# Synthesis of Halogenated $\alpha,\beta$-Unsaturated $\gamma$-Butyrolactone Derivatives by Triphenylphosphine-Catalyzed Cyclization of $\alpha$-Halogeno Ketones with Dialkyl Acetylenedicarboxylates (= Dialkyl But-2-ynedioates)

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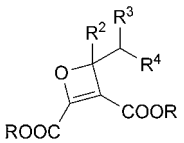
A $Ph_3P$-catalyzed cyclization of $\alpha$-halogeno ketones **2** with dialkyl acetylenedicarboxylates (=dialkyl but-2-ynedioates) **3** produced halogenated $\alpha,\beta$-unsaturated $\gamma$-butyrolactone derivatives **4** in good yields (*Scheme 1*, *Table*). The presence of electron-withdrawing groups such as halogen atoms at the $\alpha$-position of the ketones was necessary in this reaction. Cyclization of $\alpha$-chloro ketones resulted in higher yields than that of the corresponding $\alpha$-bromo ketones. Dihalogeno ketones similarly afforded the expected $\gamma$-butyrolactone derivatives in high yields.

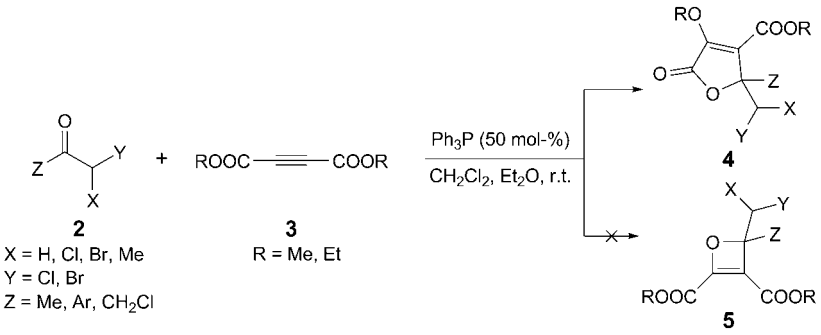
**Introduction**. – Several methods have been reported for the synthesis of $\alpha,\beta$-unsaturated $\gamma$-butyrolactones [1–10]. In 1996, *Nozaki* and co-workers described a $Ph_3P$-catalyzed lactone formation from $\alpha$-keto esters, $\alpha$-ketonitriles, or $\alpha,\alpha,\alpha$-trifluoroacetophenone and dialkyl acetylenedicarboxylate (=dialkyl but-2-ynedioate) in moderate to good yields [10]. $\alpha$-Keto esters, $\alpha$-ketonitriles, and $\alpha,\alpha,\alpha$-trifluoroacetophenone contain electron-withdrawing groups directly bound to their ketonic C=O group. The strong electrophilic nature of these ketonic groups is expected to facilitate nucleophilic additions of zwitterion intermediates derived from $Ph_3P$ and dialkyl acetylenedicarboxylates [11]. We were interested in the use of $\alpha$-halogeno ketones as trapping reagents for the zwitterionic intermediate. We reported the reaction of 1,1-dichloroacetone (=1,1-dichloropropan-2-one) and phenacyl chloride (=2-chloro-1-phenylethanone) as electron-deficient ketones with acetylenic esters in the presence of $Ph_3P$ [12]. In that report, based on spectral data ($^1$H- and $^{13}$C-NMR) and lack of X-ray quality crystal, we suggested the halogenated 2*H*-oxete-3,4-dicarboxylates **1** as the product of these reactions.




**1**

However, our complementary studies which, in part, are reported here show that compound **4** as illustrated in *Scheme 1*, is the sole product of this reaction. In fact, by NMR spectroscopy, structures **4** and **5** can hardly be distinguished. Thus, stronger

*Scheme 1*




evidence was required to confirm the definite structure of the product. In this regard, we were motivated to use a variety of $\alpha$-halogeno ketones as trapping reagents for the zwitterionic intermediate. The spectral data ($^1$H- and $^{13}$C-NMR) of the products, together with a single-crystal X-ray analysis of compound **4d** (*Fig.*), as will be discussed below, established the formation of the halogenated $\alpha,\beta$-unsaturated $\gamma$-butyrolactone derivatives **4a**–**4r** without formation of any 2*H*-oxete derivatives **5** (*Scheme 1*). In addition, to further confirm the formation of a five-membered cyclic compound **4**, the resultant product was refluxed in toluene and xylene for 10 h. The analysis (monitored by TLC) did not show any change in the product identity. Whereas, if a four-membered cyclic compound **5** would have been formed, an electrocyclic ring opening should readily take place under reflux conditions [13–17].

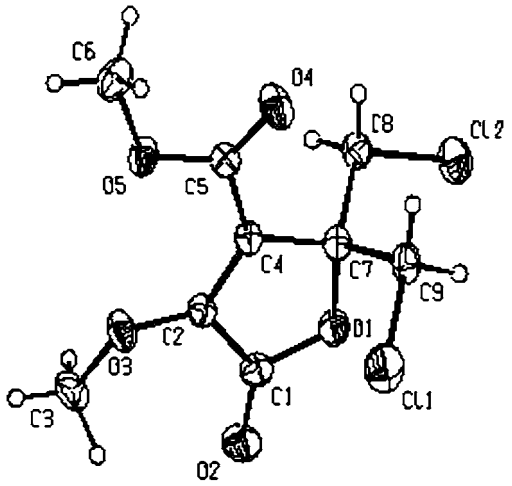



Figure. *ORTEP Diagram of* **4d**. Arbitrary atom numbering.

**Results and Discussion.** – Initially, the reaction of chloroacetone (=1-chloropropan-2-one; **2a**) and dimethyl acetylenedicarboxylate (**3**, R = Me) with $Ph_3P$ was

examined at room temperature leading to **4a** as the sole product in good yield after 2 h (*Table*). To investigate the scope and limitations of this reaction further, we extended our study to various $\alpha$-halogeno ketones (*Table*). All the reactions ran well affording the desired $\alpha,\beta$-unsaturated $\gamma$-butyrolactone derivatives **4a**–**4r** in good yields. The $\alpha$-chloro ketones were more reactive than the $\alpha$-bromo ketones (*cf.* **4f** *vs.* **4k** in the *Table*). The $\alpha,\alpha$-dichloro ketones reacted faster than $\alpha$-chloro ketones and afforded the expected products in higher yields (*cf.* **4c** *vs.* **4a** in the *Table*). These results imply that the electron-withdrawing halogen atoms at the $\alpha$-position with respect to the C=O group play an important role in the reaction. Moreover, the presence of this substituent was essential for the reaction to proceed. $\alpha$-Halogeno ketones with electron-donating groups at the $\alpha$-position gave lower yields of the expected $\gamma$-butyrolactone darivative (*Table*, **4i** and **4j**). In the case of $\alpha$-bromo *p*-substituted-aryl ketones, the strong electron-withdrawing $NO_2$ group at the *p*-position of the aryl moiety resulted in high yields of the product (*Table*, **4q** and **4r**). An interesting feature of this reaction is the fact that all reactions afforded chemoselectively the desired $\alpha,\beta$-unsaturated lactone derivatives, and no phosphorus ylides were obtained. It is also of interest to note that triphenyl or trimethyl phosphite in place of $Ph_3P$ gave complex mixtures without formation of any $\alpha,\beta$-unsaturated $\gamma$-lactone derivative.

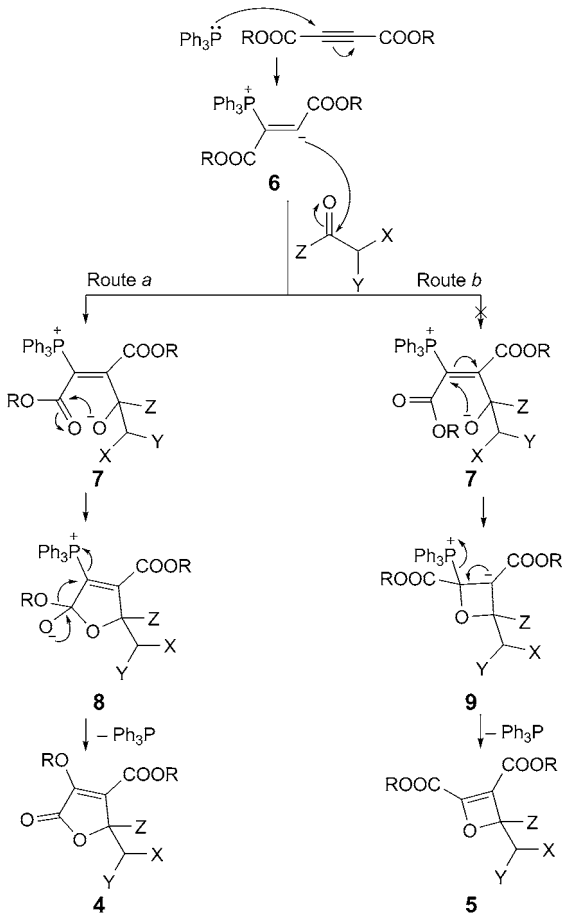
Table. *$Ph_3P$-Catalyzed Synthesis of $\gamma$-Butyrolactones Derivatives* **4** *from $\alpha$-Halogeno Ketones* **2** *and Dialkyl Acetylenedicarboxylates* **3** (alkyl = R)

| **2** and **4** | Z | X | Y | R | Yield [%][a]) | Time [h] |
|---|---|---|---|---|---|---|
| **a** | Me | H | Cl | Me | 60 | 2 |
| **b** | Me | H | Cl | Et | 62 | 2 |
| **c** | Me | Cl | Cl | Me | 70[b]) | 1 |
| **d** | $CH_2Cl$ | H | Cl | Me | 85 | 1 |
| **e** | $CH_2Cl$ | H | Cl | Et | 82 | 1 |
| **f** | Ph | H | Cl | Me | 80[b]) | 2 |
| **g** | Ph | Cl | Cl | Me | 87 | 1 |
| **h** | Ph | Cl | Cl | Et | 85 | 1 |
| **i** | Me | Me | Cl | Me | 30 | 3 |
| **j** | Me | Me | Cl | Et | trace | 3 |
| **k** | Ph | H | Br | Me | 50 | 2 |
| **l** | Ph | H | Br | Et | 52 | 3 |
| **m** | 4-Br–$C_6H_4$ | H | Br | Me | 62 | 2 |
| **n** | 4-Br–$C_6H_4$ | H | Br | Et | 60 | 2 |
| **o** | 4-Cl–$C_6H_4$ | H | Br | Me | 56 | 2 |
| **p** | 4-Cl–$C_6H_4$ | H | Br | Et | 55 | 2 |
| **q** | 4-$NO_2$–$C_6H_4$ | H | Br | Me | 80 | 1.5 |
| **r** | 4-$NO_2$–$C_6H_4$ | H | Br | Et | 78 | 1.5 |

[a]) Yield of isolated product **4**. [b]) Reported previously [12].

A possible mechanism for the presented reaction is shown in *Scheme 2*. On the basis of the well established chemistry of trivalent phosphorus nucleophiles [17–25], it is reasonable to assume that the zwitterionic intermediate **6** results from an initial addition of $Ph_3P$ to the dialkyl acetylenedicarboxylate. Then, intermediate **6** attacks the

*Scheme 2*




C=O group of the $\alpha$-halogeno ketone which leads to the dipolar species **7**. Intermediate **7** can either undergo attack at the C=O group of the ester moiety to form the five-membered cyclic dipolar species **8**, followed by anionic 1,2-alkoxy migration and loss of $Ph_3P$ to give **4** (*Route a* in *Scheme 2*), or undergo attack at the C=C bond to form the four-membered cyclic dipolar intermediate **9**, followed by loss of $Ph_3P$ to afford 2*H*-oxete derivatives **5** (*Route b* in *Scheme 2*).

The structures of **4a**–**4q** were deduced from their $^1$H- and $^{13}$C-NMR and IR spectra as well as elemental analyses. The mass spectra of the $\alpha,\beta$-unsaturated $\gamma$-lactone derivatives displayed molecular-ion peaks for the mono- and dihalogenated forms with the appropriate $m/z$ values for $M^+$ and $[M+2]^+$, and for $M^+$, $[M+2]^+$, and $[M+4]^+$, respectively. The $^1$H-NMR spectrum of **4a** in $CDCl_3$ exhibited a *s* at $\delta$(H) 1.67 for the Me group, two *s* at $\delta$(H) 3.86 and 4.28 for the two MeO groups, and two *d* at $\delta$(H) 3.85 and 4.04 ($^2J = 11.6$ Hz) for the $CH_2Cl$ group. The $^{13}$C-NMR spectrum of **4a** displayed

nine sharp lines in agreement with the proposed structure. The partial assignment of these resonances is given in the *Exper. Part*. The mass spectrum of **4a** exhibited the molecular-ion peaks at *m*/*z* 234 (9, $M^+$) and 236 (3, $[M+2]^+$) due to the presence of the isotopes of Cl-atom ($^{35}$Cl and $^{37}$Cl). The $^1$H- and $^{13}$C-NMR spectra of **4b**–**4q** were similar to those of **4a**, except for the data of the substituents at positions 2, 3, and 4, which showed characteristic resonances in the expected spectral regions. Finally, the structure of product **4d** was confirmed unambiguously by a single-crystal X-ray analysis (*Fig.*).

**Conclusions.** – In summary, we developed a highly efficient procedure for the synthesis of fully substituted $\alpha,\beta$-unsaturated $\gamma$-butyrolactone derivatives involving halogen atoms from various $\alpha$-halogeno ketones and dialkyl acetylenedicarboxylate in the presence of $Ph_3P$. The present work provides new extentions of $Ph_3P$-catalyzed organic syntheses. Scope and limitation of the reaction are described. The simplicity of the present procedure also makes it an interesting alternative to other approaches.

## Experimental Part

*General*. Dialkyl acetylenedicarboxylates, $Ph_3P$, chloroacetone (=1-chloropropan-2-one), 1,1-dichloroacetone (=1,1-dichloropropan-2-one), 1,3-dichloroacetone (=1,3-dichloropropan-2-one), 3-chlorobutan-2-one, 2-chloroacetophenone (=2-chloro-1-phenylethanone), 2,2-dichloroacetophenone (=2,2-dichloro-1-phenylethanone), 2-bromoacetophenone (=2-bromo-1-phenylethanone), 2-bromo-4-nitroacetophenone (=2-bromo-1-(4-nitrophenyl)ethanone), 2-bromo-4-chloroacetophenone (=2-bromo-1-(4-chlorophenyl)ethanone) and 2,4-dibromoacetophenone (=2-bromo-1-(4-bromophenyl)ethanone) were purchased from *Fluka* and *Merck* and used without further purification. M.p.: *Electrothermal-9100* apparatus. IR Spectra: *Bruker-Vector-22* FT-IR spectrometer; $\nu$ in cm$^{-1}$. $^1$H- and $^{13}$C-NMR spectra: *Bruker-DRX-400-Avance* instrument; at 400.1 ($^1$H) and 100.6 MHz ($^{13}$C) in $CDCl_3$; $\delta$ in ppm rel. to $Me_4Si$ as internal standard, *J* in Hz. MS: *Finnigan-Mat-8430* mass spectrometer; ionization potential 70 eV; in *m*/*z* (rel. %). Elemental analyses: *Heraeus-CHN-O-Rapid* analyzer.

*Compounds* **4**: *General Procedure. Methyl 2-(Chloromethyl)-2,5-dihydro-4-methoxy-2-methyl-5-oxofuran-3-carboxylate* (**4a**). Typical procedure: To a magnetically stirred soln. of chloroacetone (0.16 ml, 2 mmol) and dimethyl acetylenedicarboxylate (0.25 ml, 2 mmol) in $CH_2Cl_2$/$Et_2O$ 1:4 (10 ml) was added $Ph_3P$ (0.26 g, 1 mmol) at r.t. over 10 min. The mixture was stirred for 2 h. The solvent was evaporated and the residue purified by column chromatography (silica gel ($SiO_2$ *60*, 70–230 mesh; *Merck*), hexane/AcOEt 9:1): **4a** (0.33 g; 70%). White powder. M.p. 65–67°. $R_f$ (AcOEt/hexane 1:4) 0.6. IR: 1772 and 1701 (C=O), 1651 (C=C). $^1$H-NMR: 1.67 (*s*, Me); 3.85 (*d*, $^2J$ = 11.6, CH); 3.86 (*s*, MeO); 4.04 (*d*, $^2J$ = 11.6, CH); 4.28 (*s*, MeO). $^{13}$C-NMR: 23.0 (Me); 48.6 ($CH_2Cl$); 52.5, 60.1 (2 MeO); 83.4 (*s*, *C*(Me)$CH_2Cl$); 123.3 (O–C=*C*); 150.1 (O–*C*=C); 162.0, 165.2 (2 C=O). MS: 236 (3, $[M+2]^+$), 234 (9, $M^+$), 221 (3), 219 (100), 205 (5), 203 (14), 185 (100), 153 (91), 125 (14), 115 (80), 83 (32), 59 (17), 43 (38). Anal. calc. for $C_9H_{11}ClO_5$ (234.49): C 46.07, H 4.73; found: C 45.85, H 4.66.

*Ethyl 2-(Chloromethyl)-4-ethoxy-2,5-dihydro-2-methyl-5-oxofuran-3-carboxylate* (**4b**): Yield 0.36 g (68%). White powder. M.p. 53–55°. $R_f$ (AcOEt/hexane 1:4) 0.6. IR: 1774, 1703 (C=O), 1652 (C=C). $^1$H-NMR: 1.34 (*t*, $^3J$ = 7.2, Me); 1.38 (*t*, $^3J$ = 7.2, Me); 1.66 (*s*, Me); 3.85 (*d*, $^2J$ = 11.7, CH); 4.04 (*d*, $^2J$ = 11.7, CH); 4.30 (*q*, $^3J$ = 7.2, $CH_2$); 4.61–4.71 (*m*, $CH_2O$). $^{13}$C-NMR: 13.4, 15.8, 23.0 (3 Me); 48.7 ($CH_2Cl$); 61.6, 68.8 (2 $CH_2O$); 83.6 (*s*, *C*(Me)$CH_2Cl$); 127.4 (O–C=*C*); 149.7 (O–*C*=C); 161.6, 165.6 (2 C=O). MS: 264 (11, $[M+2]^+$), 262 (34, $M^+$), 218 (2), 216 (7), 203 (3), 201 (10), 183 (9), 139 (23), 130 (44), 111 (28), 97 (38), 83 (48), 77 (17), 69 (55), 57 (100), 43 (90). Anal. calc. for $C_{11}H_{15}ClO_5$ (262.51): C 50.29, H 5.76; found: C 50.15, H 5.69.

*Methyl 2,2-Bis(chloromethyl)-2,5-dihydro-4-methoxy-5-oxofuran-3-carboxylate* (**4d**): Yield 0.46 g (85%). White powder. M.p. 114–116°. $R_f$ (AcOEt/hexane 1:4) 0.5. IR: 1774 and 1730 (C=O), 1652

(C=C). $^1$H-NMR: 3.87 (*s*, MeO); 4.00, 4.02 (*AB d*, $^2J = 11.6$, 2 $CH_2Cl$); 4.32 (*s*, MeO). $^{13}$C-NMR: 45.5 ($CH_2Cl$); 52.5, 60.1 (2 MeO); 84.3 (*s*, *C*($CH_2Cl)_2$); 119.0 (O–C=*C*); 151.0 (O–*C*=C); 161.4, 164.2 (2 C=O). MS: 273 (9, $[M+5]^+$), 271 (43, $[M+1+2]^+$), 269 (75, $[M+1]^+$), 235 (8), 233 (24), 221 (31), 219 (92), 189 (36), 187 (10), 161 (3), 159 (10), 143 (3), 141 (8), 114 (62), 103 (6), 101 (16), 83 (23), 59 (18), 51 (18), 49 (26). Anal. calc. for $C_9H_{10}Cl_2O_5$ (268.94): C 40.17, H 3.75; found: C 40.8, H 3.70.

*Ethyl 2,2-Bis(chloromethyl)-4-ethoxy-2,5-dihydro-5-oxofuran-3-carboxylate* (**4e**): Yield 0.49 g (82%). White powder. M.p. 58–60°. $R_f$ (AcOEt/hexane 1:4) 0.5. IR: 1775 and 1701 (C=O), 1649 (C=C). $^1$H-NMR: 1.32 (*t*, $^3J = 7.2$, Me); 1.37 (*t*, $^3J = 7.2$, Me); 3.98, 4.00 (*AB d*, $^2J = 12.0$, 2 $CH_2Cl$); 4.28 (*q*, $^3J = 7.2$, $CH_2O$); 4.68 (*q*, $^3J = 7.2$, $CH_2O$). $^{13}$C-NMR: 14.0, 15.4 (2 Me); 46.0 (2 $CH_2Cl$); 61.6, 68.8 (2 $CH_2O$); 84.3 (*s*, *C*($CH_2Cl)_2$); 120.1 (O–C=*C*); 150.7 (O–*C*=C); 161.0, 164.5 (2 C=O). MS: 301 (2, $[M+5]^+$), 299 (12, $[M+1+2]^+$), 297 (17, $[M+1]^+$), 265 (35), 263 (100), 226 (11), 213 (52), 191 (9), 189 (27), 157 (89), 129 (23), 111 (10), 97 (7), 73 (6). Anal. calc. for $C_{11}H_{14}Cl_2O_5$ (296.96): C 44.46, H 4.75; found: C 44.35, H 4.71.

*Methyl 2-(Dichloromethyl)-2,5-dihydro-4-methoxy-5-oxo-2-phenylfuran-3-carboxylate* (**4g**): Yield 0.51 g (77%). White powder. M.p. 92–94°. $R_f$ (AcOEt/hexane 1:4) 0.6. IR: 1782 and 1696 (C=O), 1643 (C=C). $^1$H-NMR: 3.85 (*s*, MeO); 4.31 (*s*, MeO); 7.01 (*s*, $CHCl_2$); 7.38–7.44 (*m*, 3 arom. H); 7.50–7.54 (*m*, 2 arom. H). $^{13}$C-NMR: 52.6, 60.0 (2 MeO); 74.0 ($CHCl_2$); 87.8 (*s*, *C*($CHCl_2$); 125.5 (O–C=*C*); 125.6, 128.9, 129.3, 135.2 (arom. C); 148.7 (O–*C*=C); 161.9, 164.9 (2 C=O). MS: 334 (2, $[M+4]^+$), 332 (10, $[M+2]^+$), 330 (19, $M^+$), 319 (1), 317 (6), 315 (8), 303 (3), 301 (13), 299 (26), 287 (4), 285 (24), 283 (36), 279 (33), 277 (100), 264 (12), 262 (36), 247 (62), 299 (38), 219 (12), 217 (36), 201 (57), 183 (48), 173 (36), 153 (30), 115 (22), 105 (90), 83 (40), 77 (88). Anal. calc. for $C_{14}H_{12}Cl_2O_5$ (330.99): C 50.78, H 3.65; found: C 50.67, H 3.60.

*Ethyl 2-(Dichloromethyl)-4-ethoxy-2,5-dihydro-5-oxo-2-phenylfuran-3-carboxylate* (**4h**): Yield 0.50 g (70%). White powder. M.p. 67–69°. $R_f$ (AcOEt/hexane 1:4) 0.6. IR: 1782 and 1696 (C=O), 1643 (C=C). $^1$H-NMR: 1.33 (*t*, $^3J = 7.2$, Me); 1.41 (*t*, $^3J = 7.2$, Me); 4.25–4.37 (*m*, $CH_2O$); 4.60–4.80 (*m*, $CH_2O$); 7.01 (*s*, $CHCl_2$); 7.38–7.42 (*m*, 3 arom. H); 7.52–7.54 (*m*, 2 arom. H). $^{13}$C-NMR: 14.0, 15.5 (2 Me); 61.9, 68.6 (2 $CH_2O$); 74.1 ($CHCl_2$); 87.1 (*s*, *C*(Ph)$CHCl_2$); 125.5 (O–C=*C*); 125.6, 128.8, 129.2, 135.3 (arom. C); 147.8 (O–*C*=C); 161.6, 165.2 (2 C=O). MS: 362 (1, $[M+4]^+$), 360 (6, $[M+2]^+$), 358 (9, $M^+$), 317 (1), 317 (6), 315 (6), 313 (9), 275 (100), 219 (43), 201 (9), 187 (2), 173 (2), 129 (5), 105 (87), 77 (13). Anal. calc. for $C_{16}H_{16}Cl_2O_5$ (359.01): C 53.50, H 4.49; found: C 53.41, H 4.45.

*Methyl 2-(1-Chloroethyl)-2,5-dihydro-4-methoxy-2-methyl-5-oxofuran-3-carboxylate* (**4i**): Yield 0.15 g (30%). White powder. M.p. 90–93°. $R_f$ (AcOEt/hexane 1:4) 0.5. IR: 1776 and 1693 (C=O), 1644 and 1461 (C=C). $^1$H-NMR: 1.38 (*d*, $^3J = 6.8$, Me); 1.80 (*s*, Me); 3.88, 4.28 (2*s*, 2 MeO); 4.57 (*q*, $^3J = 6.8$, CH). $^{13}$C-NMR: 19.3, 23.4 (2 Me); 52.4 (CHCl); 59.7, 60.0 (2 MeO); 85.7 (*s*, *C*(Me)CH(Cl)Me); 124.7, 148.3 (O–*C*=*C*); 161.9, 165.2 (2 C=O). MS: 250 (8, $[M+2]^+$), 248 (22, $M^+$), 235 (2), 233 (6), 218 (7), 216 (20), 203 (1), 201 (4), 185 (100), 168 (6), 153 (100), 115 (100), 83 (40). Anal. calc. for $C_{10}H_{13}ClO_5$ (248.50): C 48.30, H 5.27; found: C 48.4, H 5.17.

*Methyl 2-(Bromomethyl)-2,5-dihydro-4-methoxy-5-oxo-2-phenylfuran-3-carboxylate* (**4k**): Yield 0.35 g (52%). White powder. M.p. 90–92°. $R_f$ (AcOEt/hexane 1:4) 0.6. IR: 1778 and 1697 (C=O), 1646 and 1467 (C=C). $^1$H-NMR: 3.85 (*s*, MeO); 4.19 (*d*, $^2J = 10.8$, CH); 7.38–7.46 (*m*, 5 arom. H). $^{13}$C-NMR: 37.3 ($CH_2Br$); 52.4, 60.0 (2 MeO); 84.8 (*s*, *C*(Ph)$CH_2Br$); 123.8 (O–C=*C*); 125.9, 128.9, 129.4, 136.1 (arom. C); 149.5 (O–*C*=C); 161.9, 165.0 (2 C=O). MS: 343 (3, $[M+3]^+$), 341 (3, $[M+1]^+$), 327 (2), 325 (2), 313 (5), 311 (5), 283 (3), 281 (3), 247 (100), 229 (10), 219 (34), 129 (49), 115 (100), 105 (94), 77 (97), 59 (83). Anal. calc. for $C_{14}H_{13}BrO_5$ (340.99): C 49.29, H 3.84; found: C 49.21, H 3.79.

*Ethyl 2-(Bromomethyl)-4-ethoxy-2,5-dihydro-5-oxo-2-phenylfuran-3-carboxylate* (**4l**): Yield 0.37 g (50%). White powder. M.p. 45–47°. $R_f$ (AcOEt/hexane 1:4) 0.62. IR: 1772 and 1693 (C=O), 1644 and 1430 (C=C). $^1$H-NMR: 1.31 (*t*, $^3J = 7.2$, Me); 1.44 (*t*, $^3J = 7.2$, Me); 4.19 (*d*, $^2J = 10.8$, CH); 4.23–4.34 (*m*, $CH_2O$); 4.63–4.80 (*m*, $CH_2O$); 4.59 (*d*, $^2J = 10.8$, CH); 7.37– 7.46 (*m*, Ph). $^{13}$C-NMR: 14.0, 15.5 (2 Me); 37.4 ($CH_2Br$); 61.5, 68.6 (2 $CH_2O$); 86.9 (*s*, *C*(Ph)$CH_2Br$); 124.9 (O–C=*C*); 125.9, 128.8, 129.3, 136.2 (arom. C); 149.2 (O–*C*=C); 161.5, 165.3 (2 C=O). MS: 370 (2, $[M+2]^+$), 368 (2, $M^+$), 325 (3), 323 (3), 275 (100), 247 (9), 219 (40), 201 (6), 171 (3), 163 (3), 161 (3), 115 (30), 105 (94), 77 (30). Anal. calc. for $C_{16}H_{17}BrO_5$ (369.01): C 52.05, H 4.64; found: C 51.93, H 4.59.

*Methyl 2-(Bromomethyl)-2-(4-bromophenyl)-2,5-dihydro-4-methoxy-5-oxofuran-3-carboxylate* (**4m**): Yield 0.52 g (62%). White powder. M.p. 83–85°. $R_f$ (AcOEt/hexane 1:4) 0.6. IR: 1765 and 1702 (C=O), 1639 and 1461 (C=C). $^1$H-NMR: 3.84 (*s*, MeO); 4.14 (*d*, $^2J$ = 10.8, CH); 4.33 (*s*, MeO); 4.52 (*d*, $^2J$ = 10.8, CH); 7.34 (*d*, $^3J$ = 8.8, 2 arom. H); 7.52 (*d*, $^3J$ = 8.8, 2 arom. H). $^{13}$C-NMR: 36.8 ($CH_2Br$); 52.5, 60.1 (2 MeO); 84.3 (*s*, *C*(Ar)$CH_2Br$); 123.4 (O–C=*C*); 123.7, 127.5, 132.0, 135.2 (arom. C); 149.5 (O–*C*=C); 161.8, 164.7 (2 C=O). MS: 422 (2, $[M+4]^+$), 420 (4, $[M+2]^+$), 418 (2, $M^+$), 391 (2), 389 (4), 387 (2), 363 (1), 361 (2), 359 (1), 327 (100), 325 (100), 209 (8), 207 (8), 195 (9), 193 (9), 185 (92), 183 (92), 157 (23), 155 (23), 114 (23), 83 (33), 75 (25), 59 (30). Anal. calc. for $C_{14}H_{12}Br_2O_5$ (419.89): C 40.03, H 2.88; found: C 39.2, H 2.82.

*Ethyl 2-(Bromomethyl)-2-(4-bromophenyl)-4-ethoxy-2,5-dihydro-5-oxofuran-3-carboxylate* (**4n**): Yield 0.54 g (60%). White powder. M.p. 71–73°. $R_f$ (AcOEt/hexane 1:4) 0.6. IR: 1766 and 1704 (C=O), 1641 and 1488 (C=C). $^1$H-NMR: 1.32 (*t*, $^3J$ = 7.2, Me); 1.43 (*t*, $^3J$ = 7.2, Me); 4.14 (*d*, $^2J$ = 11.2, CH); 4.26–4.34 (*m*, $CH_2O$); 4.52 (*d*, $^2J$ = 11.2, CH); 4.63–4.80 (*m*, $CH_2O$); 7.34 (*d*, $^3J$ = 8.8, 2 arom. H); 7.52 (*d*, $^3J$ = 8.8, 2 arom. H). $^{13}$C-NMR: 14.0, 15.5 (2 Me); 37.0 ($CH_2Br$); 61.6, 68.7 (2 $CH_2O$); 84.4 (*s*, *C*(Ar)$CH_2Br$); 123.6 (O–C=*C*); 124.4, 127.7, 132.0, 135.4 (arom. C); 149.2 (O–*C*=C); 161.4, 165.0 (2 C=O). MS: 450 (1, $[M+4]^+$), 448 (2, $[M+2]^+$), 446 (1, $M^+$), 405 (1), 403 (2), 401 (1), 355 (57), 353 (57), 299 (19), 297 (19), 207 (5), 185 (100), 183 (100), 157 (13), 155 (13), 142 (3), 102 (12), 69 (14). Anal. calc. for $C_{16}H_{16}Br_2O_5$ (447.91): C 42.89, H 3.60; found: C 42.78, H 3.55.

*Methyl 2-(Bromomethyl)-2-(4-chlorophenyl)-2,5-dihydro-4-methoxy-5-oxofuran-3-carboxylate* (**4o**): Yield 0.42 g (56%). White powder. M.p. 77–79°. $R_f$ (AcOEt/hexane 1:4) 0.5. IR: 1772 and 1702 (C=O), 1461 and 1488 (C=C). $^1$H-NMR: 3.84 (*s*, MeO); 4.14 (*d*, $^2J$ = 11.2, CH); 4.33 (*s*, MeO); 4.52 (*d*, $^2J$ = 11.2, CH); 7.36 (*d*, $^3J$ = 8.8, 2 arom. H); 7.40 (*d*, $^3J$ = 8.8, 2 arom. H). $^{13}$C-NMR: 36.9 ($CH_2Br$); 52.5, 60.1 (2 MeO); 84.3 (*s*, *C*(Ar)$CH_2Br$); 123.5 (O–C=*C*); 127.4, 129.1, 134.6, 135.5 (arom. C); 149.5 (O–*C*=C); 161.8, 164.7 (2 C=O). MS: 378 (1, $[M+4]^+$), 376 (4, $[M+2]^+$), 374 (3, $M^+$), 347 (2), 345 (8), 343 (6), 319 (1), 317 (4), 315 (3), 283 (35), 281 (100), 165 (3), 163 (9), 151 (6), 149 (15), 141 (33), 139 (97), 113 (9), 111 (25), 83 (1.6), 59 (1.6). Anal. calc. for $C_{14}H_{12}BrClO_5$ (375.44): C 44.77, H 3.22; found: C 44.68, H 3.18.

*Ethyl 2-(Bromomethyl)-2-(4-chlorophenyl)-4-ethoxy-2,5-dihydro-5-oxofuran-3-carboxylate* (**4p**): Yield 0.44 g (55%). White powder. M.p. 79–81°. $R_f$ (AcOEt/hexane 1:4) 0.5. IR: 1785 and 1687 (C=O), 1637 and 1494 (C=C). $^1$H-NMR: 1.32 (*t*, $^3J$ = 7.2, Me); 1.43 (*t*, $^3J$ = 7.2, Me); 4.14 (*d*, $^2J$ = 11.2, CH); 4.23–4.34 (*m*, $CH_2O$); 4.52 (*d*, $^2J$ = 11.2, CH); 7.36 (*d*, $^3J$ = 8.4, 2 arom. H); 7.41 (*d*, $^3J$ = 8.4, 2 arom. H). $^{13}$C-NMR: 14.0, 15.5 (2 Me); 37.1 ($CH_2Br$); 61.6, 68.7 (2 $CH_2O$); 84.4 (*s*, *C*(Ar)$CH_2Br$); 124.5 (O–C=*C*); 124.7, 129.0, 134.8, 135.4 (arom. C); 149.2 (O–*C*=C); 161.4, 165.0 (2 C=O). MS: 406 (1, $[M+4]^+$), 404 (4, $[M+2]^+$), 402 (3, $M^+$), 361 (2), 359 (8), 357 (6), 333 (1), 331 (4), 329 (3), 311 (32), 309 (96), 283 (2), 281 (6), 255 (10), 253 (31), 237 (3), 235 (9), 141 (35), 139 (100), 113 (6), 111 (16), 69 (9). Anal. calc. for $C_{16}H_{16}BrClO_5$ (403.46): C 47.61, H 4.0; found: C 47.54, H 3.95.

*Methyl 2-(Bromomethyl)-2,5-dihydro-4-methoxy-2-(4-nitrophenyl)-5-oxofuran-3-carboxylate* (**4q**): Yield 0.54 g (80%). White powder. M.p. 97–99°. $R_f$ (AcOEt/hexane 1:4) 0.5. IR: 1779 and 1697 (C=O), 1644 and 1471(C=C). $^1$H-NMR: 3.86 (*s*, MeO); 4.18 (*d*, $^2J$ = 11.2, CH); 4.36 (*s*, MeO); 4.54 (*d*, $^2J$ = 11.2, CH); 7.70 (*d*, $^3J$ = 8.8, 2 arom. H), 8.25 (*d*, $^3J$ = 8.8, 2 arom. H). $^{13}$C-NMR: 36.4 ($CH_2Br$); 52.6, 60.1 (2 MeO); 84.0 (*s*, *C*(Ar)$CH_2Br$); 123.1 (O–C=*C*); 124.0, 127.2, 143.0, 148.2 (arom. C); 149.6 (O–*C*=C); 161.7, 164.3 (2 C=O). MS: 387 (2, $[M+2]^+$), 385 (2, $M^+$), 311 (42), 309 (42), 292 (43), 277 (43), 262 (5), 229 (9), 178 (15), 150 (37), 139 (94), 122 (13), 97 (25), 83 (32), 69 (89), 57 (73), Anal. calc. for $C_{14}H_{12}BrNO_7$ (385.97): C 43.55, H, 3.13; found: C 42.95, H 3.80.

*Ethyl 2-(Bromomethyl)-4-ethoxy-2,5-dihydro-2-(4-nitrophenyl)-5-oxofuran-3-carboxylate* (**4r**): Yield 0.56 g (78%). White powder. M.p. 86–88°. $R_f$ (AcOEt/hexane 1:4) 0.5. IR: 1793 and 1706 (C=O), 1645 and 1430 (C=C). $^1$H-NMR 1.33 (*t*, $^3J$ = 7.2, Me); 1.44 (*t*, $^3J$ = 7.2, Me); 4.18 (*d*, $^2J$ = 11.2, CH); 4.23–4.36 (*m*, $CH_2O$); 4.53 (*d*, $^2J$ = 11.2, CH); 4.67–4.82 (*m*, $CH_2O$); 7.70 (*d*, $^3J$ = 9.2, 2 arom. CH); 8.24 (*d*, $^3J$ = 9.2, 2 arom. CH). $^{13}$C-NMR: 14.0, 15.5 (2 Me); 36.5 ($CH_2Br$); 61.8, 68.9 (2 $CH_2O$); 84.1 (*s*, *C*(Ar)$CH_2Br$); 123.5 (O–C=*C*); 123.4, 127.2, 143.2, 148.2 (arom. C); 149.3 (O–*C*=C); 161.3, 164.6 (2 C=O). MS: 415 (1, $[M+2]^+$), 413 (1, $M^+$), 386 (2), 384 (2), 370 (5), 368 (5), 334 (8), 320 (77), 264 (43), 216 (5), 150 (100), 122 (6), 104 (20), 69 (15). Anal. calc. for $C_{16}H_{16}BrNO_7$ (413.99): C 46.40, H 3.89; found: C 46.31, H 3.84.

*X-Ray Crystal Structure of* **4d**[1]). $C_9H_{10}C_{l2}O_5$, $M_r$ 269.07, crystal size $0.50 \times 0.49 \times 0.25$ mm, monoclinic; $a = 9.7761(11)$ Å, $b = 17.195(2)$ Å, $c = 7.1364(8)$ Å, $\alpha = 90°$, $\beta = 109.435(8)°$, $\gamma = 90°$, space group *C 2/c*; $Z = 4$, $V = 1131.3(2)$ Å$^3$, $D_{calc.} = 1.580$ g cm$^{-3}$; $R = 0.0724$, $R_w = 0.1233$; $-13 \leq h \leq 13$, $-23 \leq k \leq 20$; $-9 \leq l \leq 8$; Mo$K_\alpha$ radiation ($\lambda$ 0.71073 Å), $T$ 298(2)°.

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[1]) CCDC-823855 contains supplementary crystellographic data for this article. These data can be obtained free of charge *via* http://www.cdc.cam.ac.uk.data_request/cif.