneficial influence on the reaction rate. However, steric hindrance at C(β), as in **9**, retarded the ring-closing reaction, as expected (*Scheme 2*). Steric crowding at the remaining part, *i.e.*, at C(α), and at the carbonyl C-atom of the enone, *e.g.*, in 2-methyl-1-phenylpent-1-en-3-one (**6**), was beneficial in terms of preventing possible follow-up reactions.

After our first report in 1997 [10], *Hamaguchi et al.* [12] presented analogous vinylcarbonyl-ylide cyclization reactions yielding dihydrofurans. Moreover, the development of new and efficient methods for the synthesis of dihydrofurans has been continuing [13] because of various biological activities of such compounds. Furthermore, the corresponding ylides arising from (mostly s-*trans*) (*E*)-enals such as **10** and **11**, and from (*Z*)-enones such as (*Z*)-**6** and (*Z*)-**7**, yield dioxole derivatives by following a different reaction route (see *Scheme 2*) than those reported by *Huisgen* and *March* [9], or by *Doyle et al.* [14].

In the present work, we report experiments concerning the validity of similar 1,5-electrocyclic ring closures of carbonyl ylides derived from conjugated esters. When conjugated esters can be transformed to the corresponding dihydrofurans, it should be pos-

Scheme 1. *Dihydrofuran Formation by Reaction of α,β-Enones with Dimethyl Diazomalonate*



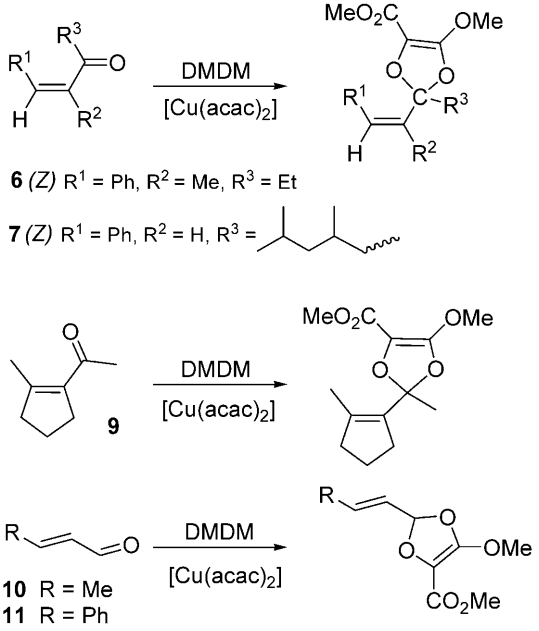
	R^1	R^2	R^3
1 *(E)*		H	Me
2 *(E)*		H	Me
3 *(E)*	Ph	H	Me
4	$(CH_2)_4$		Me
5	$(CH_2)_5$		Me
6 *(E)*	Ph	Me	Et
7 *(E)*	Ph	H	
8 *(E)*	Ph	H	

Reagents and conditions: boiling benzene, DMDM/substrate (**1** – **8**) 1:1, 0.007 mol.-equiv. of $[Cu(acac)_2]$.

sible to obtain γ-lactone derivatives (lactone lignans) with potentially biological and, perhaps, even medicinal properties [15]. Some of these target compounds might be also used as valuable intermediates in the syntheses of natural compounds such as prostaglandins, eudesmanolides, eleutherobin, and paraconic acid derivatives [16]. There are also many recent studies in the synthesis of γ-lactones by different procedures [16b][17].

In 2003, *Charette et al.* [18] worked with cinnamate esters that were analogous with our starting esters used in this study. They performed reactions with diazomethane catalyzed by bis[oxazolin-copper(II)], but obtained only cyclopropane derivatives. According to another study performed in 2005 [19], the reaction of methyl methacry-

Scheme 2. *Dioxole Formation by Reaction of α,β-Enones and Enals with Dimethyl Diazomalonate*



Reagents and conditions: boiling benzene, 1:1 molar ratio of **6**, **7**, and **9** – **11** rel. to DMDM, 0.007 mol.-equiv. of $[Cu(acac)_2]$

late and ethyl diazoacetate catalyzed by Ru complexes also yielded cyclopropane derivatives. There are also other examples of conjugated esters providing cyclopropane derivatives upon reaction with diazo compounds [20]. Finally, in 1999 and 2005, *Padwa et al.* prepared ester carbonyl ylides (by intramolecular reaction of diazo and ester functions) that underwent a [3+2] cycloaddition reaction [21].

Results and Discussion. – 1. *Structural Considerations.* In this study, we worked with conjugated esters such as ethyl crotonate (**12**), diethyl fumarate (**13**), diethyl benzalmalonate (**14**), and diethyl ethylidene malonate (**15**). First of all, we needed to confirm that the distance between the carbonyl O-atom and the β-unsaturated C-atom of these substrates was suitable. This was done by geometry optimization with the Desktop Molecular Modeling software. These predictions should also furnish a tool to rationalize the product distribution of the catalytic reaction with DMDM. In all of our previously used enones that yielded dihydrofuran derivatives [2][10] in a pericyclic reaction, the C=O ··· C(β) distances were less than *ca.* 2.9 Å. Very similar approaches had been investigated by *Birney* and co-workers [22a] in the reaction of 'α-oxocamphorketene' (**A**)[1]) with benzaldehyde, and by *Domingo* [22b] in the case of dimethyl 2,3-dimethylenesuccinate with ethylene derivatives. In the report by *Birney et al.* [22a], it was found

[1]) Systematic name: 4,7,7-trimethyl-3-(oxomethylidene)bicyclo[2.2.1]heptane-2-one.

that reactants could not undergo a *Diels–Alder*-type reaction, because the distance between C(2) and O(5) in **A** is too large (3.015 Å; *Fig. 1*). Fortunately, in our case, all of the above esters **12**–**15** gave rise to calculated C=O···C(β) distances below 2.9 Å.

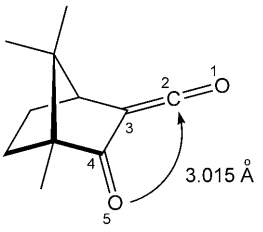
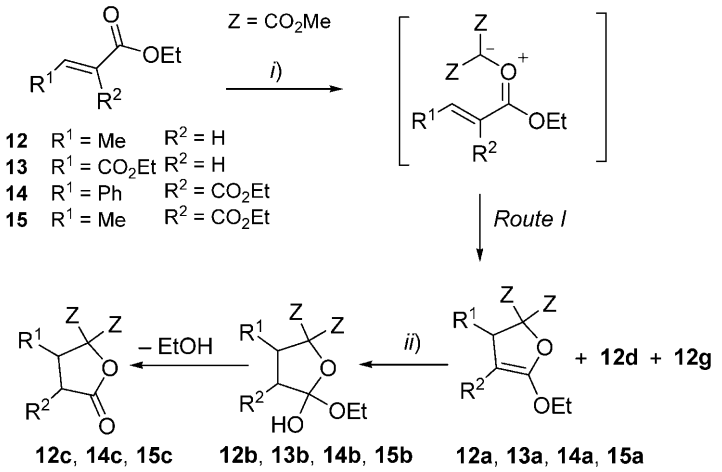


Figure. *Calculated geometry of 'α-Oxocamphorketene'*

2. *Syntheses.* The conjugated esters **12**–**15** were treated each with dimethyl diazomalonate (DMDM) in the presence of [Cu(acac)$_2$] as catalyst. Analysis of the crude mixture from the reaction with ethyl crotonate (**12**) by GC/MS and ^{1}H-NMR stereoscopy revealed the presence of compounds **12b**, **12c**, **12e**, **12f**, **12g**, and **12h** under two different reaction conditions (*Schemes* 3 and *4*)[2]).

Scheme 3. *'First-Step' Reactions*

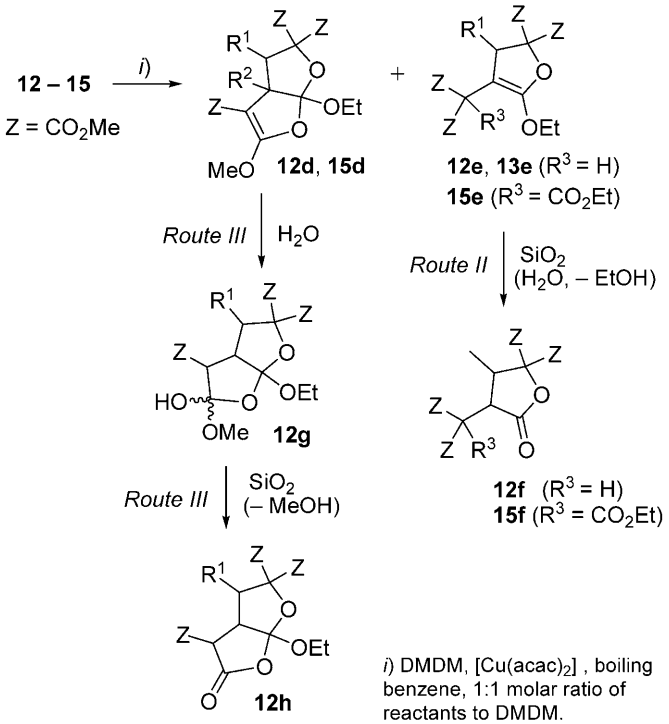


i) DMDM, [Cu(acac)$_2$] , boiling benzene, 4.5:1 molar ratio of reactants to DMDM. *ii*) Under reaction conditions and/or upon chromatography (SiO_2/H_2O).

The crude reaction mixture contained **12b** and **12c** as the 'first-step' carbene products (*Scheme 3*), with minor amounts of **12e** and **12g** as the 'second-step' carbene prod-

[2]) Products arising from, *e.g.*, substrate **12** were numered as **12a**, **12b**, **12c**, *etc.*; the same applies to the other substrates and their products. For substituents and compound names, see *Scheme 3* and *Exper. Part*, resp.

Scheme 4. *'Second-Step' Reactions*

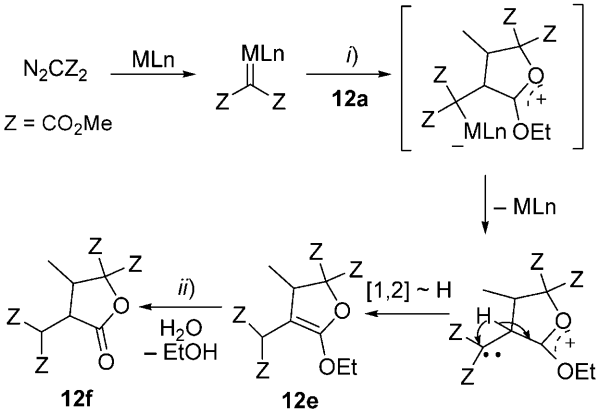


ucts (*Scheme 4*). Further attempts to purify **12b** and **12c** by column chromatography on silica gel resulted in the conversion of **12b** to **12c**.

In the 'second-step' reaction (*Scheme 4*), the main product was **12e**, a vinylic insertion product derived from **12a** with a second molecule of DMDM, together with a small amount of **12g**. There were also **12b** and **12c** present in minor amounts. Attempts to purify these two compounds chromatographically yielded the expected conversion products, *i.e.*, **12f** from **12e** (*Route II*), and **12h** from **12g** (*Route III*). The alternative route, formation of **12f** from **12c** by a carbene, was not observed under these experimental conditions: **12f** was only formed after chromatographic treatment of **12e** on silica gel.

Alonso and *Fernandez* [23] reported apparent vinyl C–H insertion products in the reaction of vinyl ethers with diazomalonates, and suggested an addition–elimination mechanism *via* highly polarized zwitterionic intermediates. *Doyle et al.* [24] proposed a similar explanation based on a competitive H-transfer step. *Davies et al.* [25] also suggested the involvement of zwitterionic intermediates in Rh-catalyzed reactions of vinyl diazoacetates with electron-rich dienes. Based on these assumptions and considering our own experimental results, we propose a vinylic-insertion mechanism for the formation of **12f** from **12e** (*Scheme 5*). An analogous rationalization was recently put forward by *Yan et al.* [26] for the unusual reaction of aryl diazoacetates with enamines in the synthesis of γ-keto esters.

Scheme 5. *A Possible Mechanism for* Route II (see *Scheme 4*)



i) DMDM, [Cu(acac)$_2$] , boiling benzene. *ii*) Under reaction conditions and/or upon chromatography (SiO_2/H_2O).

On the other hand, the formation of **12d** from **12** by a [3+2] addition mechanism with 2 equiv. of DMDM is very similar to what we had observed in our early reports [1][2][10]. Although **12d** could not be detected, the oxofuran derivative **12h** was obtained from **12g**. Similar moieties of spongiane diterpenoids have been synthesized by *Weisser et al.* from methyl 2-furoate and ethyl diazoacetate [27].

In the reaction of diethyl fumarate (**13**), compounds **13b** and **13e** were obtained under both conditions. Diethyl benzylidenemalonate (**14**) afforded **14a** and its derived compounds **14b** and **14c** upon purification. A 'second-step' product arising from the reaction of 2 equiv. of carbene and 1 equiv. of **14** was observed, but could not be purified. Finally, diethyl ethylidenemalonate (**15**) gave the products **15a**–**f** under similar reaction conditions.

Conclusions. – We have shown that a variety of substituted dihydrofurans can be accessed by 1,5-electrocyclic addition of conjugated carbonyl ylides obtained from properly chosen α,β-unsaturated esters and dimethyl diazomalonate (DMDM) in the presence of a Cu catalyst ([Cu(acac)$_2$]). The additional conjugation effect of the ester O-atom of the starting ester might facilitate the formation of the intermediary conjugated carbonyl ylides. Under our experimental conditions, dihydrofuran formation was the only initial pathway. This finding contrasts the literature data, in which mostly the formation of cyclopropane derivatives from conjugated esters and diazo compounds has been reported [18][19][20a–c]. Using diazo dicarbonyl compounds and a different catalyst might support the formation of a more stable conjugated carbonyl ylide, leading to dihydrofuran rather than cyclopopane derivatives.

Thus, 1,5-electrocyclic ring closure reactions of carbonyl ylides from conjugated esters and diazo bis(carbonyl) compounds offer an easy and highly efficient method for the preparation of polyfunctionalized γ-lactones and derivatives as valuable intermediates, especially in the synthesis of models of natural products. While the absence of

substituents at C(α) in **12** and **13** enhanced the reactivity toward a second equivalent of carbene, compounds **14** and **15**, with a CO_2Et group at C(α), notably lacked such reactivity.

Experimental Part

1. *General.* Diethyl benzylidenemalonate (**14**) was synthesized by traditional aldol condensation. Dimethyl diazomalonate (DMDM) was prepared according to a literature procedure [28]. GC/MS: *Hewlett-Packard* instrument, with *HP-1* capillary column (24 m) packed with cross-linked (phenylmethyl)siloxane; retention times t_R in min. IR Spectra: *Jasco FT-IR-5300* apparatus; in cm^{-1}. NMR Spectra: *Bruker* apparatus, at 250 MHz (^{1}H) and 60 MHz (^{13}C); δ in ppm rel. to Me_4Si, J in Hz, at 25°.

2. *General Procedure for the 'First-Step' Reaction of Conjugated Esters with DMDM*. To a soln. of the conjugated ester (4.5 mmol) in benzene (10 ml) was added [Cu(acac)$_2$] (7 µmol), and the mixture was heated at reflux. Then, a soln. of DMDM (1 mmol) in benzene (5 ml) was added to this soln. over 72 h under N_2 atmosphere. When the IR spectrum of the reaction mixture indicated total consumption of DMDM (absence of the characteristic diazo band at 2130 cm^{-1}), the mixture was filtered to remove the catalyst, evaporated, and purified by column chromatography (CC).

For the corresponding 'second-step' reactions, the above procedure was followed, with the exception that *equimolar* amounts of conjugated ester and DMDM were used.

3. *'First-Step' Reaction of* **12**. 3.1. *Analysis of the Reaction Mixture by GC/MS.* Column conditions (0.54 bar He; EI-MS detector): 150° for 7 min, then heating to 180° at 3°/min, 14 min isothermal at 180°, then heating to 290° at 5°/min, 10 min isothermal at 290°. Product distribution: **12b** (40%): t_R 8.1; m/z 263 ($[M+1]^+$). **12c** (43%): t_R 5.5; m/z 216 (M^+). **12e** (3%): t_R 22.50; m/z 375 ($[M+1]^+$). **12g** (2%): t_R 24.68; m/z 392 (M^+). Ratio **12b**/**12c** 1:1 in the crude mixture (^{1}H-NMR).

3.2. *Purification and Analytical Data*. The crude reaction mixture was passed over SiO_2, eluting with benzene, and the products were separated by prep. TLC (SiO_2; hexane/AcOEt 2:1). Total yield: 71%. Compounds **12c** and **12b** were identified as a mixture (ratio 1.45:1) by ^{1}H-NMR. To confirm the conversion of **12b** to **12c** under our chromatographic conditions, a micro-sample of the crude mixture was refluxed over SiO_2 with benzene for 1 h, which led to **12c** as the main product (GC/MS).

*Dimethyl 5-Ethoxy-4,5-dihydro-5-hydroxy-3-methylfuran-2,2(3*H*)-dicarboxylate* (**12b**). GC: t_R 8.1. ^{1}H-NMR ($CDCl_3$): 4.14 (*q*, J=7.1, 2 H); 3.86 (*s*, MeO); 3.82 (*s*, MeO); 3.07–2.93 (*m*, 1 H); 2.37–2.21 (*m*, 2 H); 1.80 (br. *s*, OH); 1.26 (*t*, J=7.1, 3 H); 0.97 (*d*, J=6.7, 3 H). ^{13}C-NMR ($CDCl_3$): 173.4–172.2 (2 C); 120.9; 62.0; 52.0–51.3 (2 C); 39.7; 17.4; 15.2, 14.9. EI-MS: 263 (1, $[M+1]^+$), 217 (40, $[M-OC_2H_5]^+$), 203 (50), 157 (100), 143 (45), 129 (85), 115 (52), 101 (30), 87 (31), 69 (33), 59 (60). HR-EI-MS: 262.1047 (M^+, $C_{11}H_{18}O_7^+$; calc. 262.1053).

*Dimethyl 3,4-Dihydro-3-methyl-5-oxofuran-2,2(3*H*)-dicarboxylate* (**12c**). GC: t_R 5.5. ^{1}H-NMR ($CDCl_3$): 3.86 (*s*, MeO); 3.84 (*s*, MeO); 3.25–3.1 (*m*, 1 H); 2.77 (*dd*, J=17.5, 8.5, 1 H); 2.4 (*dd*, J=17.5, 10.0, 1 H); 1.19 (*d*, J=6.9, 3 H). ^{13}C-NMR ($CDCl_3$): 171.5–170.5; 166.5; 87.6; 36.2; 17.2; 14.7. EI-MS: 216 (1, M^+), 172 (5), 157 (90), 129 (85), 101 (40), 59 (100). HR-EI-MS: 216.0629 (M^+, $C_9H_{12}O_6^+$; calc. 216.0634).

4. *'Second-Step' Reaction of* **12**. 4.1. *Analysis of the Reaction Mixture.* **12e** (60%): t_R 22.50; m/z 375 ($[M+1]^+$). **12g** (20%): t_R 24.68; m/z 392 (M^+). **12b** (5%): t_R 8.1; m/z 263 ($[M+1]^+$). **12c** (2%): t_R 5.5; m/z 216 (M^+).

4.2. *Purification and Analytical Data*. The crude mixture was chromatographed (SiO_2; benzene). Product distribution: **12f** (95%): t_R 15.3; m/z 346 (M^+), derived from **12e**. **12h** (5%): t_R 15.9; m/z 329 ($[M-OCH_3]^+$), derived from **12g**.

*Dimethyl 4-[Bis(methoxycarbonyl)methyl]-5-ethoxy-3-methylfuran-2,2(3*H*)-dicarboxylate* (**12e**). GC: t_R 22.50. EI-MS: 375 (40, $[M+1]^+$), 361 (56), 347 (78), 315 (27), 301 (33), 287 (76), 270 (22), 255 (40), 227 (55), 195 (44), 171 (100), 29 (40), 113 (35), 59 (42).

*Trimethyl 6a-Ethoxy-5-hydroxy-3-methyl-5-methoxytetrahydrofuro[2,3-*b*]furan-2,2,4(3*H*)-tricarboxylate* (**12g**). GC: t_R 24.68. EI-MS: 392 (1, M^+), 389 (35), 375 (79), 361 (71), 329 (26), 315 (50), 301 (59), 287 (28), 255 (43), 241 (39), 227 (43), 195 (54), 171 (100), 129 (50), 113 (36), 59 (42).

Dimethyl trans-*4-[Bis(methoxycarbonyl)methyl]-4,5-dihydro-3-methyl-5-oxofuran-2,2(3*H)*-dicarboxylate* (**12f**). Obtained in crystalline form (47% by GC) from hexane. GC: t_R: 15.3. ^{1}H-NMR ($CDCl_3$): 3.92 (*d*, *J* = 4.5); 3.87 (*s*, MeO); 3.84 (*s*, MeO); 3.78 (*s*, MeO); 3.76 (*s*, MeO); 3.26 (*dt*, *J* = 11.5, 6.7, 1 H); 3.10 (*dd*, *J* = 11.5, 4.5, 1 H); 1.14 (*d*, *J* = 6.7, 3 H). ^{13}C-NMR ($CDCl_3$): 173.1; 167.1; 167.0; 166.1; 165.9; 86.2; 53.6; 53.5; 53.0; 49.8; 45.1; 38.7; 14.7. EI-MS: 346 (1, M^+), 331 (1), 315 (10), 287 (100), 255 (30), 227 (40), 215 (32), 195 (42), 167 (38), 155 (8), 139 (9), 127 (25), 113 (28), 59 (35). HR-EI-MS: 346.0891 (M^+, $C_{14}H_{18}O_{10}^+$; calc. 346.0900).

*Trimethyl 6a-Ethoxy-3-methyl-5-oxodihydrofuro[2,3-*b*]furan-2,2,4(3*H*)-tricarboxylate* (**12h**). GC: t_R 15.9. ^{1}H-NMR ($CDCl_3$; from crude fraction): 4.24–4.19 (*m*, 2 H); 3.86 (*s*, MeO); 3.78 (*s*, MeO); 3.76 (*s*, MeO); 2.17–2.16 (*m*, 2 H); 1.23–1.29 (*m*, 3 H); 1.15 (*d*, *J* = 6.7, 3 H). EI-MS: 329 (5, $[M-OCH_3]^+$), 315 (8), 301 (100), 287 (7), 269 (25), 255 (25), 241 (30), 227 (32), 215 (28), 195 (52), 181 (10), 167 (30), 146 (32), 127 (25), 113 (26), 99 (8), 59 (20). HR-EI-MS: 360.1042 (M^+, $C_{15}H_{20}O_{10}^+$; calc. 360.1056).

5. *Reaction of* **13**. 5.1. *Analysis of Reaction Mixtures.* GC column conditions: 100° isothermal for 5 min, then heating to 290° at (*A*) 20°/min or (*B*) 10°/min; 0.54 bar He; EI-MS detector. In the 'first-step' reaction, the crude mixture contained **13a** [t_R (*A*): 11.6; *m*/*z* 302 (M^+)] and **13e** [t_R (*A*) 13.8; *m*/*z* 433 ($[M+1]^+$) in a ratio of 1:2.28, but the compounds could not be purified. In the 'second-step' reaction, **13b** [t_R (*B*) 16.3; *m*/*z* 320 (M^+)] and **13e** [t_R (*B*) 20; *m*/*z* 433 ($[M+1]^+$)] were observed in a ratio of 1:2.75. After chromatographic separation (Al_2O_3), these two compounds were obtained in 13 and 58% yield, resp.

5.2. *Analytical Data. 3-Ethyl 2,2-Dimethyl 5-Ethoxyfuran-2,2,3(3*H*)-tricarboxylate* (**13a**). GC: t_R 11.6. EI-MS: 302 (7, M^+), 270 (1), 256 (15), 229 (82), 201 (100), 173 (5), 157 (59), 142 (21), 113 (30), 59 (6).

*3-Ethyl 2,2-Dimethyl 5-Ethoxy-4,5-dihydro-5-hydroxyfuran-2,2,3(3*H*)-tricarboxylate* (**13b**). GC: t_R 16.3. ^{1}H-NMR ($CDCl_3$): 4.10 (*q*, *J* = 7.1, 2 H); 3.8 (*q*, *J* = 7.1, 2 H); 3.76 (*s*, MeO); 3.64 (*s*, MeO); 2.50–2.30 (*m*, 3 H); 1.27 (*m*, 6 H). ^{13}C-NMR ($CDCl_3$): 175.2; 166.9; 165.2; 104.2; 82.1; 59.1; 53.8; 53.2; 51.1; 45.8; 38.1; 31.2; 29.7. EI-MS: 320 (1, M^+), 275 (5), 261 (13), 244 (12), 229 (10), 215 (100), 187 (55), 159 (56), 141 (28), 127 (36), 113 (58), 59 (16). HR-EI-MS: 320.1093 (M^+, $C_{13}H_{20}O_9^+$; calc. 320.1107).

*3-Ethyl 2,2-Dimethyl 4-[Bis(methoxycarbonyl)methyl]-5-ethoxyfuran-2,2,3(3*H*)-tricarboxylate* (**13e**). GC: t_R 13.8. ^{1}H-NMR ($CDCl_3$): 4.16–4.10 (*m*, 2 H); 3.86, 3.82, 3.74, 3.67 (4*s*, 4 MeO); 3.78–3.68 (*m*, 2 H); 3.71 (*s*, 1 H); 2.50–2.30 (*m*, 3 H); 3.24 (*s*, 1 H); 1.28 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$): 177.1; 170.6; 169.1; 166.3 141.4; 77.2; 60.6; 59.3; 52.4; 52.0; 51.5; 49.6; 42.4; 30.8; 28.6. EI-MS: 433 (11, $[M+1]^+$), 432 (M^+, 3), 419 (21), 405 (28), 386 (2), 359 (32), 313 (24), 302 (8), 229 (100), 287 (29), 227 (27), 211 (95), 171 (21), 153 (4), 113 (22), 59 (3). HR-EI-MS: 432.1255 (M^+, $C_{18}H_{24}O_{12}^+$; calc. 432.1268).

6. *Reaction of* **14**. 6.1. *Analysis of Reaction Mixtures.* Column conditions: 150° isothermal for 5 min, then heating to 290° at 40°/min; 0.54 bar He; EI-MS detector. The crude mixture from the 'first-step' reaction contained mainly **14a** [57%; t_R 9.17; *m*/*z* 387 (M^+)] and a formal 'second-step' product (15%; t_R 11.67). When the oily mixture was subjected to CC (SiO_2; hexane/AcOEt 2:1), two additional compound were observed: **14b** [t_R 9.27; *m*/*z* 381 ($[M^+-CH_3]^+$)] and **14c** [t_R 9.38; *m*/*z* 350 (M^+)] derived from **14a**, which were also obtained in combined fractions (**14a**/**14b** and **14b**/**14c**).

6.2. *Analytical Data. 4-Ethyl 2,2-Dimethyl 5-Ethoxy-3-phenylfuran-2,2,4(3*H*)-tricarboxylate* (**14a**). ^{1}H-NMR ($CDCl_3$): 7.42–7.25 (*m*, 5 arom. H); 5.10 (*s*, 1 H); 4.53–4.47 (*m*, 2 H); 4.04–3.97 (*m*, 2 H); 3.88 (*s*, 3 H); 3.18 (*s*, 3 H); 1.48 (*t*, *J* = 7.1, 3 H); 0.99 (*t*, *J* = 7.1, 3 H). ^{13}C-NMR ($CDCl_3$): 166.7; 165.0; 164.9; 164.1; 142.1; 129.4; 128.8; 128.5; 86.2; 71.8; 61.8; 61.7; 61.6; 53.3; 14.1; 13.9. EI-MS: 378 (18, M^+), 333 (17), 318 (18), 304 (60), 244 (100), 203 (20), 129 (34), 77 (16), 59 (15). HR-MS: 378.1303 (M^+, $C_{19}H_{22}O_8^+$; calc. 378.1315).

*4-Ethyl 2,2-Dimethyl 5-Ethoxy-4,5-dihydro-5-hydroxy-3-phenylfuran-2,2,4(3*H*)-tricarboxylate* (**14b**). Obtained as a mixture **14b**/**14c**. GC: t_R 9.27. ^{1}H-NMR ($CDCl_3$): 7.41–7.27 (*m*, 5 arom. H); 4.54–4.50 (*m*, 1 H); 4.43 (*s*, OH); 4.22 (*q*, *J* = 7.1, 2 H); 3.85 (*s*, 3 H); 3.73–3.80 (*m*, 2 H); 3.30–3.12 (*m*, 1 H); 2.03 (*s*, 3 H); 1.26 (*t*, *J* = 7.0, 3 H); 1.24 (*t*, *J* = 7.0, 3 H). EI-MS: 396 (M^+, not. obs.), 381 (5, $[M-CH_3]^+$), 350 (1), 323 (30), 261 (29), 229 (80), 121 (87), 105 (100), 77 (18), 59 (30).

*4-Ethyl 2,2-Dimethyl 4,5-Dihydro-5-oxo-3-phenylfuran-2,2,4(3*H*)-tricarboxylate* (**14c**). Obtained as a mixture **14b**/**14c**. ^{1}H-NMR ($CDCl_3$): 7.60–7.29 (*m*, 5 arom. H); 4.54–4.50 (*m*, 1 H); 4.10 (*q*, *J* = 7.0, 2

H); 3.82 (*s*, 6 H); 3.30–3.12 (*m*, 1 H); 1.27–1.11 (*m*, 3 H). ^{13}C-NMR ($CDCl_3$): 168.5; 166.4–166.8; 165.8; 136.0–129.1; 113.4; 62.1; 53.0; 38.1; 29.6; 13.4. EI-MS: 350 (2, M^+), 323 (45), 261 (40), 229 (97), 189 (10), 173 (12), 121 (90), 105 (100), 59 (30).

Formal 'Second-Step' Product. The crude reaction mixture showed enrichment (20%) of the GC/MS peak at t_R 11.67, but attempts for chromatographic purification were not successful. EI-MS (crude fraction): 508 (M^+, not obs.), 424 (22), 379 (2), 351 (13), 333 (6), 305 (21), 279 (7), 264 (100), 247 (26), 221 (84), 189 (99), 174 (13), 146 (6), 105 (63), 77 (13), 59 (7).

7. *Reaction of* **15**. 7.1. *'First-Step' Reaction*. The crude mixture contained **15a** [t_R 12.12; *m*/*z* 316 (M^+)] and **15b** [t_R 12.23; *m*/*z* 289 ([$M+1-C_2H_5OH$]$^+$)] in a ratio of 1:1. Prep. TLC (Al_2O_3; hexane/AcOEt 3:1) gave mainly **15c** [t_R 11.71; *m*/*z* 287 ([$M-1$]$^+$)], with small amounts of **15a** and **15b**, but none of the products could be obtained in pure form. All anal. data were obtained from the crude fraction.

EI-MS Data. **15a**: 316 (25, M^+), 301 (5), 284 (4), 271 (30), 256 (14), 242 (50), 182 (100), 141 (40), 59 (20). **15b**: 334 (M^+, not obs.); 289 (12, [$M+1-C_2H_5OH$]$^+$), 275 (42), 258 (5), 243 (4), 229 (100), 215 (30), 183 (56), 141 (57), 59 (16). **15c**: 287 (8, [$M-1$]$^+$), 241 (20), 187 (60), 159 (45), 141 (100), 127 (90), 59 (15).

7.2. *'Second-Step' Reaction*. GC/MS Analysis of the mixture revealed the 'first-step' products **15a**–**c** (65%), together with the 'second-step' products **15d** [t_R 14.03; *m*/*z* 446 (M^+)], **15e** [t_R 14.07; *m*/*z* 446 (M^+)], *cis*/*trans*-**15f** [t_R 14.2; *m*/*z* 419 ([$M+1$]$^+$); t_R 14.4; *m*/*z* 419 ([$M+1$]$^+$)] in a ratio of 1:1.90:1.54:3.85. Purification attempts by prep. TLC (Al_2O_3; hexane/AcOEt 3:1) only gave a fraction enriched in **15e**, with **15d** and *cis*/*trans*-**15f** as minor compounds, the ratio **15d**/**15e**/**15f** being *ca*. 1.2:5:1. The ^{1}H-NMR data of this fraction represented mainly **15e**.

EI-MS Data (crude fraction). **15d**: 446 (1, M^+), 432 (1), 417 (2), 401 (35), 387 (100), 359 (6), 271 (40), 243 (75), 215 (5), 59 (20). *cis*/*trans*-**15f**: t_R 14.4; *m*/*z* 419 (1, M^+), 402 (1), 387 (5), 359 (60), 345 (65), 287 (100), 271 (20), 243 (25), 59 (22); the other isomer: t_R 14.4; *m*/*z* 419 (1, M^+), 403 (1), 359 (23), 345 (2), 271 (60), 243 (100), 183 (40), 59 (15).

Ethyl Dimethyl [2-Ethoxy-4,5-dihydro-4-methyl-5,5-bis(methoxycarbonyl)furan-3-yl]methanetricarboxylate (**15e**). Yield: 7%. GC: t_R: 14.07. ^{1}H-NMR ($CDCl_3$): 4.18–4.12 (*m*, 2 H); 3.89 (*m*, 2 H); 3.80 (*s*, 2 MeO); 3.75 (*s*, MeO); 3.73 (*m*, 1 H); 3.66 (*s*, MeO); 1.26 (*d*, $J=7.0$); 1.24–1.13 (*m*, 6 H). EI-MS: 446 (17, M^+), 431 (2), 415 (9), 401 (5), 387 (7), 373 (84), 313 (98), 281 (100), 243 (50), 215 (26), 158 (54), 59 (17). HR-EI-MS: 446.1411 (M^+, $C_{19}H_{26}O_{12}^+$; calc. 446.1424).

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