Ketene Chemistry 2.[1] A General Procedure for the Synthesis of 2-Alkoxycyclopropanecarboxylic Esters and Acids Starting from Aldehydes and Ketene

Preben Bødstrup Rasmussen,*[a,2] Søren Bøwadt[b]

[a] Research Department, A/S Cheminova, P.O. Box 9, DK-7620 Lemvig, Denmark
[b] Department of Chemistry, Odense University, DK-5230 Odense M, Denmark

Alkyl 3-alkoxy-4-bromocarboxylates are prepared by the Lewis acid-catalyzed reaction of α-bromoaldehyde acetals with ketene. Base-catalyzed cyclization of these intermediates affords 2-alkoxycyclopropanecarboxylic esters.

Cyclopropanecarboxylic esters and acids constitute important parts of natural compounds as well as of industrial products, e.g. pesticides.[3] General and convenient procedures for the synthesis of these intermediates[4] are therefore essential. The most common route to this class of compounds consists of adding carbene synthons, e.g., diazo compounds, to olefins. The yields of this procedure vary; the efficiency of the method has therefore been improved by the addition of transition-metal catalysts.[5–7] However, the procedure suffers from the dangerous character of diazo compounds.

Alkyl 2-alkoxycyclopropanecarboxylates can be prepared by the following methods:

(a) addition of alkyl diazoacetates to vinyl ethers;[8]

(b) reaction of alkyl 4-bromo-2-butenoates with sodium alkoxides and subsequent cyclization;[8]

(c) addition of alcohols to alkyl 4-chloro-2-butenoates followed by potassium hydroxide-mediated cyclization[9] (hydrolysis of the intermediate alkyl 4-chloro-2-alkoxybutanoate has also been reported to give the 3-alkoxy-γ-lactone[10]);

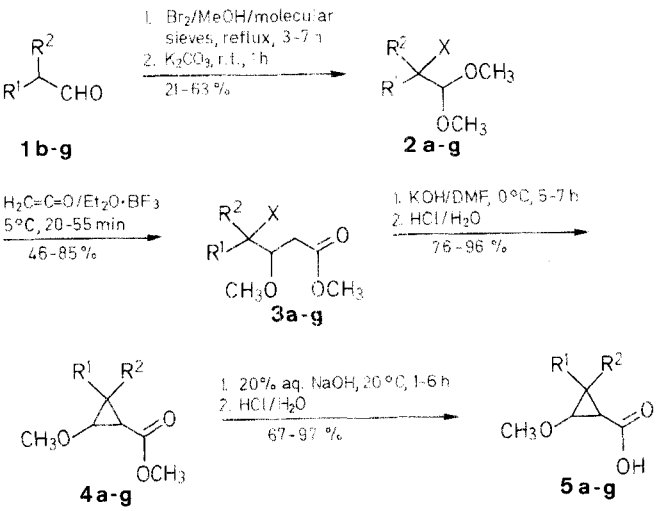
(d) simultaneous addition of bromine and an alcohol to alkyl 3-butenoates followed by sodium alkoxide-mediated cyclization.[8]

Procedure (a) has the disadvantage of an expensive starting material and of low yields even when in the reaction the alkoxide is added portionwise over several hours. Procedure (c) suffers from low yield, which is partially due to hydrolysis of the product. A low yield is also obtained in procedure (d) which has the additional disadvantage that a mixture of isomers is formed in the addition reaction, the Br-atom occurring in both the 3- and 4-positions in the products.

The procedure described here represents a general alternative route to the intermediate 3-alkoxy-4-halobutanoates **3** starting from alkanals **1**. These aldehydes are brominated and acetalized in a one-pot reaction by addition of bromine in methanol[10] to give the 2-bromoalkanal acetals **2** (X = Br) which in the presence of a Lewis acid react with ketene (which is known to undergo insertion reactions with compounds having activated C–O bonds[11]) to give 3-alkoxy-4-bromalkanoic esters **3**. Since the sodium ethoxide-mediated cyclization procedure[9] was found to be unsatisfactory for the model case **3a** we elaborated an alternative method for the cyclization **3** → **4** using solid potassium hydroxide in dimethylformamide. The resultant 2-methoxycyclopropanecarboxylic esters **4** can be easily hydrolyzed to the free carboxylic acids **5**.

In the case of **2a**, the ketene insertion is catalyzed by an acidic montmorillonite (KSF/0) to give the ester **3a** in 70% yield.

As regards the stereochemistry of compounds **4**, the ^{1}H-NMR data (Table 5) suggest that mainly the thermodynamically stable *trans* compounds are formed. Only in the case of **4d** are both *cis*- and *trans* isomers observed. This may be due to the steric restrictions imposed upon the system by the phenyl ring at C-3 of the cyclopropane ring. Second-order effects in the spectra prevent stereochemical assignment of the isomers of compounds



2a, **3a**: X = Cl (**2a** was purchased from Aldrich)
2b–g, **3b–g**: X = Br

1–5	R^1	R^2	1–5	R^1	R^2
a	H	H	**e**	C_2H_5	H
b	CH_3	H	**f**	CH_3	CH_3
c	*i*-C_3H_7	H	**g**	$CH_2C_6H_5$	H
d	C_6H_5	H			

Table 1. Preparation of 2-Bromoalkanal Dimethyl Acetals **2b–g**[a]

Product	Reaction Time (h)	Yield (%)	bp (°C)/Torr	Molecular Formula[a] or Lit. bp (°C)/Torr	MS *m/z* (%)
2b[c]	4	50	49–52/10	$C_5H_{11}BrO_2$ (183.1)	183 (MH^+, 3); 152 (99); 151 (100)
2c	3	63	66–72/13	71–74/16[15]	181 (96); 179 (100)
2d	6	52	130–133/13	84–86/0.4[16]	214 (73); 165 (100)
2e	6	61	60–64/10	66/12[17,18]	167 (98); 165 (100)
2f	6	28	52–54/10	59/16[17]	167 (98); 165 (100)
2g[d]	7	21[e]	88–90/0.15	$C_{11}H_{15}BrO_2$ (259.1)	229 (98); 227 (100)

[a] Chloroacetaldehyde dimethyl acetal (**2a**) was purchased.
[b] Microanalyses of **2b** and **2g**: C ±0.35, H ±0.24.
[c] Reported in Lit.[14] without physical data.
[d] Reported in Lit.[19] without physical data.
[e] The oxidation product methyl 3-phenylpropanoate is formed in approximately the same amount.

4a and **4e**, whereas for **4b** only one of the possible stereoisomers (*trans*) can be identified. From the ^{1}H-NMR spectra of compounds **5** (Table 5) it is evident that no isomerization occurs during hydrolysis.

Microanalyses were performed by NOVO Microanalytical Laboratory, Bagsvaerd, and by the Microanalytical Laboratory at the University of Copenhagen. Mass spectra were recorded at the MS-laboratory at Odense University using a Varian MAT 311A-spectrometer and chemical ionization with isobutene as ionization gas. ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker AC 250 spectrometer.

A ketene gas flow (≈ 0.6 mol/h) was obtained by pyrolysis of acetic anhydride.[12,13] Other reagents and solvents were used in commercially available qualities. Silica gel (230–400 mesh, Merck) was used for chromatography. The clay KSF/0 used in the conversion **2a** → **3a** is an acid-treated montmorillonite from Süd-Chemie, D-8000 München.

2-Bromoalkanal Dimethyl Acetals 2b–g; General Procedure:
Molecular sieves (3 Å; 25 g) are added to a solution of the mechanically stirred aldehyde **1b–g** (1.0 mol) in MeOH (500 mL). The mixture is heated to reflux, and Br_2 (159.8 g, 1.0 mol) is added dropwise. When the addition is complete, the mixture is refluxed until disappearance of the starting material (as detected by GC). After cooling to room temperature, the mixture is stirred with K_2CO_3 (70 g, 0.5 mol) for 1 h, and filtered. Saturated aqueous NaCl (500 mL) is added and the product is extracted with pentane (200 mL). The extract is concentrated under reduced pressure and the product is distilled.

Methyl 4-Halo-3-methoxyalkanoates 3a–g; General Procedure:
The acetal **2a–g** (0.2 mol) is cooled to ≈ 5 °C, $Et_2O \cdot BF_3$ (1 mL) is added, and ketene gas (≈ 0.3 mol) is bubbled through the mixture. After disappearance of the starting material (as detected by GC), the solution is poured into a stirred mixture of hexane (100 mL) and 25% aqueous NH_3 (75 mL). The phases are separated, the aqueous phase is washed with hexane (2 × 25 mL), the combined organic phases are dried (Na_2SO_4), and concentrated under reduced pressure, and the residue is distilled to give the pure product **3**.

Methyl 4-Chloro-3-methoxybutanoate (3a):
A solution of chloroacetaldehyde dimethyl acetal (**2a**; 31.15 g, 0.25 mol) in CH_2Cl_2 (100 mL) is cooled to 0 °C and KSF/0 (2.0 g) is added. Ketene gas (≈ 0.3 mol) is bubbled throught the mixture. When the starting material has been completely consumed (GC) the mixture is filtered immediately and the filtrate is concentrated under reduced pressure. The residue is distilled to give the pure product **3a**; yield: 29.1 g (70%); bp 80–82 °C/10 Torr.

Methyl 2-Methoxycyclopropanecarboxylates 4a–g; General Procedure:
A stirred dispersion of KOH (powdered; 5.6 g, 0.1 mol) in DMF (50 mL) is cooled to 0 °C. The methyl 4-halo-3-methoxyalkanoate **3a–g** (0.1 mol) is added dropwise, and the mixture is stirred for 2 h. Then, powdered KOH (0.56 g, 0.01 mol) is added every 1 hour (alltogether 3–5 times) with continued stirring at 0 °C for the time given in Table 3. The slow portionwise addition of base avoids the formation of a mixture of ester and free acid. The mixture is then acidified by the addition to 1 M aq. HCl (600 mL) and extracted with Et_2O (3 × 150 mL). The extract is dried (Na_2SO_4) and concentrated under reduced pressure. In most cases, the product thus obtained is analytically pure. Otherwise, further purification may be achieved by distillation or column chromatography using EtOAc/petroleum ether (1:9) as eluent.

3-Alkyl-2-methoxycyclopropanecarboxylic Acids 5a–g; General Procedure:
The methyl 3-alkyl-2-methoxycyclopropanecarboxylate **4a–g** (0.015 mol) is stirred with 4 M aq. NaOH (10 mL) for 4–5 h. The mixture is then neutralized with 4 M aq. HCl and extracted with petroleum ether (3 × 10 mL). The extract is dried (Na_2SO_4) and concentrated under reduced pressure to give the analytically pure compound **5a–g**.

Table 2. Preparation of Methyl 4-Halo-3-methoxyalkanoates **3a–g**

Product	Reaction Time (min)	Yield (%)	bp (°C)/Torr	Molecular Formula[a] or Lit. bp (°C)/Torr	MS *m/z* (%)
3a	20	70	80–82/10	87/12[10]	167 (MH^+, 100)
3b[b]	30	85	103–105/10	$C_7H_{13}BrO_3$ (225.1)	225 (MH^+, 100)
3c[b]	45	61	120–126/10	$C_9H_{17}BrO_3$ (253.1)	253 (MH^+, 35); 141 (100)
3d[b]	55	79[c]	120–122/0.2	$C_{12}H_{15}BrO_3$ (287.2)	287 (MH^+, 67); 207 (100)
3e[b]	25	76	65–67/0.2	$C_8H_{15}BrO_3$ (239.1)	239 (MH^+, 8); 75 (100)
3f	40	47	42–42/0.07	$C_8H_{15}BrO_3$ (239.1)	239 (MH^+, 24); 75 (100)
3g[b]	25	46	117–120/0.15	$C_{13}H_{17}BrO_3$ (301.2)	301 (MH^+, 100)

[a] Satisfactory microanalyses obtained: C ± 0.14, H ± 0.10; exception: **3g**, C − 0.44.
[b] Mixture of diastereoisomers.
[c] Isolated by column chromatography on silica gel using *i*-Pr_2O/petroleum ether (1 : 6) as eluent. Attempts to distil product **3d** lowered the yield to 38–40% due to decomposition.

Table 3. Preparation of Methyl 2-Methoxycyclopropanecarboxylates **4a–g**

Product	Reaction Time (h)	Yield (%)	bp (°C)/Torr	Molecular Formula[a] or Lit. bp (°C)/Torr	MS *m/z* (%)
4a	5	84	69–70/12	54.5–55.5/16[8]	131 (MH^+, 100)
4b[b]	6	84	62–8/10	$C_7H_{12}O_3$ (144.2)	145 (MH^+, 100)
4c[b]	7	96	–	$C_9H_{16}O_3$ (172.2)	173 (MH^+, 100)
4d[b]	7	76	–	$C_{12}H_{14}O_3$ (206.2)	207 (MH^+, 100)
4e[b]	7	88	90–1/12	$C_8H_{14}O_3$ (158.2)	159 (MH^+, 100)
4f	7	94	35–6/1.8	71–73/18[20]	159 (MH^+, 100)
4g[b]	6	85	–	$C_{13}H_{16}O_3$ (220.3)	221 (MH^+, 10); 129 (100)

[a] Satisfactory microanalyses obtained: C ± 0.39, H ± 0.08.
[b] Mixture of diastereoisomers.

Table 4. Preparation of 2-Methoxycyclopropanecarboxylic Acids **5a–g**

Product	Reaction Time (h)	Yield (%)	mp (°C)	Molecular Formula[a] or Lit. bp (°C)/Torr	MS *m/z* (%)
5a	1	95		*trans*-**5a**: 116/16[21] *cis*-**5a**: 105/10[22]	117 (MH^+, 78); 99 (100)
5b[b]	4	93	(1*S*,2*S*,3*R*)-**5b**: 96–97 (1*S*,2*S*,3*S*)-**5b**: 109–110	$C_6H_{10}O_3$ (130.1)	131 (MH^+, 36); 113 (100)
5c[b]	5	67		$C_8H_{14}O_3$ (158.2)	159 (MH^+, 100)
5d[b]	6	89		$C_{11}H_{12}O_3$ (192.2)	193 (MH^+, 100)
5e[b]	4	93		$C_7H_{12}O_3$ (144.2)	145 (MH^+, 100)
5f[c]	6	87		$C_7H_{12}O_3$ (144.2)	145 (MH^+, 100)
5g[b]	5	97		$C_{12}H_{14}O_3$ (206.2)	207 (MH^+, 100)

[a] Satisfactory microanalyses obtained: C ± 0.20, H ± 0.12.
[b] Mixture of diastereoisomers.
[c] Reported in Lit. 23 without physical data.

Table 5. NMR-Spectral Data of Compounds **2**–**5**

Compound	^{1}H-NMR ($CDCl_3$/TMS) δ, J(Hz)	^{13}C-NMR ($CDCl_3$) δ
2b	1.7 (d, 3H, J = 6.5); 3.5 (s, 6H); 4.1 (m, 1H); 4.3 (d, 1H, J = 5.5)	20.4 (q); 47.7 (d); 55.0 (q); 55.4 (q); 106.9 (d)
2c	0.9 (d, 3H, J = 7.5); 1.0 (d, 3H, J = 7.5); 2.1 (m, 1H); 3.4 (s, 3H); 3.5 (s, 3H); 4.0 (2d, 1H, J = 3.5, 8); 4.3 (d, 1H, J = 8)	17.2 (q); 21.9 (q); 29.4 (d); 54.1 (q); 54.2 (q); 63.1 (d); 104.5 (d)
2d	3.2 (s, 3H); 3.5 (s, 3H); 4.8 (d, 1H, J = 6.9); 4.9 (d, 1H, J = 6.8); 7.5 (m, 5H)	53.1 (d); 54.9 (q); 55.1 (q); 106.1 (d); 128.6 (d); 128.7 (d); 138.2 (s)
2e	1.1 (t, 3H, J = 7.3); 1.8 (m, 1H); 2.0 (m, 1H); 3.5 (2s, 6H); 3.9 (m, 1H); 4.5 (d, 1H, J = 5.9)	11.9 (q); 26.3 (t); 54.9 (q); 55.3 (q); 56.8 (d); 106.0 (d)
2f	1.8 (s, 6H); 3.6 (s, 6H); 4.2 (s, 1H)	28.4 (q); 58.2 (2 × q); 66.1 (s); 111.0 (d)
2g	3.0 (2d, 1H, J = 10, 14); 3.5 (2d, J = 4.5, 14, 1H); 3.5 (2s, 6H); 4.2 (m, 1H); 4.5 (d, 1H, J = 5.6); 7.3 (m, 5H)	39.1 (t); 54.7 (d); 55.1 (q); 55.7 (q); 105.6 (d); 126.7 (d); 128.3 (d); 129.3 (d); 138.0 (s)
3a	2.6 (m, 2H); 3.4 (s, 3H); 3.6 (d, 2H, J = 4.9); 3.7 (s, 3H); 3.9 (m, 1H)	37.2 (t); 44.9 (t); 51.8 (q); 57.7 (q); 77.1 (d); 171.3 (s)
3b[a]	1.7 (m, 3H); 2.7 (m, 2H); 3.4 (s, 3H); 3.7 (s, 3H); 3.7 (m, 1H); 4.2 (m, 1H)	20.5 (q); 21.6 (q); 36.0 (t); 37.2 (t); 49.3 (q); 50.4 (q); 51.6 (d); 58.59 (q); 58.63 (q); 80.7 (d); 81.4 (d); 171.7 (s); 171.8 (s)
3c[a]	1.10 (d, 6H, J = 6); 1.15 (d, 6H, J = 6); 2.1 (m, 2H); 2.7 (m, 4H); 3.5 (d, 3H, J = 5.5); 3.5 (d, 3H, J = 5.5); 3.7 (s, 3H); 3.7 (s, 3H); 3.9 (m, 2H); 4.0 (m, 2H)	18.8 (q); 20.9 (q); 21.5 (q); 21.6 (q); 30.1 (d); 32.2 (d); 37.4 (t); 38.1 (t); 51.8 (q); 51.9 (q); 58.2 (q); 58.3 (q); 65.8 (d); 66.9 (d); 78.70 (d); 78.71 (d); 171.8 (s); 172.0 (s)
3d[a]	2.3–2.9 (m, 4H); 3.2 (s, 3H); 3.5 (s, 3H); 3.7 (s, 3H); 3.8 (s, 3H); 4.1 (m, 2H); 5.1 (m, 2H); 7.5 (m, 10H)	37.3 (t); 38.1 (t); 51.8 (q); 55.6 (d); 56.5 (d); 59.28 (q); 59.33 (q); 81.6 (d); 81.8 (d); 128.47 (d); 128.49 (d); 128.53 (d); 128.61 (d); 128.64 (d); 128.73 (d); 138.42 (s); 138.47 (s); 171.3 (s); 171.6 (s)
3e[a]	1.1 (m, 6H); 1.9 (m, 4H); 2.8 (m, 4H); 3.6 (s, 6H); 3.8 (s, 6H); 3.9 (m, 2H); 4.1 (m, 2H)	12.5 (q); 12.8 (q); 27.0 (t); 27.8 (t); 36.3 (t); 37.5 (t); 51.8 (q); 58.3 (q); 58.5 (q); 58.9 (d); 59.6 (d); 80.2 (d); 80.3 (d); 171.8 (s); 171.9 (s)
3f	2.0 (s, 3H); 2.1 (s, 3H); 2.8 (2d, 1H, J = 8.6, 16.1); 3.2 (2d, 1H, J = 3.1, 16.1); 3.8 (s, 3H); 4.0 (s, 3H); 4.1 (m, 1H)	29.0 (q); 31.2 (q); 37.5 (t); 51.8 (q); 60.5 (q); 67.4 (s); 85.3 (d); 172.3 (s)
3g[a]	2.6–3.4 (m, 8H); 3.44 (s, 3H); 3.46 (s, 3H); 3.70 (s, 3H); 3.72 (s, 3H); 3.7–3.9 (m, 2H); 4.3 (m, 2H); 7.2 (m, 10H)	36.4 (t); 37.3 (t); 40.3 (t); 40.9 (t); 51.82 (q); 51.87 (q); 57.0 (d); 57.3 (d); 58.1 (q); 58.3 (q); 78.8 (d); 80.1 (d); 126.85 (d); 126.94 (d); 128.5 (d); 129.1 (d); 137.9 (s); 138.2 (s); 171.6 (s); 171.7 (s)
4a	1.2–1.3 (m, 2H); 1.8–1.9 (m, 1H); 3.3 (s, 3H); 3.5–3.6 (m, 1H); 3.8 (s, 3H)	15.8 (t); 20.7 (d); 51.7 (q); 58.4 (q); 62.2 (d); 173.0 (s)
4b[a]	1.2 (d, 6H); 1.4 (2d, 1H, J = 2, 5.5); 1.6–1.9 (m, 3H); 3.3 (s, 3H); 3.4 (s, 3H); 3.4–3.5 (m, 1H); 3.6 (2d, 1H, J = 2, 7); 3.65 (s, 3H); 3.67 (s, 3H)	10.0 (q); 10.2 (q); 23.2 (d); 24.1 (d); 26.0 (d); 27.3 (d); 51.3 (q); 51.5 (q); 57.9 (q); 58.6 (q); 66.1 (d); 67.7 (d); 171.5 (s); 173.0 (s)
4c[a]	0.8 (d, 3H); 0.9–1.1 (m, 9H); 1.2–1.3 (m, 2H); 1.4 (2d, 1H, J = 2.5, 6); 1.4–1.7 (m, 2H); 1.8 (2d, 1H, J = 3, 10); 3.2 (s, 3H); 3.3 (s, 3H); 3.4 (2d, 1H, J = 3, 4.5); 3.5 (2d, 1H, J = 2.5, 7); 3.65 (s, 3H); 3.66 (s, 3H)	21.7 (d); 22.1 (d); 22.2 (d); 22.4 (d); 24.5 (d); 26.0 (q); 26.1 (q); 26.1 (q); 37.1 (d); 38.3 (d); 51.57 (q); 51.64 (q); 58.0 (q); 58.9 (q); 66.7 (d); 66.8 (d); 171.8 (s); 173.4 (s)
4d[a]	2.2 (2d, 1H, J = 2.7, 6.2); 2.3 (2d, 1H, J = 3.1, 10.8); 2.7 (2d, 1H, J = 6.2, 7); 2.9 (2d, 1H, J = 4.7, 10.8); 3.3 (s, 3H); 3.42 (s, 3H); 3.43 (s, 3H); 3.7 (s, 3H); 3.8 (2d, 1H, J = 2.7, 7); 4.2 (2d, 1H, J = 3.1, 4.7); 7.3 (m, 10H)	27.9 (d); 29.3 (d); 32.6 (d); 33.7 (d); 51.4 (q); 51.9 (q); 58.1 (q); 58.6 (q); 65.0 (d); 66.0 (d); 126.7 (d); 127.0 (d); 128.2 (d); 128.4 (d); 129.0 (d); 134.6 (s); 134.7 (s); 169.7 (s); 172.5 (s)
4e[a]	1.0 (t, 3H, J = 7); 1.1 (t, 3H, J = 7); 1.5 (m, 8H); 3.34 (s, 3H); 3.39 (s, 3H); 3.6 (m, 2H); 3.66 (s, 3H); 3.67 (s, 3H)	13.3 (q); 13.7 (q); 18.2 (t); 19.0 (t); 25.7 (d); 26.3 (d); 30.9 (d); 31.9 (d); 51.5 (q); 51.6 (q); 58.0 (q); 58.8 (q); 66.4 (d); 67.0 (d); 171.7 (s); 173.3 (s)
4f	1.2 (s, 3H); 1.3 (s, 3H); 1.6 (d, 1H, J = 3); 3.4 (s, 3H); 3.5 (d, 1H, J = 3); 3.7 (s, 3H)	18.5 (q); 19.8 (q); 30.0 (s); 32.5 (d); 51.4 (q); 58.4 (q); 71.3 (d); 171.6 (s)
4g[a]	1.7 (2d, 1H, J = 2.4, 5.5); 1.8 (m, 2H); 1.9 (2d, 1H, J = 2.8, 9.5); 2.9 (m, 4H); 3.3 (s, 3H); 3.4 (s, 3H); 3.63 (s, 3H); 3.64 (s, 3H); 3.75 (2d, 1H, J = 2.8, 4.4); 3.8 (2d, 1H, J = 2.2, 7.1); 1H); 7.2 (m, 10H)	26.0 (d); 26.7 (d); 29.5 (d); 30.6 (t); 30.7 (d); 31.5 (t); 51.6 (q); 51.7 (q); 58.0 (q); 58.9 (q); 66.0 (d); 66.9 (d); 126.2 (d); 128.3 (d); 128.40 (d); 128.44 (d); 128.48 (d); 140.4 (s); 140.5 (s); 171.6 (s); 172.8 (s)
5a	1.4 (m, 2H); 1.7 (m, 1H); 3.4 (s, 3H); 3.7 (m, 1H); 11.8 (s, 1H)	16.4 (t); 20.8 (d); 58.5 (q); 62.9 (d); 178.8 (s)
5b[a]	1.2 (d, 6H); 1.3 (2d, 1H, J = 2, 5.5); 1.7–1.9 (m, 3H); 3.3 (s, 3H); 3.4 (s, 3H); 3.5 (m, 1H); 3.7 (2d, 1H, J = 2, 7); 11.9 (s, 2H)	10.2 (q); 10.3 (q); 24.2 (d); 25.2 (d); 26.3 (d); 27.8 (d); 57.8 (q); 58.8 (q); 66.9 (d); 68.5 (d); 177.8 (s); 179.1 (s)
5c[a]	0.9 (d, 3H); 1.1 (m, 9H); 1.5 (m, 3H); 1.7 (m, 1H); 1.8 (m, 1H); 1.9 (2d, 1H, J = 2.7, 10.3); 3.4 (s, 3H); 3.5 (s, 3H); 3.6 (2d, 1H, J = 2.7, 4.7); 3.7 (2d, 1H, J = 2.9, 6.3); 11.9 (s, 2H)	21.6 (q); 22.0 (q); 22.2 (q); 24.4 (d); 26.0 (d); 26.1 (d); 37.8 (d); 39.2 (d); 57.9 (q); 58.7 (q); 67.3 (d); 67.4 (d); 177.9 (s); 179.3 (s)
5d[a]	2.2 (2d, 1H, J = 2.5, 6); 2.25 (2d, 1H, J = 2.9, 10.7); 2.8 (2d, 1H, J = 6.5, 6.7); 2.9 (2d, 1H, J = 4.9, 10.7); 3.3 (s, 3H); 3.5 (s, 3H); 3.9 (2d, 1H, J = 2.5, 7.1); 4.1 (2d, 1H, J = 3.1, 4.8); 7.2 (m, 10H); 11.9 (s, 2H)	27.9 (d); 29.1 (d); 33.2 (d); 34.6 (d); 58.1 (q); 58.7 (q); 65.5 (d); 66.5 (d); 126.8 (d); 127.1 (d); 128.2 (d); 128.4 (d); 129.1 (d); 133.9 (s); 134.2 (s); 175.8 (s); 178.4 (s)
5e[a]	1.0 (m, 8H); 1.4 (m, 1H); 1.7 (m, 4H); 1.9 (m, 1H); 3.4 (s, 3H); 3.5 (s, 3H); 3.6 (m, 1H); 3.7 (m, 1H); 11.8 (s, 2H)	13.0 (q); 13.3 (q); 18.0 (t); 18.8 (t); 25.6 (d); 26.3 (d); 31.5 (d); 32.7 (d); 57.7 (q); 58.5 (q); 66.9 (d); 67.5 (d); 177.7 (s); 179.1 (s)
5f	1.24 (s, 3H); 1.27 (s, 3H); 1.5 (d, 1H, J = 3); 3.4 (s, 3H); 3.5 (d, 1H, J = 3); 11.8 (s, 1H)	18.5 (q); 19.9 (q); 31.3 (s); 32.7 (d); 58.3 (q); 72.0 (d); 178.0 (s)
5g[a]	1.6 (2d, 1H, J = 2.2, 5.6); 1.9 (m, 3H); 2.9 (m, 4H); 3.3 (s, 3H); 3.5 (s, 3H); 3.66 (t, 2H, J = 3.8); 3.7 (2d, 1H, J = 2.2, 7); 7.2 (m, 10H); 11.9 (s, 2H)	26.1 (d); 26.8 (d); 30.4 (d); 30.6 (t); 31.4 (t); 31.6 (d); 58.0 (q); 58.8 (q); 66.7 (d); 67.6 (d); 126.2 (d); 128.2 (d); 128.3 (d); 128.40 (d); 128.46 (d); 128.51 (d); 128.8 (d); 140.2 (s); 140.3 (s); 177.8 (s); 178.9 (s)

[a] Mixture of diastereoisomers.

The diastereoisomers of compound **5d** can be separated by column chromatography [100 × 4 cm; silica gel; 800 mL; benzene/dioxane/AcOH (80:19:1)]. The isomers are identified by ^{1}H-NMR spectrometry.

(1S,2S,3R)-2-Methoxy-3-phenylcyclopropanecarboxylic Acid; mp 96–97 °C.

(1S,2S,3S)-2-Methoxy-3-phenylcyclopropanecarboxylic Acid; mp 109–110 °C.

The authors thank Drs. J. Møller and G. Bojesen for recording the mass spectra and Dr. T. Bjorholm for the NMR work.

Received: 14 April 1988; revised: 15 August 1988

(1) For Part 1, see: Jacobsen, N., Winckelmann, I. *J. Chem. Res. (S)* **1985**, 80.
(2) New Address: Grindsted Products A/S, Edwin Rahrs Vej 38, DK-8220 Brabrand, Denmark.
(3) Hassall, K.E., in: *The Chemistry of Pesticides*, Macmillan Press, London, 1982, p. 148.
(4) For syntheses of cyclopropanes, see: Preparation of Cyclopropyl Derivatives, Tsuji, T., Nishida, S., in: *The Chemistry of the Cyclopropyl Group*, Rappoport, Z. (ed.), John Wiley & Sons, Chichester, 1987, p. 307.
(5) Dave, V., Warnhoff, E.W. *Org. React.* **1970**, *18*, 217.
(6) Doyle, M.P., Van Leusen, D., Tamblyn, W.H. *Synthesis* **1981**, 787.
(7) Anciaux, A.J., Hubert, A.J., Noels, A.F., Petiniot, N., Teyssié, P. *J. Org. Chem.* **1980**, *45*, 695.
(8) Rambaud, R., Brini-Fritz, M., Durif, S. *Bull. Soc. Chim. Fr.* **1957**, 681.
(9) Rambaud, R. *Bull. Soc. Chim. Fr.* **1938**, 1552.
(10) Rambaud, R., Brini-Fritz, M. *Bull. Soc. Chim. Fr.* **1958**, 1426.
(11) Garbisch, E.W. *J. Org. Chem.* **1965**, *30*, 2109.
(12) See Borrmann, D., in: *Houben-Weyl*, 4th ed., Vol. VII/4, Georg Thieme Verlag, Stuttgart, 1968, p. 53.
(13) Kapernaum, M., Kuth, G., Bachmaier, F. *Fresenius' Z. Anal. Chem.* **1986**, *323*, 487.
(14) Gall, M., Kamdar, B.V. *J. Org. Chem.* **1981**, *46*, 1575.
(15) Nazarov, I.N., Makin, S.M., Kruptsov, B.K., Mironov, V.A. *Zh. Obshch. Khim.* **1959**, *29*, 111; *C.A.* **1960**, *54*, 255.
(16) Baldwin, J.E., Walker, L.E. *J. Org. Chem.* **1966**, *31*, 3985.
(17) Aben, R.W.M., Hanneman, E.J.M., Scheeren, J.W. *Synth. Commun.* **1980**, *10*, 821.
(18) Esterbauer, H., Weger, W. *Monatsh. Chem.* **1967**, *98*, 1884.
(19) Marsi, M., Brinkmann, K.C., Lisensky, C.A., Vaughn, G.D., Gladysz, J.A. *J. Org. Chem.* **1985**, *50*, 3396.
(20) Reichelt, I., Reissig, H.U. *Chem. Ber.* **1983**, *116*, 3895.
(21) Kusuyama, Y., Ikeda, Y. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 724.
(22) Kusuyama, Y. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1944.
(23) Grueter, H., Bissig, P., Martin, P., Flueck, V., Gsell, L. *Pestic. Sci.* **1980**, *11*, 148.