# Lactone Synthesis by Mn(III)-Mediated Oxidative Cyclization of Allylic β-Diesters

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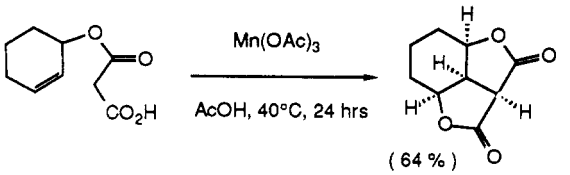
Oxidative free-radical cyclization of allylic β-diesters with $Mn(OAc)_3$–$Cu(OAc)_2$ leads to various γ-lactones resulting exclusively from a 5-exo cyclization. The products depend on the α substituent on the malonic ester, on the stereoselectivity of the intramolecular addition step, and on the nature of the intermediate radical.

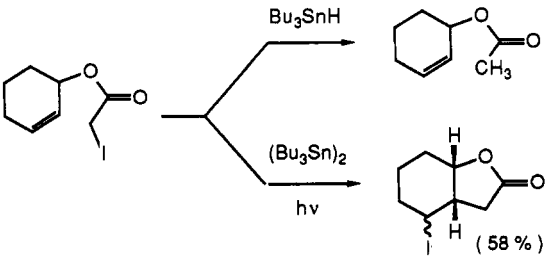
Lactone synthesis by free-radical pathways has been largely developed during the last decade.[1] Among these methods, the oxidative addition of carboxylic acids to olefins has drawn considerable attention as a route of γ-lactones.[2-4] This method emerged from the pioneering work of Heiba and Dessau[2a-d] and Bush and Finkbeiner,[2f] who showed that $Mn(OAc)_3$ was especially suitable to perform these reactions and this reactant has been widely used as an oxidizing agent of carbonyl compounds.[3a]

Although most of the reports in this field are concerned with intermolecular reactions,[2,3] examples of intramolecular additions have been reported.[4] Fristad described the synthesis of bicyclic lactones by oxidative cyclization of monoalkylated cyanoacetic acid and malonic acid[4a] derivatives. Corey reported the first example of cyclization of a monoester derived from malonic acid[4b] in which the lactone is formed in the intramolecular addition step (eq 1). This last result was most intriguing, since previous




eq 1

attempts to perform free-radical ring closures from such esters had failed.[5] More recently Curran has shown that such an intramolecular addition is slow and cannot compete with radical reduction by $Bu_3SnH$[6] (eq 2), although a lactone is formed with an iodine-atom-transfer process. We report in this paper the results of oxidative cyclization of various unsaturated β-diesters.




eq 2

## Results and Discussion

The oxidative cyclization of compounds **1–9** (vide infra) was performed in glacial acetic acid (25 mL) by treating 5 to 10 mmol of the substrate with 2 equiv of $Mn(OAc)_3$ and 1 equiv of $Cu(OAc)_2$ in the presence of NaOAc (1 equiv) (except with compounds **1**, **2**, and **5b**, see Table I). The reaction mixture was heated until the amber color of Mn(III) disappeared. Although intermolecular addition of acids to olefins, initiated by Mn(III), without cooxidant, produces lactones in high yields,[3e-f] we observed[7] that allyl acetoacetate underwent oxidation more efficiently and selectively in the presence of a stoichiometric amount of $Cu(OAc)_2$. Therefore, the same experimental conditions were applied to substrates **1–9**. Other authors[8a] have reported similar observations. The results indicate that the structure of the reaction product is very sensitive to the nature of the substituents. No attempts at optimization were carried out. The isolated products can be rationalized as indicated in Scheme I.

The mechanism of oxidation of β-dicarbonyl compounds has been extensively studied by Fristad[4a] and Snider.[8a,e] In agreement with these studies and the very first reports,[2d] a complex (A) formed between the substrate and Mn(III) is transformed into the complexed radical C via enolate B. We have observed exclusively γ-lactone ring closure resulting from the exo cyclization mode to form radical D. This radical can then be oxidized by Mn(III), or, more efficiently, by Cu(II). According to Kochi,[9] an alkylcopper (E) is the precursor of the products. The free-radical cyclizations of malonic and cyanoacetic acid derivatives are known to be reversible and normally give endo cyclization products, as a result of thermodynamic control.[10] In the presence of Cu(II), a fast oxidative transfer step traps the kinetic radical D and prevents reversibility.[10b]

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(8) (a) Snider, B. B.; Mohan, R.; Kates, S. A. *J. Org. Chem.* **1985**, *50*, 3659. (b) Mohan, R.; Kates, S. A.; Dombroski, M. A.; Snider, B. B. *Tetrahedron Lett.* **1987**, *28*, 845. (c) Snider, B. B.; Mohan, R.; Kates, S. A. *Ibid.* **1987**, *28*, 841. (d) Snider, B. B.; Dombroski, M. A. *J. Org. Chem.* **1987**, *52*, 5487. (e) Snider, B. B.; Patricia J. J.; Kates, S. A. *Ibid.* **1988**, *53*, 2137. (f) Snider, B. B.; Patricia, J. J. *Ibid.* **1989**, *54*, 38. (g) Merritt, J. E.; Sasson, M.; Kates, S. A.; Snider, B. B. *Tetrahedron Lett.* **1988**, *29*, 5209. (h) Peterson, J. R..; Egler, R. S.; Horsley, D. B.; Winter, T. J. *Tetrahedron Lett.* **1987**, *28*, 6109.

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(10) (a) Julia, M. *Acc. Chem. Res.* **1971**, *4*, 386. (b) Julia, M.; Barreau, M. *C. R. Acad. Sci. Paris, Ser. C.* **1975**, *280*, 957.

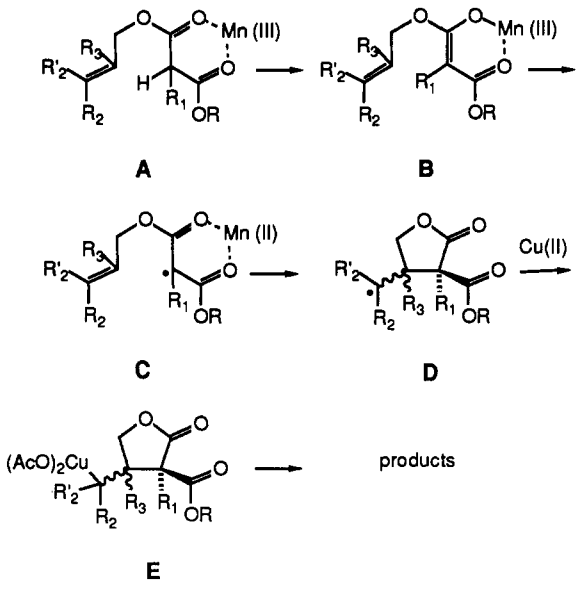
0022-3263/89/1954-5684$01.50/0 

**Table I. Oxidative Cyclization of Compounds 1-9**

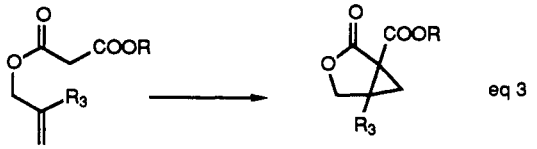
| substr | products (%)[a] | substr | products (%)[a] |
|---|---|---|---|
| 1a | **10a** (42)[b] | 5b | **16** (66)[d] |
| 1b | **10b** (43)[b] | 6 | **17** (54) |
| 2 | **11** (7)[b] | 7 | **18** (30), **19** (17) |
| 3 | **12** (53), **13** (20) | 8 | **20** (20), **21** (43) |
| 4 | **14** (21), **15** (5)[c] | 9 | **13** (38), **22** (33) |
| 5a | | | |

[a] Yields of purified products refer to the amount of converted substrate (0–15% was recovered unchanged). [b] This reaction was performed with 2 equiv of NaOAc. [c] In the absence of $Cu(OAc)_2$, **14** is suppressed and **15** is the only product obtained (17% yield). [d] The reaction was accomplished with 4 equiv of Mn(III) and 2 equiv of Cu(II).

**Scheme I**



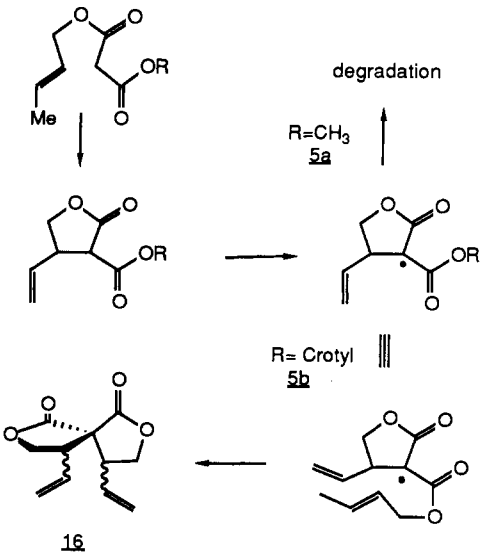

The oxidation of compounds **1a,b** and **2**, which are unsubstituted malonic esters, led to bicyclo[3.1.0] lactones **10a,b** (42, 43%) and **11** (7%) (eq 3). In this case, the




1a (R = Me, $R_3$ = H) **10a**
1b (R = Allyl, $R_3$ = H) **10b**
2 (R = Et, $R_3$ = Me) **11**

primary intermediate E in its enol form undergoes a fast ring closure to a cyclopropane. The same behavior was observed with allyl acetoacetate.[7] Similar cyclopropanations have also been reported for the Cu(II)-mediated addition of ethyl cyanoacetate to various olefins.[11] Obtaining only five-membered-ring lactones from these experiments contrasts with the results of the oxidative cyclization of methyl 3-oxo-6-heptenoate, which lead in nearly quantitative yield to a six-membered-ring product,[8b,f,h] under similar experimental conditions.[12] The presence of a heteroatom in the chain is known to facilitate the exo cyclization mode.[13] Of course, since yields of

**Scheme II**




γ-lactones are not quantitative, we cannot rule out the possibility of some endo cyclization, which would lead to a product capable of being degraded by further oxidation. However, given the 73% yield of γ-lactones from **3** (vide infra), endo cyclization is probably not usually a major pathway. The low yield observed with **2** is consistent with the known retarding effect of the methyl group on the ring closure rate.[13]

The oxidation of the crotyl esters **5a** and **5b** gave contrasting results. Whereas **5a** gave no isolable lactone, the dicrotyl ester **5b** gave a diastereomeric mixture of spirolactones **16**. Surprisingly, cyclopropanation was not observed with these compounds. As proposed in Scheme II, the first cyclization step proceeds in a similar manner to give a secondary radical. The resulting alkylcopper intermediate undergoes a rapid β-elimination to give a vinyl-substituted γ-lactone. In agreement with Snider's observations on 2-cyclopentanone carboxylate esters,[8a] the primary product is oxidized even more rapidly than the starting material and consequently undergoes oxidative degradation, unless the substrate contains a second radical trap. The latter is clearly demonstrated by the fate of dicrotyl malonate **5b**, which bears two allylic chains. In this instance, through a second cyclization, **5b** leads to a mixture of three isomeric spirodilactones **16** (66%) in the relative proportions of 38:54:8. Analysis by $^1H$ and $^{13}C$ NMR allows the identification of the major isomer **16b** as the unsymmetrical one. The structures of symmetrical isomers **16a** and **16c** are tentatively assigned on the basis of steric considerations, which suggest that the syn isomer should be formed in smaller quantities.

With the methyl malonates **3**, **4**, **6**, **7**, and **8**, the methylgroup blocks further reaction at the reactive center. With these substrates the nature of the products depends on the stereoselectivity of the initial cyclization step (C → D) and the substitution of the radical D, which subsequently influences the fate of E.

Compound **3** generates a primary radical, which undergoes oxidative substitution to give dilactone **12** (53%) or oxidative elimination to give the methylene lactone **13** (20%) (eq 4). If **13** is not further oxidized under the reaction conditions, the ratio of **12**:**13** is an indication of the stereoselectivity of the radical cyclization since only

(11) Barreau, M.; Bost, M.; Julia, M.; Lallemand, J.-Y. *Tetrahedron Lett.* **1975**, 3465.

(12) In the case of such an α-oxo radical the six-membered-ring product is the kinetic one. See: Clive, D. L. J.; Cheschire, D. R. *J. Chem. Soc., Chem. Commun.* **1987**, *20*, 1520, and ref 1b (p 502).

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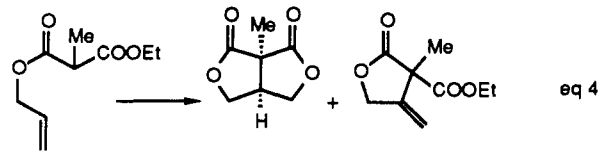
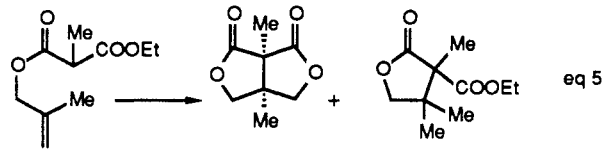


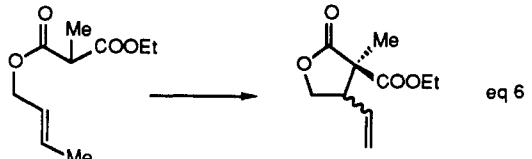

3 12 13




4 14 15

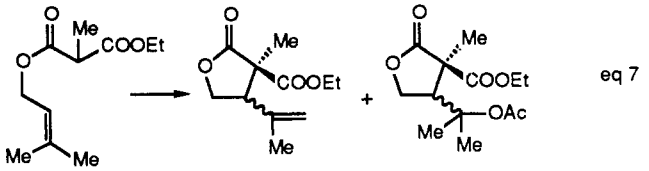
the stereoisomer of the radical in which the ester is syn to the reactive center can produce the dilactone. A similar pathway leads to dilactone **14** (21%) from compound **4** although the yields are significantly lower (eq 5). The reduction product **15** (5%) was formed as a minor product in this case, where oxidative elimination is not possible. Formally the dilactones could originate either from direct radical addition to the neighboring carbethoxy group or from oxidative substitution. These two pathways have already been suggested in the literature.[2d,e,8d] Oxidation of compound **4** in the absence of $Cu(OAc)_2$ gave **15** in 17% yield as the only product. Since the formation of lactone **14** is suppressed, this experiment argues in favor of oxidative substitution and confirms that primary radical oxidation by Mn(III) is slow.[9]

The oxidation of crotyl ester **6** gives an intermediate secondary radical, which upon cyclization is transformed to vinyl lactone **17** as the only observed product (54%) (eq 6). This lactone is a mixture of isomers whose analysis by $^1H$ NMR spectroscopy indicates a *Z*:*E* ratio of 70:30. This suggests that the *Z* isomer of D is favored in the cyclization step.

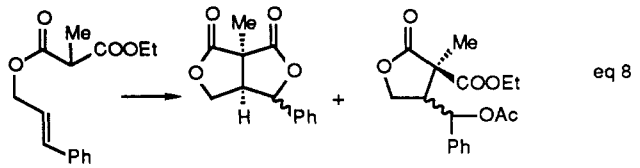



6 17

With the more highly substituted olefin present in **7** two different types of products are observed (eq 7). Product **18** (30%) is derived from similar oxidative elimination, whereas **19** (17%) results from oxidative substitution. The phenyl-substituted substrate **8** gave only products from oxidative substitution (eq 8). The lactone **20** (20%) is




7 18 19

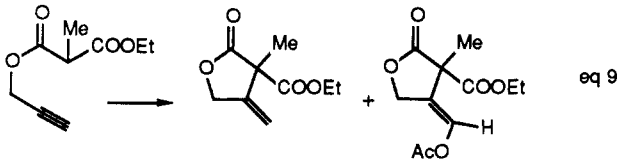



8 20 21

formed by intramolecular attack on an intermediate benzyl cation, whereas **21** (43%) is derived from solvent attack on this intermediate. Whereas the dilactonization seems to be the favored product of primary intermediates resulting from **3** and **4**, provided the stereochemistry is correct, no dilactone was obtained from **6** or **7** (secondary and tertiary radical intermediates). Since oxidative elimination is known to predominate over oxidative substitution for primary radicals,[9] these results demonstrate that elimination leading to methylene-substituted five-membered ring is a disfavored process.

Snider reported kinetic evidence for simultaneous complexation of the double bond during Mn(III) oxidation of some unsubstituted ethylenic β-keto esters.[8e] Whether such an interaction is involved in the fate of intermediate C is not substantiated with our models. This interaction with a metallic ion should have direct consequences on the stereoselectivity of the reaction. At this time, no definitive conclusions can be drawn. We can only point out that such a complexation fits well with the fact that the major products result from the intermediate D, where the carbethoxy group and the side chain bearing the radical are cis to one another.

Intramolecular addition to the triple bond seems to be readily accessible. The oxidation of **9** gave the methylene lactone **13** (38%) and the vinyl acetate **22** (33%) (eq 9). These two products can be explained on the basis of an intermediate vinyl radical, which leads to **13** by hydrogen-atom transfer from the solvent or the substrate and to **23** by oxidative substitution with Cu(II). The unsubstituted ethyl propargyl malonate gave polymer material under the reaction medium.




9 13 22

In summary, these results show that oxidative cyclization of allylic β-diesters with $Mn(OAc)_3$ is a general method for the formation of γ-lactone ring. Very different products can be obtained by varying the structure of the ethylenic chain and the fate of each type of substrate has been clearly delineated. Since allylic esters of activated acids do not give cyclic products under classical free-radical initiation, this study provides additional evidence that complexed radicals are more prone to intramolecular addition.[1] We are further investigating the stereoselectivity of the reaction and its utility for polycyclizations of suitable models.

## Experimental Section

$Mn(OAc)_3 \cdot 2H_2O$ was purchased from Aldrich Chemical Co. and used without purification. Column chromatography was performed on silica gel 60 (Merck 7734). Melting points are uncorrected. IR spectra were recorded on Perkin-Elmer 297 and Nicolet 20 SXB spectrometers. NMR spectra were recorded in $CDCl_3$ solution (unless otherwise stated) on VARIAN XL 200, BRUKER AC 100, and AC 200 spectrometers. Chemical shifts are measured in ppm downfield from TMS. GC-coupled MS spectra were recorded on a RIBERMAG R.10-10-C spectrometer.

Starting materials were prepared either by reacting malonoyl dichloride with the appropriate alcohol[14] or by alkylating ethyl potassium malonate under phase-transfer catalysis conditions. The potassium salt was treated with a stoichiometric amount of allylic halide in $CH_2Cl_2$ with tetrabutylammonium bromide as a catalyst.[15,16] The β-diesters were purified by column chro-

(14) Raha, C. *Org. Syntheses*; Wiley: New York, 1963; Collect. Vol. 4, p 263.

matography (silica, 20% EtOAc/petroleum ether). Compounds **1a**,[17a] **1b**,[17b] **5a**,[17c] **6**,[17c] and **7**[17d] had previously been prepared. Structural data for the other β-diesters are given below.

**Propanedioic acid ethyl 2-methyl-2-propenyl diester (2)**: IR (neat) 3100, 1770, 1740, 1670, 855 $cm^{-1}$; $^1H$ NMR δ 1.28 (t, $J$ = 7.1 Hz, 3 H), 1.76 (s, 3 H), 3.42 (s, 2 H), 4.21 (q, $J$ = 7.1 Hz, 2 H), 4.57 (s, 2 H), 4.95 (s, 1 H), 5.00 (s, 1 H). Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 58.06; H, 7.55.

**2-Methylpropanedioic acid ethyl 2-propenyl diester (3)**: IR (neat) 1760, 1740, 1680, 990, 930 $cm^{-1}$; $^1H$ NMR δ 1.28 (t, $J$ = 7.1 Hz, 3 H), 3.40 (s, 2 H), 4.21 (q, $J$ = 7.1 Hz, 2 H), 4.65 (dt, $J$ = 5.6, 1.2 Hz, 2 H), 5.20–5.40 (m, 2 H), 5.92 (ddt, $J$ = 16.2, 10.4, 5.6 Hz, 1 H). Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 58.14; H, 7.56.

**2-Methylpropanedioic acid ethyl 2-methyl-2-propenyl diester (4)**: IR (neat) 3100, 3000, 1760, 1750, 1670, 920 $cm^{-1}$; $^1H$ NMR δ 1.27 (t, $J$ = 7.1 Hz, 3 H), 1.44 (d, $J$ = 7.3 Hz, 3 H), 1.75 (s, 3 H), 3.48 (q, $J$ = 7.3 Hz, 1 H), 4.20 (q, $J$ = 7.1 Hz, 2 H), 4.56 (AB quartet, $\Delta\nu$ = 10.5 Hz, $J_{AB}$ = 13 Hz, 2 H), 4.93 (s, 1 H), 4.98 (s, 1 H). Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 59.96; H, 8.00.

**Propanedioic acid 2-butenyl methyl diester (5b)**: IR (neat) 1765, 1745, 1680, 970 $cm^{-1}$; $^1H$ NMR (since commercial crotyl alcohol is a cis/trans mixture, the resulting β-diester is a mixture of isomers, chemical shifts specific of the minor cis double bond are indicated with an asterisk, relative integrations of the doublets at 4.57 and 4.71 indicate 17% of cis double bond) δ 1.71 and 1.74* (s, 6 H), 3.39 (s, 2 H), 4.57 and 4.71* (d, $J$ = 6.4, 6.6* Hz, 4 H), 5.60 (m, 2 H), 5.80 (m, 2 H); $^{13}C$ NMR ppm 166.5*, 166.3, 132.0, 130.2*, 124.5, 123.6*, 66.2, 61.1*, 41.6, 17.8, 13.1*. Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.6. Found: C, 61.99; H, 7.67.

**2-Methylpropanedioic acid ethyl 3-phenyl-2-propenyl diester (8)**: IR (neat) 1760, 1740, 1620, 1600, 1610, 760, 710 $cm^{-1}$; $^1H$ NMR δ 1.25 (t, $J$ = 7.1 Hz, 3 H), 1.44 (d, $J$ = 7.3 Hz, 3 H), 3.48 (q, $J$ = 7.3 Hz, 1 H), 4.19 (q, $J$ = 7.1 Hz, 2 H), 4.79 (dd, $J$ = 6.4, 1.1 Hz, 2 H), 6.26 (dt, $J$ = 15.9, 6.4 Hz, 1 H), 6.66 (d, $J$ = 15.9 Hz, 1 H), 7.31 (m, 5 H). Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92. Found: C, 68.85; H, 6.81.

**2-Methylpropanedioic acid ethyl 2-propynyl diester (9)**: IR (neat) 3300, 2135, 1765, 1735 $cm^{-1}$; $^1H$ NMR δ 1.27 (t, $J$ = 7 Hz, 3 H), 1.42 (d, $J$ = 7 Hz, 3 H), 2.55 (t, $J$ = 2 Hz, 1 H), 3.45 (q, $J$ = 7 Hz, 1 H), 4.15 (q, $J$ = 7 Hz, 2 H), 4.69 (d, $J$ = 2 Hz, 2 H). Anal. Calcd for $C_9H_{12}O_4$: C, 58.68; H, 6.56. Found: C, 58.70; H, 6.47.

**Representative Oxidative Cyclization Experiment**. In a flask equipped with a magnetic stirrer and a reflux condenser, 1.06 g (5 mmol) of **5b**, 5.36 g (20 mmol) of manganese(III) acetate dihydrate, 2 g (10 mmol) of copper(II) acetate monohydrate, and 0.8 g (10 mmol) of sodium acetate were mixed together in 25 mL of glacial acetic acid. The heterogenous solution was stirred at reflux, under inert atmosphere (argon), until the brown color of Mn(III) dissipated (this coincides with the color becoming blue-turquoise). After cooling, the reaction mixture was filtered, diluted with water (200 mL), and extracted successively with three portions of $CH_2Cl_2$. The combined extracts were washed twice with water and then with saturated $NaHCO_3$, dried ($Na_2SO_4$), and concentrated. Separation by column chromatography on silica gel employed EtOAc/pentane mixtures of gradually increased polarity (5 to 50%). After recovery of 80 mg of starting material, the following were successively eluted: 250 mg of the symmetrical dilactone **16a**, 230 mg of the unsymmetrical dilactone **16b**, and 172 mg of a 70:30 mixture of **16b** and the third isomer **16c** (These relative proportions were determined by gas chromatography on Chromosorb PAW (80/100), 10% SE 30 as stationnary phase. This analysis was performed on an Intersmat IGC 120FL chromatograph equipped with an Intersmat ICR 1B integrator.)

**Structural Data for Compounds in Table I. Methyl 3-oxa-2-oxobicyclo[3.1.0]hexane-1-carboxylate (10a)**: IR (neat) 1785, 1735 $cm^{-1}$; $^1H$ NMR δ 1.46 (dd, $J$ = 6, 4 Hz, 1 H), 2.13 (dd, $J$ = 8, 4 Hz, 1 H), 2.86 (m, 1 H), 3.90 (s, 3 H), 4.30 (d, $J$ = 10 Hz, 1 H), 4.48 (dd, $J$ = 10, 5 Hz, 1 H); $^{13}C$ NMR ppm 170.5, 167.2, 67.1, 52.8, 29.3, 28.1, 20.9. Anal. Calcd for $C_7H_8O_4$: C, 53.85; H, 5.16. Found: C, 53.89; H, 5.17.

**2-Propenyl 3-oxa-2-oxobicyclo[3.1.0]hexane-1-carboxylate (10b)**: IR (neat) 1780, 1735, 1655, 1000, 940 $cm^{-1}$; $^1H$ NMR δ 1.45 (dd, $J$ = 6, 4 Hz, 1 H), 2.10 (dd, $J$ = 8, 4 Hz, 1 H), 2.86 (m, 1 H), 4.17 (d, $J$ = 10 Hz, 1 H), 4.44 (dd, $J$ = 10, 5 Hz, 1 H), 4.75 (d, $J$ = 6 Hz, 2 H), 5.34 (dd, $J$ = 10, 2 Hz, 1 H), 5.46 (dd, $J$ = 18, 2 Hz, 1 H), 6.02 (m, 1 H); $^{13}C$ NMR ppm 170.3, 166.4, 131.3, 118.9, 67.6, 66.3, 29.3, 28.0, 20.8. Anal. Calcd for $C_9H_{10}O_4$: C, 59.34; H, 5.53. Found: C, 59.38; H, 5.42.

**Ethyl 5-methyl-3-oxa-2-oxobicyclo[3.1.0]hexane-1-carboxylate (11)**: IR (neat) 1780, 1730 $cm^{-1}$; $^1H$ NMR δ 1.32 (t, $J$ = 7.1 Hz, 3 H), 1.43 (d, $J$ = 4.9 Hz, 1 H), 1.44 (superimposed s, 3 H), 1.99 (d, $J$ = 4.9 Hz, 1 H), 4.17 (AB quartet, $\Delta\nu$ = 12.8 Hz, $J_{AB}$ = 9.6 Hz, 2 H), 4.28 (superimposed q, $J$ = 7.1 Hz, 2 H); $^{13}C$ NMR ppm 171.6, 166.1, 72.2, 62.2, 35.8, 34.6, 25.3, 14.5, 14.3. Anal. Calcd for $C_9H_{12}O_4$: C, 58.68; H, 6.56. Found: C, 58.27; H, 6.73.

**3,7-Dioxa-2-methylbicyclo[3.3.0]octane-2,8-dione (12)**: mp 145–146 °C (cyclohexane); IR (KBr) 1800, 1785, (ep.), 1775 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$) δ 1.47 (s, 3 H), 3.42 (m, 1 H), 4.26 (dd, $J$ = 10, 4 Hz, 2 H), 4.58 (dd, $J$ = 10, 8 Hz, 2 H); $^{13}C$ NMR ppm 172.9, 69.6, 50.3, 42.6, 17.4. Anal. Calcd for $C_7H_8O_4$: C, 53.85; H, 5.16. Found: C, 53.75; H, 5.19.

**Ethyl 3-methyl-4-methylene-2-oxotetrahydrofuran-3-carboxylate (13)**: IR (neat) 1795, 1745, 1650, 870 $cm^{-1}$; $^1H$ NMR δ 1.25 (t, $J$ = 7 Hz, 3 H), 1.58 (s, 3 H), 4.20 (q, $J$ = 7 Hz, 2 H), 4.75–5.01 (m, 2 H), 5.27 (m, 2 H); $^{13}C$ NMR ppm 175.0, 168.3, 144.2, 109.8, 70.6, 62.4, 53.3, 19.1, 13.9. Anal. Calcd for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 56.21; H, 6.92.

**1,5-Dimethyl-3,7-dioxabicyclo[3.3.0]octane-2,8-dione (14)**: mp 164 °C (cyclohexane); IR (neat) 1797, 1747 $cm^{-1}$; $^1H$ NMR δ 1.34 (s, 3 H), 1.40 (s, 3 H), 4.18 (AB quartet, $\Delta\nu$ = 20.4 Hz, $J_{AB}$ = 9.7 Hz, 4 H); $^{13}C$ NMR ppm 155.3, 74.9, 54.3, 48.3, 16.9, 13.9. Anal. Calcd for $C_8H_{10}O_4$: C, 56.46; H, 5.92. Found: C, 56.46; H, 5.77.

**Ethyl 3,4,4-trimethyl-2-oxotetrahydrofuran-3-carboxylate (15)**: IR (neat) 1790, 1750 $cm^{-1}$; $^1H$ NMR δ 1.05 (s, 3 H), 1.11 (s, 3 H), 1.30 (t, $J$ = 7 Hz, 3 H), 1.32 (superimposed s, 3 H), 3.95 (d, $J$ = 8.3 Hz, 1 H), 4.1–4.4 (m, 3 H); $^{13}C$ NMR ppm 172.1, 169.9, 77.8, 62.1, 57.7, 42.8, 24.0, 21.4, 14.4, 14.2. Anal. Calcd for $C_{10}H_{14}O_4$: C, 59.98; H, 8.05. Found: C, 59.97; H, 8.18.

**2,7-Dioxa-4,9-divinylspiro[4.4]nonane-1,6-dione (16).** Symmetrical isomer (**16a**): mp 87–88 °C (cyclohexane); IR (KBr) 1781, 1764 (strongest C=O), 1644, 997, 931 $cm^{-1}$; $^1H$ NMR δ 3.17 (dt, $J$ = 10, 8 Hz, 2 H), 4.41 (t, $J$ = 10 Hz, 2 H), 4.59 (dd, $J$ = 10, 8 Hz, 2 H), 5.29–5.43 (m, 4 H), 6.0 (ddd, $J$ = 16, 11, and 10 Hz, 2 H); $^{13}C$ NMR ppm 170.4, 130.0, 123.0, 70.3, 58.3, 46.4. Anal. Calcd for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81. Found: C, 63.49; H, 5.83. Unsymmetrical isomer (**16b**): mp 69 °C (cyclohexane); IR (KBr) 1785, 1767, 1644, 922, 936 $cm^{-1}$; $^1H$ NMR δ 3.47 (dt, $J$ = 10, 8 Hz, 1 H), 3.90 (dt, $J$ = 10, 8 Hz, 1 H), 4.14 (t, $J$ = 8 Hz, 1 H), 4.30–4.50 (m, 2 H), 4.58 (t, $J$ = 8 Hz, 1 H), 4.28–5.55 (m, 4 H), 5.65–5.95 (m, 2 H); $^{13}C$ NMR ppm 172.5, 171.5, 130.6, 130.1, 122.9, 122.0, 70.5, 69.0, 58.2, 45.9, 45.5. Anal. Calcd for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81. Found: C, 63.36; H, 5.84. An analytical sample of the minor symmetrical isomer (**16c**) could not be isolated; our identification is based on GC-coupled MS analysis: $m/e$ (rel intensity) 209 (5), 208 (47), 163 (27), 151 (10), 160 (10), 149 (44), 135 (16), 121 (19), 119 (59), 107 (13), 106 (10), 105 (76), 93 (14), 92 (13), 91 (100), 79 (44), 78 (17), 77 (57), 65 (21), 42 (17), 27 (29).

**Ethyl 3-methyl-2-oxo-4-vinyltetrahydrofuran-3-carboxylate (17)**: IR (neat) 1790, 1785, 1750, 1730, 1645, 990, 970, 930, 915 $cm^{-1}$; the product is a mixture of $Z$ and $E$ isomers in a ratio of 70:30, determined by the integration of the protons in the α position relative to the vinyl substituent. They are very easily distinguished by $^1H$ NMR. Chemical shifts of the major $Z$ isomer are distinguished by an asterisk. $^1H$ NMR: δ 1.29* and

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1.30 (t, $J$ = 7 Hz, 3 H), 1.38 and 1.47* (s, 3 H), 3.04* and 3.69 (m, 1 H), 4.06-4.54 (m, 4 H), 5.17-5.43 (m, 2 H), 5.53-5.79 (m, 1 H); $^{13}$C NMR ppm 175.6*, 168.3* (C=O of the minor isomer were not detected), 131.4*-130.7, 120.9*-120.3, 69.5-69.3*, 62.2-62.0*, 54.0-53.8, 51.8*-47.4, 18.7*, 14.2*-14.8, 14.6. Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.21; H, 7.16.

**Ethyl 4-isopropenyl-3-methyl-2-oxotetrahydrofuran-3-carboxylate (18)**: IR (neat) 1780, 1740, 1645 cm$^{-1}$; $^1$H NMR; $Z$ isomer $\delta$ 1.25 (t, $J$ = 7 Hz, 3 H), 1.61 (s, 3 H), 1.83 (s large, 3 H), 3.01 (dd, $J$ = 7.9, 11 Hz, 1 H), 4.0-4.6 (m, 4 H), 4.78 (s, 1 H), 5.00 (s, 1 H); $^{13}$C NMR ppm 14.1, 20.6, 23.1, 53.2, 61.9, 139.0, 168.4, 175.7; $E$ isomer (data from the two isomer mixture) 1.31 (t, $J$ = 7 Hz, 3 H), 1.63 (s, 3 H), 1.69 (s br, 3 H), 3.65 (t, $J$ = 7.8 Hz, 1 H), 4.0-4.6 (m, 4 H), 4.76 (s, br, 1 H), 5.03 (s br, 1 H); $^{13}$C NMR ppm 175.6, 170.7, 139.4, 114.5, 68.6, 62.3, 53.0, 50.0, 22.1, 20.06, 14.1. $Z$:$E$ = 58:42 (from $^1$H NMR). Anal. Calcd for $C_{11}H_{16}O_4$ (mixture): C, 62.24; H, 7.69. Found: C, 62.23; H, 7.67.

**Ethyl 4-(2-acetoxy-2-propenyl)-3-methyl-2-oxotetrahydrofuran-3-carboxylate (19)**: IR (neat) 1780, 1740 cm$^{-1}$; $^1$H NMR; $Z$ isomer $\delta$ 1.29 (t, $J$ = 7 Hz, 3 H), 1.54 (s, 3 H), 1.63 (s, 3 H), 1.70 (s, 3 H), 1.96 (s, 3 H), 2.55 (dd, $J$ = 8.2, 10.7 Hz, 1 H), 4.0-4.60 (m, 4 H); $^{13}$C NMR ppm 176.0, 169.4, 169.0, 80.2, 66.3, 61.8, 58.1, 51.9, 24.9, 14.0, 22.0, 21.9, 13.9; $E$ isomer (data from the two isomer mixture) 1.30 (t, $J$ = 7 Hz, 3 H), 1.51 (s, 3 H), 1.56 (s, 3 H), 2.00 (s, 3 H), 2.02 (s, 3 H), 3.29 (dd $J$ = 10.7, 8 Hz, 1 H), 4-4.6 (m, 4 H); $^{13}$C NMR ppm 175.7, 170.8, 169.4, 80.0, 66.5, 62.3, 53.6, 53.1, 24.9, 24.1, 22.3, 15.3, 14.0. $Z$:$E$ = 65:35 (from $^1$H NMR). Anal. Calcd for $C_{13}H_{20}O_6$ (mixture): C, 57.34; H, 7.40. Found: C, 57.29; H, 7.41.

**3,7-Dioxa-1-methyl-4-phenylbicyclo[3.3.0]octane-2,8-dione (20).** Oxidation of 1 g of diester 8 leads after column chromatography to 70 mg of recovered 8, 110 mg of acetate 21, and 700 mg of a mixture of 20 and 21, whose ratio determined by $^1$H NMR (based on benzylic proton signals) is 75:25, respectively. Yields were calculated from this result. Rechromatography of the mixture gave a sample of compound 20 for which only $^1$H NMR and MS data were obtained. $^1$H NMR: $\delta$ 1.45 (s, 3 H), 3.18 (td, $J$ = 6, 3 Hz, 1 H), 4.36-4.68 (AB part of a ABX multiplet, $J_{AB}$ = 10 Hz, 2 H), 5.3 (d, $J$ = 6 Hz, 1 H), 7.2-7.6 (m, 5 H). MS: $m/e$ (rel intensity 233 (7), 232 (42), 131 (11), 129 (27), 128 (20), 126 (11), 115 (22), 110 (26), 107 (30), 106 (20), 105 (60), 99 (100), 98 (34), 91 (46), 83 (13), 82 (17), 79 (15), 78 (20), 77 (62), 69 (63), 64 (10), 55 (13), 54 (19), 53 (16), 52 (10), 51 (34), 50 (4), 44 (25), 41 (35), 39 (50), 29 (19), 27 (27).

**Ethyl 4-($\alpha$-acetoxybenzyl)-3-methyl-2-oxotetrahydrofuran-3-carboxylate (21)**: IR (neat) 1774, 1740, 1717, 765, 706 cm$^{-1}$; the product is a mixture of four stereoisomers whose ratio could not be determined from the complex $^1$H NMR spectra. Major stereoisomer (data from the mixture): $^1$H NMR $\delta$ 1.00 (s, 3 H), 1.35 (t, $J$ = 7.1 Hz, 3 H), 2.03 (s, 3 H), 2.98 (q, $J$ = 9 Hz, 1 H), 4.20-4.60 (m, 4 H), 5.84 (d, $J$ = 9 Hz, 1 H), 7.27-7.41 (m, 5 H), (the spectra of the other isomers differ mainly by the chemical shift of the methyl groups and of the cyclic C$H$ whose signals appear at 3.6-4.1 ppm); $^{13}$C NMR ppm 175.3, 169.4, 168.7, 137.4, 129.2, 128.7, 127.2, 73.8, 68.5, 68.4, 52.2, 48.1, 32.4, 20.9, 19.7, 14.1. Anal. Calcd for $C_{17}H_{20}O_6$ (mixture): C, 63.75; H, 6.25. Found: C, 63.74; H, 6.19.

**Ethyl 4-(acetoxymethylene)-3-methyl-2-oxotetrahydrofuran-3-carboxylate (22)**: IR (neat) 3000, 1780, 1740, 1690 cm$^{-1}$; $^1$H NMR $\delta$ 1.27 (t, $J$ = 7 Hz, 3 H), 1.62 (s, 3 H), 2.19 (s, 3 H), 4.21 (q, $J$ = 7 Hz, 2 H), 4.92-5.01 (AB part of an ABX multiplet; $J_{AB}$ = 13 Hz, 2 H), 7.29 (t, $J$ = 2 Hz, 1 H); $^{13}$C NMR ppm 174.6, 168.5, 166.6, 130.9, 120.9, 67.1, 62.6, 51.1, 24.5, 19.9, 13.9. Anal. Calcd for $C_{11}H_{14}O_6$: C, 54.54; H, 5.83. Found: C, 54.49; H, 5.85.

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# Monosubstitution versus Disubstitution in the $S_{RN}1$ Reaction of Dihalobenzenes with Sulfanions. The Role of the Monosubstitution Product and of Its Anion Radical

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The competition between mono- and disubstitution of dihalobenzenes by a series of aromatic sulfanions, via the $S_{RN}1$ reaction, is shown to involve two radical chains. The first one, recognized in the earliest works, involves one branching point at the level of the monosubstituted product anion radical. Reoxidation of the latter via electron transfer to the parent dihalide affords the monosubstituted product. Conversely, the route to the disubstituted product is opened when cleavage of the carbon-halogen bond in the monosubstituted product anion radical occurs before the electron transfer takes place; the disubstitution product is then obtained in its reduced (anion radical) form. Reoxidation of the latter, to afford the neutral disubstituted product, may involve competitively the parent dihalide or the neutral monosubstituted product, depending on the electron affinity of the arylthio moiety. In the first case the electron transfer propagates the first chain; in the second a new chain leading to the disubstitution is activated. The role of the two imbricated chains, under photochemical conditions, and thus that of the monosubstitution product is discussed quantitatively on the basis of the pertinent rate constants determined by cyclic voltammetry.

## Introduction

The photostimulated $S_{RN}1$ reactions of dihalobenzenes ($IC_6H_4X$, X = $o$, $m$, $p$-Br, Cl) with various nucleophiles are known to give monosubstitution or disubstitution products according to the nature of X and the nucleophile.[1,2] $m$-Chloroiodobenzene (**1,m**) is reported to afford only the monosubstitution product when treated with diethyl

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