Silver-ion Assisted Methanolysis of 2,2-Dibromo-1-methylcyclopropanecarboxylic Acid and 2,2-Dibromo-1,3-dimethylcyclopropanecarboxylic Acid

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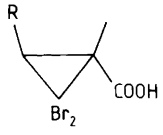
For both title acids the course of methanolysis depends to a large extent on the substrate concentrations and the silver salt employed. In dilute solution the reaction between 2,2-dibromo-1-methylcyclopropanecarboxylic acid and silver trifluoroacetate yields only 4-bromo-3-methyl-2(5*H*)-furanone and 3-bromo-2-methoxy-2-methyl-3-butenoic acid, whereas in more concentrated solution a number of other products arising from ring opening are formed. The yield of one of these products, 4-methoxy-2-butanone increases as the reaction time is increased. When silver perchlorate ($AgClO_4$) is used most of the acid is converted into methyl 2,2-dibromo-1-methylcyclopropanecarboxylate. The 1,3-dimethyl acid reacts similarly, but is not converted into the corresponding methyl ester even in the presence of $AgClO_4$. Possible reaction pathways for product formation are discussed taking into account experiments carried out in CD_3OD and D_2O.

Solvolysis of *gem*-dibromocyclopropanes in the presence of a silver salt generally leads to ring opening and, depending on the reaction medium, formation of allylic derivatives and/or dienes.[1-6] When an acyl or alkoxycarbonyl group is attached to the ring, however, the cyclopropane is unreactive under such conditions.[7] For comparison, we wished to perform solvolysis experiments with 2,2-dibromocyclopropanecarboxylic acids **1a** and **1b** which we expected to be almost unreactive. Surprisingly enough, both acids turned out to be fairly reactive and were converted, as reported here, into product mixtures the compositions of which were sensitive to the reaction conditions.



1a R=H
1b R=CH_3

Results and discussion

The title compounds[8] were solvolysed in methanol in the presence of various silver salts. Exploratory experiments revealed that the acids did not react at or slightly above room temperature and all preparative reactions were therefore carried out in refluxing methanol (65 °C). With the exception of silver nitrate which is rather insoluble in methanol, all the salts employed dissolved easily, to give 0.7 M solutions under these conditions. The reaction mixtures were separated into acidic and neutral fractions which were analysed by GLC, GLC/MS, and ^1H NMR spectroscopy prior to chromatographic work-up.

When a methanolic solution of **1a** (0.08 M) and silver trifluoroacetate (AgTFA) (0.12 M) was refluxed the acid was consumed rather slowly; after 144 h the reaction mixture still contained 45 %

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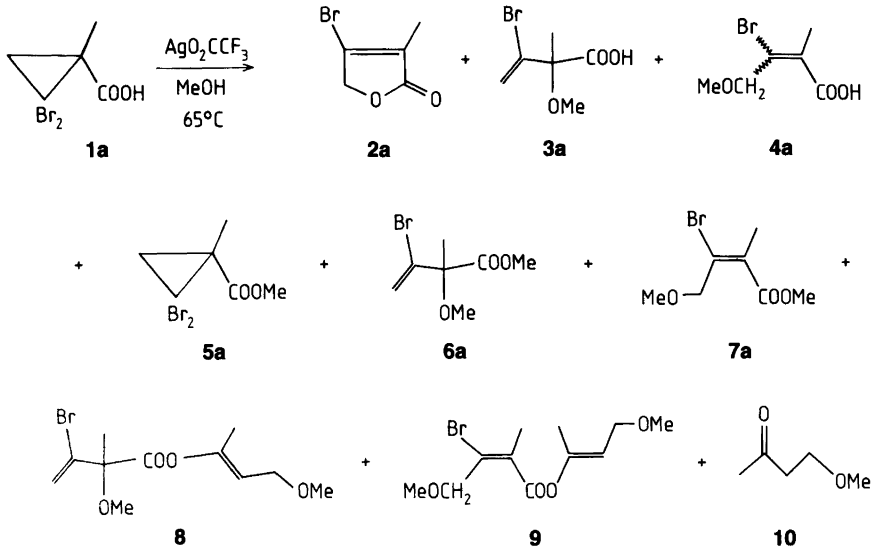
Table 1. Product distribution in reactions of **1a** (0.37 M) with silver salts (AgX, 0.70 M) in methanol in the dark at 65 °C.

Entry	X	Reaction time/h	Yield (%)[a]											
			1a	**2a**	**3a**	*E*-**4a**	*Z*-**4a**	**5a**	**6a**	*E*-**7a**	*Z*-**7a**	**8**	**9**	**10**
1	TFA	17	69	5	11	10	5	0	0	0	0	0	0	0
2		42	30	7	34	6	6	0	4	<1	0	5	6	2
3		96	0	7	48	5	6	0	3	<1	0	9	8	14
4		122	0	9	40	4	6	0	5	<1	0	8	9	19
5		158	0	16	33	5	6	0	5	<1	0	8	4	23
6		288	0	25	11	0	3	0	8	1	<1	3	3	46
7	F	48	0	20	4	4	4	7	3	4	0	0	0	5
8	NO_3	56	45	16	<1	<1	<1	34	3	2	<1	0	0	0
9	ClO_4	56	0	<1	<1	0	2	73	3	17	<1	0	0	0

[a]Percentage of reaction mixture as determined by a combination of GLC and ^{1}H NMR analyses; for isolated yields, see Experimental.

unchanged starting material. Two products were formed, 4-bromo-3-methyl-2(5*H*)-furanone (**2a**, 30 %) and 3-bromo-2-methoxy-2-methyl-3-butenoic acid (**3a**, 25 %). The lactone was easily obtained pure by washing an ether solution of the product mixture with aqueous sodium carbonate.

In order to make the reaction more efficient the concentrations of **1a** and AgTFA were increased to 0.37 and 0.70 M, respectively. The mixture was stirred at 65 °C and the reaction was monitored by GLC. The results are summarized in Table 1, entries 1–6. As expected, on the basis of the rate expression for similar reactions,[9] the rate of consumption of the acid increased considerably, but concomitantly the number of products increased drastically (Scheme 1). Altogether ten products were detected, the distribution of which varied as the reaction proceeded.



Scheme 1.

Among the primary products compounds **2a** and **3a** were always present, but in addition a significant amount of 3-bromo-4-methoxy-2-methyl-2-butenoic acid (**4a**) was formed at an early stage (Table 1, entry 1). This new product was formed as a 2:1 mixture of the *E* and *Z* isomers (^{1}H NMR). As the reaction proceeded the methyl esters of **1a**, **3a** and **4a**, methyl 2,2-dibromo-1-methylcyclopropanecarboxylate (**5a**), methyl 3-bromo-2-methoxy-2-methyl-3-butenoate (**6a**) and methyl 3-bromo-4-methoxy-2-methyl-2-butenoate (**7a**) were formed in low yields (Table 1, entries 2–6). Interestingly, **7a** was obtained as a single isomer. Since its ^{1}H NMR spectrum exhibits a 3H triplet at 2.15 ppm and a 2H quartet at 4.48 ppm this compound probably has the *E* configuration. Two other esters were also formed, *viz.* 3-methoxy-1-methyl-1-propenyl 3-bromo-2-methoxy-2-methyl-3-butenoate (**8**) and 3-methoxy-1-methyl-1-propenyl 3-bromo-4-methoxy-2-methyl-2-butenoate (**9**), but were consumed during the reaction; their yields dropping from approximately 10% after 96 h (Table 1, entry 3) to 3% after 288 h (entry 6). The final product isolated was 4-methoxy-2-butanone (**10**) which was identical with an authentic sample.[10] This product was present in very low yield after 42 h reflux (Table 1, entry 2) but was predominant (46%) after 288 h (entry 6).

The structure elucidation of products **2–10** was carried out by employing spectroscopic and spectrometric techniques on purified samples of the compounds. Mass spectrometry proved to be very useful for the identification of the isomeric esters **6a**, **7a**, **8** and **9**. The reason for this is the systematic variation in the intensities of characteristic peaks in their mass spectra (Table 2) caused by the butenoate moieties which strongly direct the fragmentation processes. The structural similarity between **3a**, **6a** and **8** and between **4a**, **7a** and **9** was also reflected in their ^{1}H NMR spectra. All the unconjugated compounds gave rise to a 2H AB system around 6.0 ppm and a 3H singlet at ca. 1.7 ppm. The conjugated compounds, on the other hand, displayed a 2H quartet around 4.5 ppm and a 3H triplet at ca. 2.2 ppm; the coupling constant was in this case ca. 0.9 Hz which is characteristic of homoallylic coupling.[11]

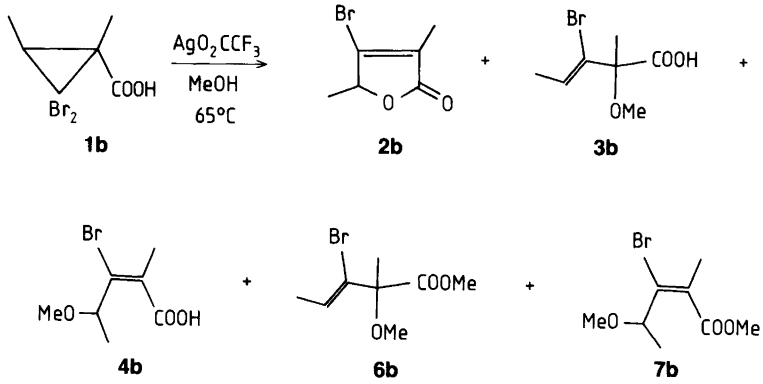
A comment on the stereochemical assignments of esters **8** and **9** is necessary. The signals due to the acid moiety of **9** were almost identical with those exhibited by that of *E*-**4a** and of *E*-**7a**; **9** is thus probably derived from (*E*)-2-butenoic acid. Furthermore, the signals caused by the 3-methoxy-1-methyl-1-propenyl group were essentially identical which indicates that the configuration of the alkenyl moieties is the same. As borne out by decoupling experiments, the methyl group attached to C-1 is coupled to the olefinic proton with $|J| < 0.5$ Hz which strongly suggests that the double bond has an *E* configuration.[7,12]

When the acid **1b** was treated with AgTFA suspended in methanol at 65 °C, the course of reaction was similar to that observed for **1a** (Scheme 2 and Table 3, entry 1). Thus, the main products were 4-bromo-3,5-dimethyl-2(5*H*)-furanone (**2b**), (*Z*)-3-bromo-2-methoxy-2-methyl-3-pentenoic acid (**3b**) and (*E*)-3-bromo-4-methoxy-2-methyl-2-pentenoic acid (**4b**); in addition

Table 2. Selected mass spectrometric fragments of the esters **6–9** as percentages of the base peak.[a]

Ion[b]	6a	7a	8	9	6b	7b
$M^{+\cdot}$	1	18	0	0	0	20
$M^{+\cdot}-RO$	3	52	1	100	2	16
$M^{+\cdot}-ROH$	0	4	1	0	2	6
$M^{+\cdot}-ROH-CH_3$	0	74	1	4	1	26
$M^{+\cdot}-COOR$	100	34	100	45	100	20
$M^{+\cdot}-COOR-CH_2O$	14	0	56	3	10	0
$M^{+\cdot}-Br$	10	100	0	0	0	100
$M^{+\cdot}-Br-CO$	0	30	22	0	0	0
$M^{+\cdot}-Br-ROH$	0	25	0	5	0	74

[a]The intensity of a fragment containing bromine is equal to the sum of the intensities of the isotope peaks.
[b]R denotes the alkyl groups of the alkyl alkenoates.



Scheme 2.

small amounts of methyl (*Z*)-3-bromo-2-methoxy-2-methyl-3-pentenoate (**6b**) and methyl (*E*)-3-bromo-4-methoxy-2-methyl-2-pentenoate (**7b**) were obtained along with five minor, unidentified compounds. Interestingly, 3-methoxy-1-alkenyl esters corresponding to **8** and **9** were not formed and no trace of a methoxy ketone analogous to **10** could be detected. Finally, it is noteworthy that the **3**:**4** ratio decreases from 4.4 in the case of **1a** to 1.5 during the methanolysis of **1b**.

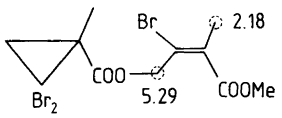
The identification of compounds **2b**–**7b** is mainly based on their MS and ^{1}H NMR spectroscopic properties. The mass spectral fragmentation patterns of **6b** and **7b** were very similar to those of **6a** and **7a**, respectively (Table 2). The ^{1}H NMR spectrum of **3b** consisted of a quartet at δ 6.21 due to the C-4 methine proton, a doublet at 1.82 ppm due to the terminal methyl group, and a singlet at 1.62 ppm associated with the methyl group attached to C-2. In order to establish the stereochemistry of the double bond ^{1}H–{H} difference NOE experiments were performed. Irradiation at 1.62 ppm gave a small enhancement of the quartet at 6.21 ppm and when the methine proton was irradiated an NOE was observed at 1.62 ppm and INDOR at 1.82 ppm. It may therefore be concluded that the C=C bond has the *Z* configuration.

The methanolyses of **1a** and **1b** proceeded quite differently when AgTFA was replaced by silver fluoride. The most striking features are the much lower yields of the acids **3** and **4**, and the formation of more than 13 products which were not formed in the AgTFA-mediated reactions. None of the new products could be isolated in a pure state but on the basis of ^{1}H NMR and MS studies the structures of four compounds present in the neutral fraction from the solvolysis of **1a** were tentatively assigned as 2-bromo-4-methoxycarbonyl-2*E*-butenyl 2,2-dibromo-1-methylcyclopropanecarboxylate (**11**), 2-bromo-3-methoxy-

Table 3. Product distribution in reactions of **1b** (0.37 M) with silver salts (AgX) (0.70 M) in methanol in the dark at 65 °C.

Entry	X	Reaction time/h	Yield (%)[a]					
			2b	***Z*-3b**	***E*-4b**	***Z*-6b**	***E*-7b**	Unknown (number)
1	TFA	45	21	43	28	4	2	2 (5)
2	F	45	27	1	4	<1	12	56 (13)
3	NO_3	56	12	2	8	21	57	0
4	ClO_4	56	18	1	1	44	36	0

[a]Percentage of reaction mixture as determined by a combination of GLC and ^{1}H NMR analyses.



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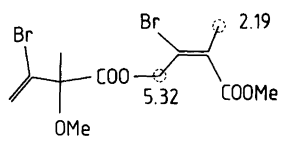

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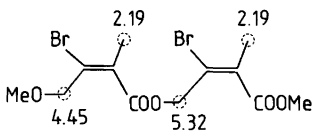

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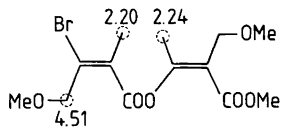

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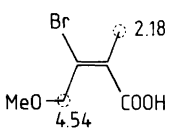
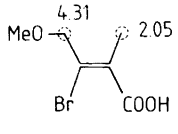
Fig. 1.

carbonyl-2*E*-butenyl 3-bromo-2-methoxy-2-methyl-3-butenoate (**12**), 2-bromo-3-methoxycarbonyl-2*E*-butenyl 3-bromo-4-methoxy-2-methyl-2*E*-butenoate (**13**), and 3-methoxy-2-methoxycarbonyl-1-methyl-1-propenyl 3-bromo-4-methoxy-2-methyl-2*E*-butenoate (**14**). The stereochemical assignments are mainly based on the chemical shifts of the methyl groups attached to the C=C bonds; these shifts (Fig. 1) are almost identical with those observed for the corresponding groups in *E*-**4a** and *E*-**7a** but are significantly different from that of the corresponding methyl group in *Z*-**4a**.



E-**4a**

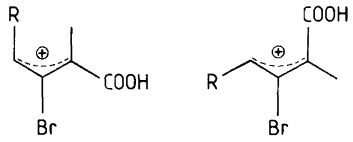


Z-**4a**

When **1a** and **1b** were solvolysed at 65 °C in methanol in the presence of silver nitrate, ester formation was even more pronounced than in the AgF-assisted reactions. The reaction of **1a** appeared to proceed much more sluggishly than under any other set of conditions. This may be due to the heterogenous nature of the reaction, caused by the low solubility of $AgNO_3$ in methanol. The main product from **1a** was the corresponding methyl ester (**5a**) which is reported to be inert under our reaction conditions.[7] Lactone **2a** and esters **6a** and **7a** were the only ring-opened products observed, albeit in very low yield. When **1b** was solvolysed under the same conditions the corresponding ring-opened products (**2b**, **6b**, and **7b**) amounted to 90 % of the reaction mixture (Table 3, entry 3). In this case, however, no trace of the methyl ester of the starting material was observed.

Finally, both acids were solvolysed in the presence of silver perchlorate. Once more their chemical reactivity turned out to be significantly different. Acid **1a** was mainly (73 %) converted into the corresponding, unreactive methyl ester **5a**; the rest of the reaction mixture consisted of six products, of which the predominant one was **7a** (17 %) (Table 1, entry 9). As observed in the AgTFA- and AgF-mediated reactions **7a** was formed almost esclusively in the *E* configuration. On the other hand, solvolysis of **1b** gave the esters **2b**, *Z*-**6b**, and *E*-**7b** in 98 % total yield, with no trace of a cyclopropyl ester.

With the exception of the ester **5a**, which results from the esterification of **1a** catalysed by the silver salt present, all of the products **2–7** and **11–13** are primarily due to nucleophilic trapping of the allylic cations **15** and **16** formed by silver-assisted electrolytic opening of the cyclopropane ring. Intramolecular attack of **16** by the carboxy group yields the lactone **2**.[13–15] Furthermore, attack of methanol on C–α and C–γ gives the acids **3** and **4**, respectively, which are converted, to various extents, into esters **6** and **7**, respectively, under our experimental conditions. Finally, nucleophilic trapping of **16** by **1**, **3** and **4** results in formation of three compounds which are converted into the esters **11**, **12** and **13**, respectively, after reaction with methanol. All these reactions are sensitive to the nature of the salt present. The salts that yield the largest total amount of the esters **5–7**, i.e. $AgNO_3$ and $AgClO_4$, give the lactone **2** in lowest yield. This is in accordance with the theory that ester formation is



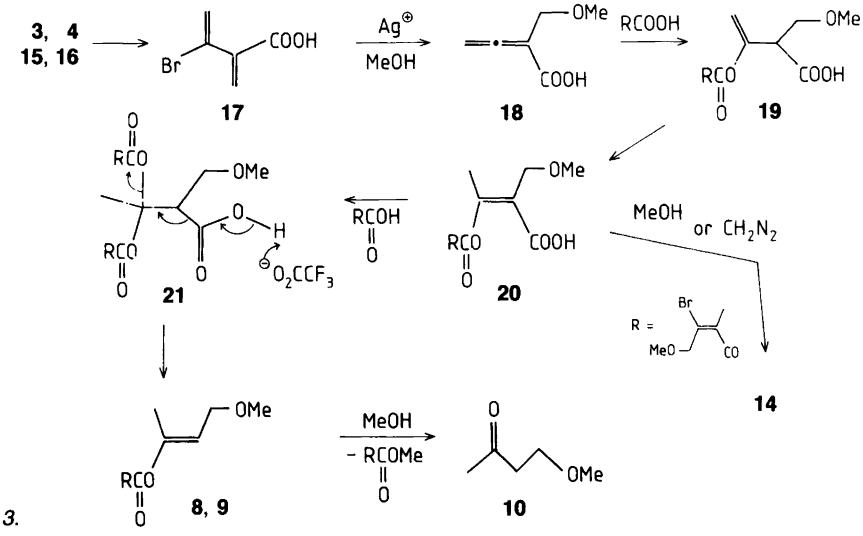
catalysed by Ag^+ complexation of the carboxy group. The stronger the complexation, the more difficult the intramolecular reaction of **16** becomes.

Esters **8**, **9** and **14** and ketone **10** cannot be accounted for on the basis of reactions usually observed during solvolysis of *gem*-dihalocyclopropanes. However, by invoking the transient existence of 3-bromo-2-methylene-3-butenoic acid **17** and 2-methoxymethyl-2,3-butadienoic acid **18** the formation of these esters can be rationalized (Scheme 3). Hydrogen abstraction from cations **15** and **16** and methanol elimination from the acids **3** and **4** give the diene **17** which belongs to a group of compounds showing remarkable solvolytic activity in alcoholic solvents even in the absence of silver ions.[16,17] As a result, the allene **18** is formed.[7] Carbonyl compounds conjugated to an allene moiety are rapidly attacked, in a Michael fashion, by nucleophilic species (**3**, **4** and HTFA) and **18** is therefore transformed into **19** which isomerizes to the acid **20**.[18] Neither of these acids could be detected in any of the reaction mixtures but when the methanolysis was carried out in the presence of AgF one of the products was the ester **14**. Compound **14** can conceivably be formed by silver- or acid-catalysed esterification of **20**, which is trapped when reaction mixtures, after AgTFA-mediated solvolysis, were treated with diazomethane prior to work-up.

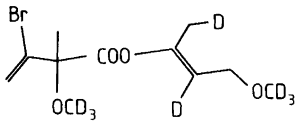
Acid **20** may also undergo Michael addition to form the acid **21** which yields **8** and **9** upon tandem decarboxylation/elimination. The carbon dioxide evolution observed during the reaction prior to hydrolysis may substantiate this conclusion.

The reaction path depicted in Scheme 3 is supported by results from AgTFA-assisted solvolysis in CD_3OD. In a representative experiment 1.85 mmol of **1a** were solvolysed in 1.0 ml (22.5 mmol) of CD_3OD. ^1H NMR and MS analyses of the deuteriated analogues of **8** and **9** thus obtained, i.e. **22** and **23**, revealed that partial deuteriation had taken place in the expected positions. Thus, two CD_3 groups had been incorporated and, in addition, partial deuteriation of the methine group and the other methyl group had occurred. The deuterium content of the methyl and the methine groups was 20 and 80%, respectively, which is as expected from the mechanism outlined above.

When a purified mixture of the esters **8** and **9** was refluxed in methanol in the absence of a silver salt the compounds underwent slow trans-



Scheme 3.



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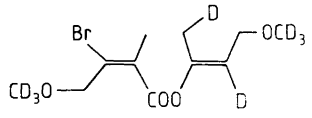

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esterification and gave a mixture of **6a** and **7a** in addition to the ketone **10**. The presence of AgTFA increased the rate of reaction significantly and the lactone **2a** was formed in addition to **6a**, **7a** and **10**. The lactone formation is therefore catalysed by the silver salt. As expected, **8** and **9** were not obtained from mixtures of **3a**, **4a** and **10**.

The fact that transesterification of **8** and **9** and formation of **10** took place prior to hydrolytic work-up was also proved by deuterium experiments. Thus, treatment of **1a** with AgTFA–CD_3OD and subsequent hydrolysis using either H_2O–HCl or D_2O–DCl gave 1,1,1,3,3-pentadeuterio-4-trideuteriomethoxy-2-butanone as the primary product.

Experimental

General. IR spectra were recorded on a Shimadzu IR-435 spectrophotometer with the compounds as liquid films or dissolved in tetrachloromethane. ^{1}H NMR spectra were obtained on Jeol PMX 60SI (60 MHz) and Jeol FX90Q (90 MHz) spectrometers. $CDCl_3$ and CCl_4 were used as solvents and tetramethylsilane (TMS) as an internal standard. Chemical shifts are reported in ppm downfield from TMS. ^{1}H-{^{1}H} difference nuclear Overhauser enhancement (NOE) spectra were recorded on a Jeol FX90Q instrument using degassed samples dissolved in $CDCl_3$. The pulse sequence was a phase-cycled sequence of a $\pi/2$ pulse with homonuclear gated decoupling followed by a $-\pi/2$ pulse without decoupling. GLC/MS was performed on a VG Micromass 7070H spectrometer combined with a Hewlett–Packard 5710 gas chromatograph equipped with a Supelco SPB 5 fused silica column (30 m × 0.25 mm I.D.). The spectrometer was operated in the EI mode at 70 eV. GLC analyses were carried out on a Carlo Erba Mega 5300 gas chromatograph equipped with FID and a Supelco SPB 5 fused silica column (30 m × 0.25 mm I.D.) and connected to an LDC Milton Roy CC-10B integrator. Response ratios were determined by GLC analysis of samples analysed by ^{1}H NMR spectroscopy.

Solvolysis of the gem*-dibromocyclopropanecarboxylic acids* **1**; *general procedure.* A mixture of **1** (0.37 M) and a silver salt (0.70 M) in methanol was refluxed in the dark until all the starting material had been consumed (approximately 48 h). Dilute hydrochloric acid was added and the resulting mixture was thoroughly extracted with ether. The combined ether extracts were analysed using GLC and ^{1}H NMR spectroscopy and subsequently washed with aqueous sodium hydrogen carbonate and dried ($MgSO_4$). The results are compiled in Tables 1 and 3. The hydrogen carbonate phases were acidified (aq. HCl) and extracted with ether. The ether extracts were combined and dried ($MgSO_4$) separately.

The ether extracts were worked up separately. The residues were analysed by GLC and ^{1}H NMR spectroscopy prior to chromatographic separation of the products.

1a/*Silver trifluoroacetate (AgTFA)/MeOH.* Treatment of **1a** (2.50 g) with AgTFA gave a complex reaction mixture. The acidic residue (0.789 g) consisted of three products in a 81:9:10 ratio (GLC). The main product was identified as 3-bromo-2-methoxy-2-methyl-3-butenoic acid (**3a**). The two minor products were (*E*)- and (*Z*)-3-bromo-4-methoxy-2-methyl-2-butenoic acid (**4a**).

3a: IR (film): 3250–2850 (m), 1720 (s), 1630 (m), 910 (m) cm^{-1}; ^{1}H NMR (60 MHz; CCl_4): δ 1.65 (3 H, s), 3.40 (3 H, s), 5.88 (1 H, d, *J* 2 Hz), 6.07 (1 H, d, *J* 2 Hz), 9.85 (1 H, broad s); MS [*m/z* (% rel. int.)]: 193 (12), 192 (46), 191 (13), 190 (46), 177 (4), 175 (4), 165 (12), 163 (13).

E-**4a**: ^{1}H NMR (90 MHz; $CDCl_3$): δ 2.18 (3 H, narrow t), 3.37 (3 H, s), 4.54 (2 H, narrow q), 9.85 (1 H, broad s); MS [*m/z* (% rel. int.)]: 178 (20), 176 (20), 149 (9), 147 (9), 121 (10), 119 (12), 97 (100).

Z-**4a**: ^{1}H NMR (60 MHz; $CDCl_3$): δ 2.05 (3 H,

m), 3.37 (3 H, s), 4.31 (2 H, m), 8.20 (1 H, broad s); mass spectrum indistinguishable from that of *E*-**4a**.

The neutral residue (0.261 g) was subjected to preparative TLC [SiO_2; chloroform–hexane (4:1)].

Three distinct bands were formed. The first band consisted of a 2:2:1 mixture of methyl 2,2-dibromo-1-methylcyclopropanecarboxylate (**5a**), methyl 3-bromo-4-methoxy-2-methyl-2-butenoate (**7a**), and methyl 3-bromo-2-methoxy-2-methyl-3-butenoate (**6a**), respectively.

6a: IR (CCl_4): 3020 (w), 1745 (s), 1635 (w), 1225 (m), 1140 (s), 900 (m), 860 (s) cm^{-1}; ^1H NMR (90 MHz; $CDCl_3$): δ 1.67 (3 H, s), 3.34 (3 H, s), 3.82 (3 H, s), 5.86 (1 H, d, *J* 2.5 Hz), 6.07 (1 H, d, *J* 2.5 Hz); MS [*m/z* (% rel. int.)]: 224 (5, M^+), 222 (5, M^+), 209 (3), 207 (3), 193 (15), 191 (15), 166 (34), 165 (100), 164 (36), 163 (100), 143 (52), 135 (69), 133 (73), 117 (9), 113 (9), 85 (11), 83 (19).

7a: ^1H NMR (90 MHz; $CDCl_3$): δ 2.15 (3 H, t, *J* 0.97 Hz), 3.37 (3 H, s), 3.82 (3 H, s), 4.48 (2 H, q, *J* 0.97 Hz); MS [*m/z* (% rel. int.)]: 224 (9, M^+), 222 (9, M^+), 193 (26), 191 (26), 177 (36), 175 (38), 165 (17), 163 (17), 143 (100), 115 (30), 101 (25).

The second band consisted of a 1:4 mixture of the ester **6a** and 4-bromo-3-methyl-2(5*H*)-furanone (**2a**), respectively.

2a: m.p. 56–57 °C; IR (CCl_4): 1770 (s), 1660 (m), 1270 (m), 1070 (m), 1005 (m), 905 (s) cm^{-1}; ^1H NMR (90 MHz; $CDCl_3$): δ 1.94 (3 H, t, *J* 2.06 Hz), 4.80 (2 H, q, *J* 2.06 Hz); MS [*m/z* (% rel. int.)]: 178 (33), 176 (34), 149 (10), 147 (11), 121 (12), 119 (14), 97 (100). Anal. $C_5H_5BrO_2$: C, H.

The third band was made up of two compounds in a 70:30 ratio. The compounds were identified as (*E*)-3-methoxy-1-methyl-1-propenyl 3-bromo-2-methoxy-2-methyl-3-butenoate (**8**) and (*E*)-3-methoxy-1-methyl-1-propenyl (*E*)-3-bromo-4-methoxy-2-methyl-2-butenoate (**9**).

8: ^1H NMR (90 MHz; $CDCl_3$): δ 1.74 (3 H, s), 2.00 (3 H, broad s), 3.31 (3 H, s), 3.38 (3 H, s), 3.96 (2 H, unresolved d), 5.27 (1 H, unresolved t), 5.92 (1 H, d, *J* 0.73 Hz), 6.17 (1 H, d, *J* 0.73 Hz); MS [*m/z* (% rel. int.)]: 263 (0.5), 261 (0.5), 185 (22), 165 (100), 163 (100), 135 (56), 133 (59).

9: ^1H NMR (90 MHz; $CDCl_3$): δ 2.00 (3 H, broad s), 2.22 (3 H, t, *J* 0.93 Hz), 3.31 (3 H, s), 3.38 (3 H, s), 3.96 (2 H, unresolved d), 4.52 (2 H, q, *J* 0.93 Hz), 5.27 (1 H, unresolved t); MS [*m/z* (% rel. int.)]: 193 (100), 191 (100), 165 (44), 163 (46), 112 (44), 97 (27).

When the neutral fraction was subjected to ^1H NMR spectroscopy prior to chromatographic work-up, signals caused by an additional compound were observed. This compound was shown to be identical with 4-methoxy-2-butanone (**10**).[10]

GLC analysis revealed that the crude neutral residue consisted of the above-mentioned seven main products together with several minor components. The minor components comprised less than 5 per cent (GLC) of the total amount. The main products, compounds **10**:**2a**:**6a**:**5a**:**7a**:**8**:**9** were formed in a ratio of 34:18:7:1:2:20:18 (in order of increasing retention time).

In another experiment a methanolic solution of **1a** (2.50 g) was refluxed with AgTFA according to the general procedure. Samples (0.2 ml) of the reaction mixture were collected after 17, 42, 96, 122, 158 and 188 h to which aqueous HCl (0.2 ml) and ether (0.4 ml) were added. The samples were vigorously shaken and the organic phase was separated, dried ($MgSO_4$), and analysed by GLC. The results are summarized in Table 1.

1a/*AgF*/*MeOH*. The acid **1a** (1.25 g) was treated with AgF as described in the general procedure. Following the usual procedure an acidic (0.121 g) and a neutral (0.105 g) residue were obtained. The acidic residue consisted of the acids **3a**, *E*-**4a** and *Z*-**4a** in a 1:1:1 ratio, comprising 35 % of the total acidic mixture (GLC). In addition, four unidentified acids of oligomeric nature were observed.

The neutral fraction was subjected to preparative TLC [SiO_2; chloroform–hexane (4:1)]. The first band contained the lactone **2a** and esters **6a**, **7a** and **5a** in a 59:9:11:21 ratio. The next band contained 2-bromo-3-methoxycarbonyl-2-butenyl 2,2-dibromo-1-methylcyclopropanecarboxylate (**11**).

11: ^1H NMR (90 MHz; $CDCl_3$): δ 1.64 (1 H, d, *J* 7.8 Hz), 1.67 (3 H, s), 2.18 (3 H, t, *J* 0.98 Hz), 2.47 (1 H, d, *J* 7.8 Hz), 3.48 (3 H, s), 5.29 (2 H, q, *J* 0.98 Hz); MS [*m/z* (% rel. int.)]: 435 (1), 433 (1), 421 (1), 419 (2), 417 (2), 415 (1), 371 (1), 369 (2), 367 (1), 243 (50), 241 (100), 239 (55), 215 (24), 213 (53), 211 (27), 193 (16), 191 (18), 133 (24), 131 (27).

The third band consisted of two compounds: 2-bromo-3-methoxycarbonyl-2-butenyl 3-bromo-2-methoxy-2-methyl-3-butenoate (**12**) and 2-bromo-3-methoxycarbonyl-2-butenyl 3-bromo-4-methoxy-2-methyl-2-butenoate (**13**) in a 40:60 ratio.

12: ^{1}H NMR (90 MHz; $CDCl_3$): δ 1.68 (3 H, s), 2.19 (3 H, broad s), 3.38 (3 H, s), 3.85 (3 H, s), 5.32 (2 H, m), 5.95 (1 H, d, *J* 2.55 Hz), 6.15 (1 H, d, *J* 2.55 Hz); MS [*m/z* (% rel. int.)]: 343 (1), 340 (2), 338 (1), 290 (34), 288 (33), 243 (2), 241 (5), 238 (2), 193 (6), 191 (5), 163 (100), 161 (96), 135 (37), 133 (41).

13: ^{1}H NMR (90 MHz; $CDCl_3$): δ 2.19 (6 H, broad s), 3.38 (3 H, s), 3.85 (3 H, s), 4.15 (2 H, broad s), 5.32 (2 H, m); MS [*m/z* (% rel. int.)]: 321 (7), 319 (8), 240 (4), 209 (26), 207 (28), 193 (51), 191 (54), 178 (10), 177 (67), 176 (13), 175 (64), 165 (41), 163 (44), 83 (100).

The fourth band consisted of five compounds of which four remain unknown. The major component, constituting 40 % of the mixture, was tentatively assigned the structure 3-methoxy-2-methoxycarbonyl-1-methyl-1-propenyl 3-bromo-4-methoxy-2-methyl-2-butenoate (**14**).

14: ^{1}H NMR (90 MHz; $CDCl_3$): δ 2.20 (3 H, broad s), 2.24 (3 H, broad s), 3.32 (3 H, s), 3.37 (3 H, s), 3.80 (3 H, s), 4.51 (2 H, broad s), 5.33 (2 H, broad s); MS [*m/z* (% rel. int.)]: 285 (10), 284 (8), 252 (12), 193 (65), 192 (45), 191 (60), 190 (43), 177 (31), 175 (31), 165 (50), 163 (98).

1a/*$AgNO_3$/MeOH*. The acid **1a** (1.25 g) was treated with $AgNO_3$ as described above. Usual work-up gave an acidic (0.271 g) and a neutral (0.318 g) fraction. The acidic fraction consisted of unchanged **1a** (967 %) together with traces of the acids **3a**, *E*-**4a** and *Z*-**4a**. The neutral fraction contained the lactone **2a** and esters **6a**, *Z*-**7a** and **5a** in a 27:6:4:63 ratio.

1a/*$AgClO_4$/MeOH*. The acid **1a** (2.50 g) was treated with $AgClO_4 \cdot H_2O$ as described above. Usual work-up yielded an acidic (0.170 g) and a neutral (1.069 g) residue. The acidic residue consisted of a 1:9 mixture of the acids **3a** and *Z*-**4a**, respectively. The neutral fraction contained the esters *E*-**7a**, **6a**, **2a** and **5a** in a 18:7:1:74 ratio.

1b/*AgTFA/MeOH*. Treatment of **1b** (2.20 g) with AgTFA gave an acidic (0.544 g) and a neutral (0.198 g) fraction. The acidic fraction consisted of (*Z*)-3-bromo-2-methoxy-2-methyl-3-pentenoic acid (**3b**) and (*E*)-3-bromo-4-methoxy-2-methyl-2-pentenoic acid (**4b**) in a 6.4 ratio.

3b: ^{1}H NMR (60 MHz; $CDCl_3$): δ 1.62 (3 H, s), 1.82 (3 H, d, *J* 6.2 Hz), 3.21 (3 H, s), 6.21 (1 H, q, *J* 6.2 Hz), 7.9 (1 H, broad s); MS [*m/z* (% rel. int.)]: 177 (24), 175 (30), 147 (7), 143 (57), 119 (15), 111 (95), 97 (100).

4b: ^{1}H NMR (60 MHz; $CDCl_3$): δ 1.28 (3 H, d, *J* 5.8 Hz), 2.12 (3 H, s), 3.21 (3 H, s), 4.68 (1 H, q, *J* 5.8 Hz), 7.9 (1 H, broad s); MS [*m/z* (% rel. int.)]: 179 (96), 177 (100), 165 (20), 163 (23), 149 (17), 147 (22), 119 (10), 111 (19), 97 (15).

2b and **3b**: IR (film): 3050 (m), 1710 (s), 1650 (m), 1610 (m), 930 (m), 910 (m), 810 (w), 730 (s).

The neutral fraction consisted of 4-bromo-3,5-dimethyl-2(5*H*)-furanone (**2b**), methyl (*Z*)-3-bromo-2-methoxy-2-methyl-3-pentenoate (**6b**) and methyl (*E*)-3-bromo-4-methoxy-2-methyl-2-pentenoate (**7b**) in a 77:14:9 ratio.

2b: ^{1}H NMR (90 MHz; $CDCl_3$): δ 1.49 (3 H, d, *J* 6.3 Hz), 1.92 (3 H, d, *J* 1.1 Hz), 4.96 (1 H, qq, *J* 1.1 and 6.3 Hz); MS [*m/z* (% rel. int.)]: 192 (3), 191 (1), 190 (4), 189 (1), 188 (2), 187 (12), 175 (12), 149 (8), 147 (9), 121 (16), 119 (17), 111 (100).

6b: ^{1}H NMR (90 MHz; $CDCl_3$): δ 1.65 (3 H, s), 1.85 (3 H, d, *J* 6.6 Hz), 3.28 (3 H, s), 3.79 (3 H, s), 6.24 (1 H, q, *J* 6.6 Hz); MS data: see Table 2.

7b: ^{1}H NMR (90 MHz; $CDCl_3$): δ 1.32 (3 H, d, *J* 6.4 Hz), 2.12 (3 H, s), 3.22 (3 H, s), 3.81 (3 H, s), 4.05 (1 H, q, *J* 6.4 Hz); MS data: see Table 2.

1b/*AgF/MeOH*. The acid **1b** (0.77 g) was treated with AgF as described above. The acidic fraction (0.003 g) contained the acids *Z*-**3b** and *E*-**4b** in a 1:4 ratio. The neutral fraction (0.351 g) consisted of the lactone **2b** and ester *E*-**7b** in a 70:30 ratio. In addition, traces of the ester *Z*-**6b** and seven unidentified products were detected. The compounds amounted to 57 % of the neutral mixture.

1b/*$AgNO_3$/MeOH*. The acid **1b** (1.35 g) was treated with $AgNO_3$ as described previously. Usual work-up gave an acidic (0.010 g) and a neutral (0.912 g) fraction. The acidic fraction consisted of the acids *Z*-**3b** and *E*-**4b** in a 1:1 ratio. The neutral fraction consisted of the lactone **2b** and esters *Z*-**6b** and *E*-**7b** in a 18:45:37 ratio.

1b/*$AgClO_4$/MeOH*. The acid **1b** (2.63 g) was treated with $AgClO_4 \cdot H_2O$ as described previously. Usual work-up yielded an acidic (0.187 g) and a neutral (1.758 g) fraction. The acidic fraction consisted of the acids *Z*-**3b** and *E*-**4b** in a 20:80 ratio. The neutral fraction consisted of lactone **2b** and esters *Z*-**6b** and *E*-**7b** in a 13:23:64 ratio.

Diazomethane trapping experiment. An AgTFA-mediated methanolysis of the acid **1a** was performed as described above. Prior to being quenched with aqueous hydrochloric acid, the reaction mixture was treated with ethereal diazomethane. Extractive work-up yielded a very complex mixture which was analysed by GLC and GLC/MS. The main products were the esters **6a**, **7a** and **9** together with the lactone **2a** and ketone **10**. In addition, small amounts of **14** were detected.

Solvolysis of **1a** *using AgTFA/CD_3OD.* The reaction was performed as described previously using 0.48 g (1.85 mmol) of the acid **1a** in methanol-d_4 (1.0 ml). The reaction mixture was worked up in the usual way to yield an acidic fraction (0.103 g) consisting of 3-bromo-2-(methoxy-d_3)-2-methyl-3-butenoic acid (**15**) and very small amounts (less than 5 % according to GLC) of a product tentatively assigned the structure 3-bromo-4-(methoxy-d_3)-2-methyl-2-butenoic acid (**16**).

3a-d_3: ^{1}H NMR (90 MHz; $CDCl_3$): δ 1.65 (3 H, s), 5.86 (1 H, d, *J* 2.0 Hz), 6.05 (1 H, d, *J* 2.0 Hz), 9.8 (1 H, broad s); MS [*m/z* (% rel. int.)]: 196 (1), 195 (1), 194 (1), 193 (1), 179 (3), 178 (4), 177 (3), 176 (3), 168 (98), 166 (100).

4a-d_3: ^{1}H NMR (90 MHz; $CDCl_3$): δ 2.17 (3 H, unresolved t), 4.52 (2 H, unresolved q), 9.8 (1 H, broad s).

The neutral fraction (0.040 g) was subjected to preparative TLC [SiO_2; chloroform–hexane (4:1)]. The first band consisted of the lactone **2a** and methyl-d_3 3-bromo-2-(methoxy-d_3)-2-methyl-3-butenoate (**6a**-d_6) in a 9:1 ratio.

6a-d_6: ^{1}H NMR (90 MHz; $CDCl_3$): δ 1.65 (3 H, s), 5.84 (1 H, d, *J* 2.6 Hz), 6.05 (1 H, d, *J* 2.6 Hz); MS [*m/z* (% rel. int.)]: 230 (1), 228 (1), 215 (1), 213 (1), 196 (2), 194 (2), 168 (100), 166 (100).

The second band consisted of the ester **6a**-d_6, lactone **2a**, 3-(methoxy-d_3)-1-(methyl-d_1)-1-propenyl-2-d_1, 3-bromo-2-(methoxy-d_3)-2-methyl-3-butenoate (*22*) and 3-(methoxy-d_3)-1-(methyl-d_1)-1-propenyl-2-d_1 3-bromo-4-(methoxy-d_3)-2-methyl-2-butenoate (**23**) in a 9:58:15:18 ratio.

22: ^{1}H NMR (90 MHz; $CDCl_3$): δ 1.71 (3 H, s), 1.96 (2.6 H, broad s), 3.87 (2 H, m), 5.30 (0.3 H, m), 5.90 (1 H, d, *J* 2.6 Hz), 6.14 (1 H, d, *J* 2.6 Hz); MS [*m/z* (% rel. int.)]: 193 (2), 192 (6), 191 (2), 168 (98), 166 (100), 136 (6), 134 (6).

23: ^{1}H NMR (90 MHz; $CDCl_3$): δ 1.96 (2.6 H, broad s), 2.20 (3 H, m), 3.87 (2 H, m), 4.49 (2 H, m), 5.30 (0.3 H, m); MS [*m/z* (% rel. int.)]: 196 (96), 194 (100), 177 (2), 175 (2), 168 (29), 166 (29), 149 (5), 115 (7).

^{1}H NMR spectroscopy and combined GLC/MS analysis of the neutral residue prior to chromatographic work-up revealed the presence of 4-(methoxy-d_3)-2-butanone-1, 1, 1, 3, 3-d_5 (**24**) in approximately 10 % yield (GLC).

24: ^{1}H NMR (90 MHz; $CDCl_3$): δ 3.64 (2 H, m); MS [*m/z* (% rel. int.)]: 110 (32), 109 (11), 92 (100), 81 (30), 76 (35), 75 (47), 74 (33), 57 (62), 56 (47).

Treatment of **8** *and* **9** *with MeOH.* A 7:3 mixture of the esters **8** and **9** was refluxed in methanol for 48 h. GLC analysis revealed the presence of the methyl esters **6a** and **7a** in a 7:3 ratio together with the ketone **10**. When a similar experiment was performed in the presence of AgTFA, the conversion of the esters **8** and **9** was complete after 20 h, and the products were the ketone **10**, methyl esters **6a** and **7a**, and the lactone **2a**. The ratio **6a**:**7a**:**2a** was 40:40:20.

Treatment of **3a** *and* **4a** *with MeOH.* A mixture of the acids **3a**, *E*-**4a** and *Z*-**4a** in a 78:11:11 ratio was refluxed in methanol for 8 h. GLC analysis revealed the presence of the esters **6a** and **7a**, lactone **2a** and acids **3a**, *E*-**4a** and *Z*-**4a** in 56:2:5:33:1:3 ratio. When the same reaction was performed in the presence of AgTFA for 20 h, a product mixture of **6a**, **7a**, **2a** and **3a** in a 39:10:39:28 ratio was formed.

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