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Cyclopropane formation by nickel-catalysed electroreductive coupling of activated olefins and unactivated *gem*-dibromo compounds

Stéphane Sengmany, Eric Léonel,* Jean Paul Paugam and Jean-Yves Nédélec

Laboratoire d'Electrochimie, Catalyse et Synthèse Organique, UMR CNRS 7582, CNRS-Université Paris XII, 2, Rue Henri Dunant, B.P. 28, F-94320 Thiais, France

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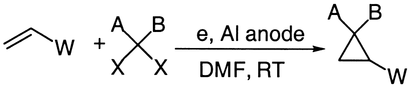
Abstract—Cyclopropyl derivatives have been prepared with good yields by transition-metal catalysed electroreductive coupling of activated olefins and unactivated *gem*-dibromo compounds. This electrolysis is characterized by the use of a Fe/Ni catalyst system, acetonitrile as the solvent and a catalytic amount of triphenylphosphine as ligand. This procedure is a good alternative to the classical preparations of cyclopropyl derivatives from activated olefins (Simmons–Smith reaction, 1,3-dipolar addition of diazomethane, 1,4-addition of phosphorus and sulfur ylides). © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

We previously reported[1,2] that cyclopropyl rings can be formed with satisfactory yields by direct electroreductive coupling of activated olefins and polyhalo compounds (alkyl *gem*-dihalides or α,α,α-trichlorides) using an aluminium rod as the sacrificial anode (Eq. (1)). We also found that this process (referred to, in this paper, as method a) is efficient only when the olefin is more easily reducible than the organic halide.



(1)

W: electrowithdrawing group

It has therefore come out that the ring formation likely occurs through two nucleophilic displacements between the reduced forms of the olefin and the *gem*-alkyldihalide in a non-concerted process. As a consequence, the most stable compound is mainly formed, i.e. for example dimethyl *trans*-3,3-dimethylcyclopropane-1,2-dicarboxylate from dimethyl maleate and 2,2-dibromopropane. A survey of the results, some of them having not yet been published, obtained from typical reagents and using method a are given in Table 1.

It appears that, apart from the coupling between dimethyl itaconate **III** and methyl trichloroacetate **IV** (Table 1, entries A3), for each polyhalo compound (entries A, B, C, D, E, F), the more negative the reduction potential of the olefin, the lower the cyclopropane yield.

Since direct electrosyntheses (i.e. method a) fail to produce cyclopropane compounds when the activated olefin is reduced at a potential lower than for the *gem*-dihalo compounds, we tried to find an alternative allowing the activation of alkyl *gem*-dihalides. This can be expected from indirect electrolyses involving electrogenerated low-valent transition metal species which would react readily with the *gem*-dihalo compounds. The approach reported here is based on the use of nickel salts or complexes already applied to the arylation, alkenylation, and alkylation of activated olefins.[3] The nickel species can be either introduced before the electrolysis (method b1),[3] or generated in situ by oxidation of Ni- or Fe/Ni-anode (method b2). We may expect from this approach the formation of either a α-halogenated alkyl-nickel species or a nickel carbene. Would the latter intermediate be formed, a concerted cycloaddition may occur, which can eventually be evidenced from an unsaturated substrate with a suitable configuration about the original double bond.

2. Results and discussion

The first approach employing added nickel salts (method b1)[3] was conducted at 60°C in an undivided cell using an iron rod as the anode, and a nickel grid as the cathode; the reactants in a 2.5/1 olefin/*gem*-polyhalo compound ratio and the catalyst $NiBr_2 \cdot xH_2O$ (ca. 20% vs the limiting reactant)[†]

Keywords: carbenoids; cyclopropanecarboxylates; electro-organic synthesis; organonickel reagents; ring closure.

* Corresponding author. Tel.: +1-49-78-11-27; fax: +1-49-78-11-48; e-mail: leonel@givt-cnrs.fr

[†] $NiBr_2 \cdot xH_2O$, from Aldrich, delivered as $NiBr_2 \cdot 3H_2O$:98%.

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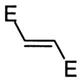
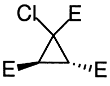
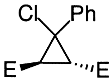
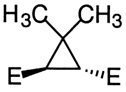
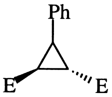
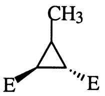
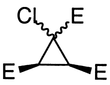
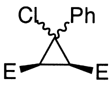
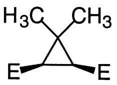
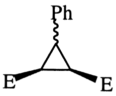
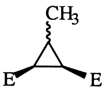
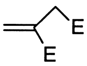
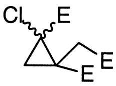
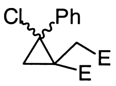
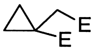
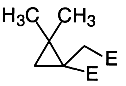
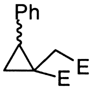
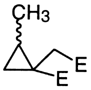
Table 1. Direct electrochemical coupling of activated olefins and polyhalo compounds (method a)

Entries	→	A Isolated yield **Product Nr**	B Isolated yield **Product Nr**	C Isolated yield **Product Nr**	D Isolated yield **Product Nr**	E Isolated yield **Product Nr**	F Isolated yield **Product Nr**
↓	Halo compound **Reagent Nr** (Reduction potential (V/SCE)) →	$Cl_3CCO_2CH_3$ **IV** (−1.6)	$PhCCl_3$ **V** (−1.7)	CH_2Br_2 **VI** (−2.1)	$(CH_3)_2CBr_2$ **VII** (−2.1)	$PhCHCl_2$ **VIII** (−2.2)	CH_3CHBr_2 **IX** (−2.3)
	Olefin[a] **Reagent Nr** (Reduction potential (V/SCE)) ↓						
1	 **I** (−1.45)	 43%[b] **1**	 34%[b] **4**	 30% **7**	 60%[b] **10**	 25%[b] **13**	 35%[b] **16**
2[c]	 **II** (−1.6)	 **2**[d] 20%[b] **1**	 **5**[d] 16%[b] **4**	 6% **8** 24% **7**	 **11**[d] 34%[b] **10**	 **14**[d] 10%[b] **13**	 **17**[d] 30%[b] **16**
3	 **III** (−2.05)	 53% **3**	 Traces **6**	 Traces **9**	 13%[b] **12**	 Traces **15**	 Traces **18**

DMF (45 ml), NBu_4Br (250 mg), NBu_4I (125 mg), I=0.1 A, an aluminium rod as the anode, a nickel foam as the cathode.

[a] E=CO_2Me.

[b] See Ref. 2.

[c] *trans* Cyclopropanes are identified by comparison with spectral data of entry 1.

[d] No (1*r*,2*c*) isomer was detected by GC.

Table 2. Indirect electrochemical coupling of activated olefins and polyhalo compounds catalysed by added nickel salts (method b1)

Entry	Olefin	Polyhalo compound	Results
1	R^1=R^2=H, R^3=CO_2CH_3. **I**	$Cl_3CCO_2CH_3$: **IV**	Reduction of trichloromethylacetate and no coupling for the three olefins: **I**, **II**, **III**
2	R^1=CO_2CH_3, R^2=R^3=H. **II**	$Cl_3CCO_2CH_3$: **IV**	
3	R^1=R^3=H, R^2=$CH_2CO_2CH_3$. **III**	$Cl_3CCO_2CH_3$: **IV**	
4	**I**	$PhCCl_3$: **V**	Reduction and dimerisation of $PhCCl_3$ followed by reduction to dichlorostilbene for the three olefins: **I**, **II**, **III**
5	**II**	$PhCCl_3$: **V**	
6	**III**	$PhCCl_3$: **V**	
7	**I**	CH_2Br_2: **VI**	No detectable reaction by GC for the three olefins: **I**, **II**, **III**
8	**II**	CH_2Br_2: **VI**	
9	**III**	CH_2Br_2: **VI**	
10	**I**	$(CH_3)_2CBr_2$: **VII**	**10**: 45%
11	**II**	$(CH_3)_2CBr_2$: **VII**	**11**: 4%, **10**: 17%, (20/80: (*cis*/*trans*))
12	**III**	$(CH_3)_2CBr_2$: **VII**	**12**: 44%
13	**I**	$PhCHCl_2$: **VIII**	Essentially dimerisation of benzalchloride and reduction to stilbene for the three olefins: **I**, **II**, **III**
14	**II**	$PhCHCl_2$: **VIII**	
15	**III**	$PhCHCl_2$: **VIII**	
16	**I**	CH_3CHBr_2: **IX**	**16**: 27% (24% of dimethyl 2-ethylidenebutane-1,4-dioate was also isolated and characterized by MS)
17	**II**	CH_3CHBr_2: **IX**	**17**: Traces (1α,2α,3β (**17a**)/1α,2α,3α (**17b**)), **16**: 20% (9% of dimethyl 2-ethylidenebutane-1,4-dioate was also isolated and characterized by MS)
18	**III**	CH_3CHBr_2: **IX**	**18**: 45%

Table 3. Investigations on nickel-catalysed electroreductive coupling of dimethyl maleate and dibromomethane

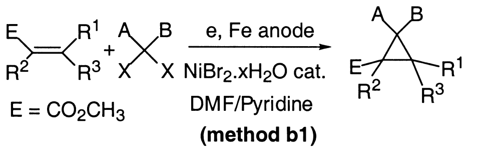
Entry	Anode	Solvent—CH_2Br_2/maleate, ligand	$NiBr_2 \cdot xH_2O$ (%)	Temperature (°C)	Yield (%) **8**+**7**	Stereoselectivity (*cis*/*trans*)
1[a]	Fe	DMF/Py[b]-1/2.5, no ligand	20	60	0	–
2	Fe	ACN/Py[b]-1/2.5, no ligand	20	60	Heterogeneous mixture	–
3	Fe	ACN-1/2.5, no ligand	20	60	11	90/10
4	Fe	ACN-1/2.5, no ligand	50	60	21	85/15
5	Fe	ACN-1/2.5, no ligand	50	RT	50	94/6
6	Fe	ACN-4/1, no ligand	50	RT	65	75/25
7	Fe	ACN-4/1, no ligand	50	60	50	77/23
8	Ni	ACN-4/1, no ligand	0	RT	Traces	Anodic passivation
9	Stainless steel	ACN-4/1, no ligand	0	RT	46	43/57
10	Fe/Ni 64/36	ACN-4/1, no ligand	0	RT	65	75/25
11[c]	Fe/Ni 64/36	ACN-4/1, PPh_3	0	RT	77	80/20
12	Fe/Ni 64/36	ACN-4/1, Bpy	0	RT	60	84/16
13	Fe/Ni 64/36	ACN-4/1, DPA	0	RT	59	88/12
14	Fe/Ni 64/36	ACN-4/1, DME	0	RT	72	86/14

[a] The reaction conditions used in entry 1 are referred to as method b1.

[b] 90/10 (v/v).

[c] The reaction conditions used in entry 11 are referred to as method b2.

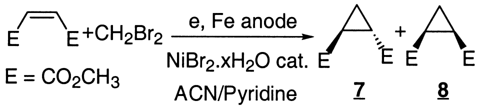
were dissolved in a 90/10 (V/V) dimethylformamide (DMF)/pyridine (Py) mixture, and the reactions were run under constant current intensity (0.1 A). During the electrolysis the working-electrode potential was near −1.2 V/SCE (Eq. (2)). Results are shown in Table 2.



(2)

The most interesting result is that cyclopropanes can be obtained in good yields from alkyl-*gem*-dibromides, even when the reduction potential of the halo compound is close to the reduction potential of the olefin (**12**: 44% and **18**: 45%), (Table 2, entries 12 and 18). On the contrary, activated polychloro compounds are either reduced (**IV**, **V**, **VIII**), (Table 2, entries 1–6 and entries 13–15) and/or dimerised (**V** and **VIII**), (Table 2, entries 3–5 and 13–15) under these reaction conditions. Also, the stereoselectivity of the cyclopropanation is not much improved since starting from dimethyl maleate we obtained the two stereoisomers in only 20/80 *cis*/*trans* ratio (**11**, **10**), (Table 2, entry 11).

When CH_2Br_2 (**VI**) is used (Table 2, entries 7–9), no product is formed from any olefin. An hypothetical reaction between a carbenoid species and DMF can been considered, by analogy to what was observed in the reduction of CCl_4 or CF_2Br_2 in DMF.[4a,b] Therefore, we replaced DMF by acetonitrile (ACN) as the solvent, and we investigated again the cyclocondensation between dimethyl maleate and dibromomethane with the aim of improving both the yield and the stereoselectivity (Eq. (3)). The results are reported in Table 3.



(3)

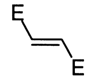
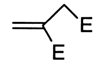
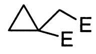
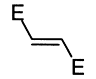
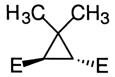
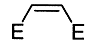
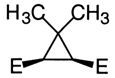
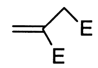
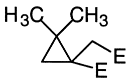
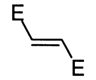
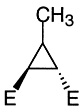
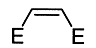
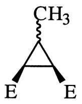
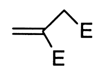
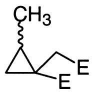
We first found (Table 3, entries 2, 3) that nickel salts are not very soluble in ACN/pyridine mixture, but more soluble in ACN alone. We next studied the effect of the amount of

Table 4. Indirect electrochemical coupling of activated olefins and polyhalo compounds catalysed by electrogenerated nickel salts (method b2)

Entry	Olefin	Polyhalo compound	Results
1	$R^1=R^2=H$, $R^3=CO_2CH_3$. **I**	$Cl_3CCO_2CH_3$: **IV**	Reduction of trichloromethylacetate and no coupling for the three olefins: **I**, **II**, **III**
2	$R^1=CO_2CH_3$, $R^2=R^3=H$. **II**	$Cl_3CCO_2CH_3$: **IV**	
3	$R^1=R^3=H$, $R^2=CH_2CO_2CH_3$. **III**	$Cl_3CCO_2CH_3$: **IV**	
4	**I**	$PhCCl_3$: **V**	Reduction and dimerisation of $PhCCl_3$ followed by reduction to dichlorostilbene for the three olefins: **I**, **II**, **III**
5	**II**	$PhCCl_3$: **V**	
6	**III**	$PhCCl_3$: **V**	
7	**I**	CH_2Br_2: **VI**	**7**: 56%
8	**II**	CH_2Br_2: **VI**	**8**: 62%, **7**: 15%, (80/20 (*cis*/*trans*))
9	**III**	CH_2Br_2: **VI**	**9**: 90%
10	**I**	$(CH_3)_2CBr_2$: **VII**	**10**: 45%
11	**II**	$(CH_3)_2CBr_2$: **VII**	**11**: 16%, **10**: 16%, (50/50: (*cis*/*trans*))
12	**III**	$(CH_3)_2CBr_2$: **VII**	**12**: 65%
13	**I**	$PhCHCl_2$: **VIII**	Essentially dimerisation of benzalchloride and reduction to stilbene for the three olefins: **I**, **II**, **III**
14	**II**	$PhCHCl_2$: **VIII**	
15	**III**	$PhCHCl_2$: **VIII**	
16	**I**	CH_3CHBr_2: **IX**	**16**: 50%
17	**II**	CH_3CHBr_2: **IX**	**17**: 30% 33/67 (1α,2α,3β (**17a**)/1α,2α,3α (**17b**)), **16**: 28%
18	**III**	CH_3CHBr_2: **IX**	**18**: 30%

$NiBr_2$ (Table 3, entries 3, 4), of the temperature (Table 3, entries 4, 5), and of the dibromomethane/dimethyl maleate ratio (Table 3, entries 5, 6). The best experimental conditions we found are given at entry 6 (Table 3). This result indicates that large amounts of nickel salts and a room temperature are notably needed to obtain satisfactory yield and selectivity. However, these two conditions can be hardly simultaneously met due to the low solubility of nickel salts at room temperature in ACN; this can only be overcome by heating the mixture at 60°C until an homogeneous medium is obtained, the yield then falls down to 50% with a similar stereoselectivity 77/23 (Table 3, entry 7). For that reason, we thought of generating Ni(II) by anodic oxidation of a nickel-containing electrode. With a nickel rod as the anode, however, we did not observe any cyclopropanation, but polymerization occurred at the surface of the anode (Table 3, entry 8). Interestingly, results identical to those reported in Table 3 entry 6, combining added nickel salts and an iron anode, were obtained with a Fe/Ni (64/36) anode (Table 3, entry 10). This clearly indicates that the presence of iron salts in the reaction medium is a key factor, but which may possibly be masked by the presence of chromium, when a stainless steel anode is used (Table 3, entry 9). under these reaction conditions (Table 3, entry 10), we examined the effect of various ligands on the yield and the stereoselectivity (Table 3, entries 11–14). The best yield was obtained with triphenylphosphine (Table 3, entry 11), and the highest stereoselectivity with dipyridylamine, at the expense however of the yield (Table 3, entry 13). The reaction conditions given at entry 11 (Table 3), and referred to as method b2, have then been applied to the coupling between various activated

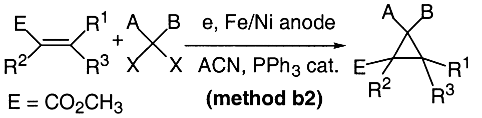
Table 5. Ring formation by indirect electroreductive coupling of activated olefins and alkyl *gem*-dibromo compounds

Entry	Olefin[a]	E (V/SCE)	Polyhalo compound	E (V/SCE)	Product [CAS RN]	Nr	Isolated yield%, method[b]
1		−1.45	CH_2Br_2	−2.1	 [826-35-7]	**7**	56, b2
2		−1.6	CH_2Br_2	−2.1	 [826-34-6]	**8**	62 (**8**), 15 (**7**) (80 *cis*/20 *trans*), b2
3		−2.05	CH_2Br_2	−2.1	 [6081-67-0]	**9**	90, b2
4		−1.45	$(CH_3)_2CBr_2$	−2.1	 [16601-23-3]	**10**	60, a
5		−1.6	$(CH_3)_2CBr_2$	−2.1	 [20315-30-4]	**11**	16 (**11**), 16 (**10**) (50 *cis*/50 *trans*), b2
6		−2.05	$(CH_3)_2CBr_2$	−2.1	 [205320-55-4]	**12**	65, b2
7		−1.45	CH_3CHBr_2	−2.3	 1,2-*t*-[28363-79-3]	**16**	50, b2
8		−1.6	CH_3CHBr_2	−2.3	 1α,2α,3β[14661-79-1] (**17a**) 1α,2α,3α[87421-39-4] (**17b**)	**17**	30 (**17**), 33 (**17a**)/67 (**17b**), 28 (**16**), b2
9		−2.05	CH_3CHBr_2	−2.3	 ***new compound***	**18**	45, b1

[a] $E=CO_2CH_3$.

[b] For typical procedure see Sections 4.2.1–4.2.3.

olefins and various polyhalo compounds (Eq. (4)). The results for the different polyhalides **IV–IX** are reported in Table 4.



(4)

Thus the nickel-catalysed electroreductive coupling (i.e. method b2) is efficient in the presence of activated olefins and non-activated polyhalo compounds, no matter what their relative reduction potentials are. However, the previous nickel catalysed electroreductive process in DMF/pyridine (method b1) is more efficient with the couple **IX/III** to give cyclopropane **18** (Table 4, entry 18 and Table 2, entry 18), and, more surprisingly, these two nickel catalysed processes fail with activated polychloro compounds (Cl_3CCO_2Me, $PhCCl_3$, $PhCHCl_2$), (Table 4, entries 1–6 and entries 13–15).

These nickel-catalysed electrochemical methods can be related to the work described by Kanai et al.,[5a,b] in which zinc powder is used in large excess (3 equiv.) as the reductant (yields obtained are: **7**: 78%;[5b] **8**+**7**: 78% (91/9, *cis/trans*);[5b] **10**: 44%;[5b] **11**+**10**: 39% (87/13, *cis/trans*);[5b] **16**: 58%[5b]). Kanai has suggested that the nickel-catalysed cyclopropanation proceeds via the formation of a metallacyclobutane complex formed from a metallocarbene and the olefin. Our approach may be in keeping with such an analysis on the basis of the good stereoselectivity in the formation of **8** and **7** from dimethyl maleate and CH_2Br_2 in a *cis/trans* ratio of 4:1.

Our nickel-catalysed electrochemical method is an alternative to the Simmons–Smith reaction (CH_2I_2, Zn–Cu)[6a] (**9**: 72%),[6b] the 1,3-dipolar addition of diazomethane to activated olefins followed by thermolysis or photolysis (**7**: 33%,[7a] **9**: 80%[7b]), the use of phosphorus ylides or diphenylsulfonium isopropylide with conjugated carbonyl compounds[8a,b] (**10**: 82%),[8b] the McCoy reaction[9a,b] (**8**: 39%,[9b] **7**: 19%[9b]), the intramolecular oxidative coupling of the bis-enolate derived from dimethylglutarates[10a,b] (**11**+**10**: 81%, 80/20 *cis/trans*,[10a] **17a**: 75%[10b]), and the electrochemical 1,3-debromination reaction of dimethyl 2,4-dibromopentanedioate[11] (**7**+**8**: 75%, 70/30 *trans/cis*).

We have summarized in Table 5 our best results for the electroreductive coupling of activated olefins and unactivated polyhalo compounds.

3. Conclusion

We have developed a successful electrochemical cyclopropanation of activated olefins from alkyl *gem*-dibromo compounds. This one step process is characterized by the use of a Fe/Ni catalyst system, ACN as solvent, and triphenylphosphine as ligand, and does not require the preparation of reactive intermediates. The yields compare favorably to those reported in the literature, and the stereoselectivity is moderately good. Very surprisingly, this procedure fails with activated polychloro compounds (α,α,α-trichlorotoluene, methyltrichloroacetate, benzalchloride), and we are now searching for another metallic system enabling the indirect activation of this type of polyhalo compounds.

4. Experimental

4.1. General information

Melting point were determined with an Electrothermal IA 9100 digital melting point apparatus. ^1H, ^{13}C NMR spectra were recorded on a Bruker AC-200 (200 MHz, 50 MHz, respectively) or Bruker AM-300 (300 MHz, 75 MHz, respectively) spectrometer. Mass spectra (electron impact) were obtained on a GCQ Thermoquest spectrometer coupled to a Finigan-GCQ with a DB 5MS capillary column. High-resolution mass spectral analyses and elemental analyses were carried out at 'Service Central d'Analyse du CNRS', Vernaison, France. Gas chromatography was performed on a Varian 3300 chromatograph fitted with a SIL-5 CP capillary column. Solvents and chemicals were used as received without further purification.

4.2. General procedure

4.2.1. Method a, direct electrolysis with aluminium anode. The reactions were conducted in an undivided cell fitted with an aluminium rod as anode and a nickel foam as cathode (area: ca. 40 cm^2). A solution of the activated olefin (10 mmol), polyhalo compound (20 mmol) in DMF (45 ml) containing Nbu_4Br (250 mg) and NBu_4I (125 mg) was electrolysed at constant intensity (0.1 A) at room temperature until complete olefin consumption. The reaction mixture was poured into a cold mixture of 1 M HCl (50 ml) and diethyl ether (50 ml). The layers were separated and extracted with diethyl ether (3 portions of 25 ml). The combined ethereal extracts were washed with brine, dried over Na_2SO_4 and evaporated. Products were isolated by column chromatography on silica gel (230–400 mesh) using pentane/ether as eluent.

4.2.2. Method b1, indirect electrolysis with iron anode and added nickel salts. The reactions were conducted in an undivided cell fitted with XC10 iron rod as anode and a nickel foam as cathode (area: ca. 40 cm^2). A solution of the activated olefin (25 mmol) and polyhalo compound (10 mmol) in DMF/pyridine (45 ml/5 ml) containing $NiBr_2{\cdot}xH_2O$ (436 mg), NBu_4Br (250 mg) and NBu_4I (125 mg) was electrolysed at constant intensity (0.1 A) at 60°C until complete consumption of the limiting reagent. The products were isolated using the procedure described in method a.

4.2.3. Method b2, indirect electrolysis with iron/nickel 64/36 anode. The reactions were conducted in an undivided cell fitted with an Fe/Ni 64/36 rod as anode and a nickel foam as cathode (area: ca. 40 cm^2). A solution of the activated olefin (10 mmol), polyhalo compound (40 mmol) and PPh_3 (1 mmol) in acetonitrile (45 ml) containing NBu_4Br (250 mg) and NBu_4I (125 mg) was electrolysed at constant intensity (0.1 A) and at room temperature until complete consumption of the limiting reagent. The products were isolated using the procedure described in method a.

4.3. Isolated products

4.3.1. Dimethyl 1-chloro-2-methoxycarbonylmethylcyclopropane-1,2-dicarboxylate 3 (new compound). ($C_{10}H_{13}ClO_6$); MW: 264.5; FAB-HR-MS calcd for $C_{10}H_{14}ClO_6$ $(M+H)^+$ *m/z* 265.0479, found 265.0476.

Anal. Calcd for $(1R^*2R^*)$ $C_{10}H_{13}ClO_6$: C, 45.38; H, 4.95; O, 36.27; Cl, 13.40. Found: C, 45.33; H, 5.00; O, 36.51; Cl, 13.23. Anal. Calcd for $(1R^*2S^*)$ $C_{10}H_{13}ClO_6$: C, 45.38; H, 4.95; O, 36.27; Cl, 13.40. Found: C, 45.58; H, 5.08; O, 36.27; Cl, 13.64.

Pentane/ether: (95/5)–(80/20); obtained: 1.4 g (yield: 53%, method a); liquid; two diastereoisomers $(1R^*2R^*)$ and $(1R^*2S^*)$ in ratio 70/30. $(1R^*,2R^*)$ ^{1}H NMR (200 MHz, CDCl$_3$) δ 3.76 (OCH$_3$, 3H, s), 3.70 (OCH$_3$, 3H, s), 3.61 (OCH$_3$, 3H, s), 3.00 (H-4, 1H, d, *J*=17 Hz), 2.55 (H-4, 1H, d, *J*=17 Hz), 2.20 (H-3, 1H, d, *J*=6.8 Hz), 1.90 (H-3, 1H, d, *J*=6.8 Hz), for the couple H-3 ($\Delta\nu/J$=8.1 Hz AB system): *E*/*E trans*. $(1R^*,2S^*)$ ^{1}H NMR (200 MHz, CDCl$_3$) δ 3.76 (OCH$_3$, 3H, s), 3.70 (OCH$_3$, 3H, s), 3.64 (OCH$_3$, 3H, s), 3.10 (H-4, 1H, d, *J*=17.4 Hz), 2.70 (H-4, 1H, d, *J*=17.4 Hz), 2.36 (H-3, 1H, d, *J*=7.2 Hz), 1.41 (H-3, 1H, d, *J*=7.2 Hz), for the couple H-3 ($\Delta\nu/J$=26.1 Hz AX system): *E*/*E cis*. ^{13}C NMR (50 MHz, CDCl$_3$) δ (mixture of the two diastereoisomers, $1R^*2R^*$,$(1R^*2S^*)$): *C*O: 170.4, 167.7, 167.3, (170.6, 169.4, 166.5); OCH$_3$: 53.4, 52.4, 51.6, (53.2, 53.1, 52.6); C-1: 44.7 (48.5); C-4: 36.4, (35.8); C-2: 33.8, (32.8); C-3: 25.5, (26.2). EI-MS *m/z* $(1R^*,2R^*)$: 266, 264, 235, 234, 233, 232, 228, 205, 203, 202, 201, 200, 198, 197, 192, 191, 178, 175, 174, 173, 172, 171, 170, 169 (base peak), 165, 146, 145. $(1R^*,2S^*)$: 266, 265, 235, 234, 233, 232, 228, 205, 203, 202, 201, 200, 198, 197, 192, 191, 178, 175, 174, 173, 172, 171, 170, 169 (base peak), 165, 146, 145; IR ν cm^{-1} (CCl$_4$) 1760–1720.

4.3.2. Dimethyl *trans*-cyclopropane-1,2-dicarboxylate 7. ($C_7H_{10}O_4$); MW: 158; CAS RN: 826-35-7. Pentane/ether: 80/20; obtained: 0.89 g (56% yield, method b2); liquid. ^{1}H NMR[9b] (200 MHz, CDCl$_3$) δ 3.7 (OCH$_3$, 6H, s), 2.20–2.10 (H-1 and H-2, 2H, m), 1.45–1.35 (H-3, 2H, m); ^{13}C NMR[9b] (50 MHz, CDCl$_3$) δ *C*O: 171.9; O*C*H$_3$: 51.8; C-1, C-2: 21.9; C-3: 15; EI-MS[9b] *m/z* 158, 127, 126, 99, 98 (base peak), 83, 71, 68, 59, 55; IR[9b] ν cm^{-1} (CCl$_4$) 1735.

4.3.3. Dimethyl *cis*-cyclopropane-1,2-dicarboxylate 8. ($C_7H_{10}O_4$); MW: 158; CAS RN: 826-34-6. Pentane/ether: 80/20; obtained: 0.98 g (62% yield, method b2); liquid. ^{1}H NMR[10b] (200 MHz, CDCl$_3$) δ 3.40 (OCH$_3$, 6H, s), 1.90 (H-1 and H-2, 2H, dd, *J*=8.4, 6.7 Hz), 1.40 (H-3a, 1H, td, *J*=6.7, 4.9 Hz), 1.00 (H-3b, 1H, td, *J*=8.4, 4.9 Hz); ^{13}C NMR[10b] (50 MHz, CDCl$_3$) δ*C*O: 170.2; O*C*H$_3$: 51.9; C-1, C-2: 21.2; C-3: 11.6; EI-MS *m/z* 158, 127 (base peak), 99, 71; IR ν cm^{-1} (CCl$_4$) 1735.

4.3.4. Methyl 1-methoxycarbonylmethylcyclopropane-1-carboxylate 9. ($C_8H_{12}O_4$); MW: 172; CAS RN: 6081-67-0. Pentane/ether: 80/20; obtained: 1.55 g (90% yield, method b2); liquid. ^{1}H NMR[7b] (200 MHz, CDCl$_3$) δ 3.63 (OCH$_3$, 3H, s), 3.59 (OCH$_3$, 3H, s), 2.50 (H-4, 2H, s), 1.30 (H-1b and H-2b, 2H, m) 0.80 (H-1a and H-2a, 2H, m); ^{13}C NMR (50 MHz, CDCl$_3$) δ *C*O: 174.3, 171.7; O*C*H$_3$: 51.7, 51.3; C-4: 38.1; C-1: 19.8; C-2, C-3: 15.2; EI-MS *m/z* 172, 157, 141, 113 (base peak), 81, 59, 53; IR[7b] ν cm^{-1} (CCl$_4$) 1740, 1735.

4.3.5. Dimethyl *trans*-3,3-dimethylcyclopropane-1,2-dicarboxylate 10. ($C_9H_{14}O_4$); MW: 186; CAS RN: 16601-23-3. Pentane/ether: 90/10; obtained: 1.12 g (60% yield, method a); liquid. ^{1}H NMR[10a] (200 MHz, CDCl$_3$) δ 3.7 (OCH$_3$, 6H, s), 2.20 (H-1 and H-2, 2H, s), 1.20 (H-4 and H-5, 6H, s); ^{13}C NMR (50 MHz, CDCl$_3$) δ *C*O: 170.1; O*C*H$_3$: 51.2; C-1, C-2: 33; C-3: 29.7; C-4, C-5: 19.8; EI-MS *m/z* 186, 155, 127 (base peak), 95, 67; IR ν cm^{-1} (CCl$_4$) 1735.

4.3.6. Dimethyl *cis*-3,3-dimethylcyclopropane-1,2-dicarboxylate 11. ($C_9H_{14}O_4$); MW: 186. CAS RN: 20315-30-4. Pentane/ether: 90/10; obtained: 0.3 g (16% yield, method b2); liquid. ^{1}H NMR[10b] (200 MHz, CDCl$_3$) δ 3.68 (OCH$_3$, 6H, s), 1.89 (H-1 and H-2, 2H, s), 1.40 (H-4, 3H, s), 1.25 (H-5, 3H, s); ^{13}C NMR[10b] (50 MHz, CDCl$_3$) δ *C*O: 169.5; O*C*H$_3$: 51.6; C-1, C-2: 31.8; C-5: 27.9; C-3: 26; C-4: 15.5; EI-MS[10b] *m/z* 186, 155, 127 (base peak), 95, 85, 73, 67, 65, 59, 55, 53; IR[10b] ν cm^{-1} (CCl$_4$) 1735.

4.3.7. Methyl 2,2-dimethyl-1-methoxycarbonylmethylcyclopropane-1-carboxylate 12. ($C_{10}H_{16}O_4$); MW: 200. CAS RN: 205320-55-4. Pentane/ether: 90/10; obtained: 1.3 g (65% yield, method b2); liquid. ^{1}H NMR[2] (200 MHz, CDCl$_3$) δ 3.46 (OCH$_3$, 3H, s), 3.45 (OCH$_3$, 3H, s), 2.83 (H-6, 1H, d, ^2J=17.3 Hz), 2.15 (H-6, 1H, d, ^2J=17.3 Hz), 1.3 (H-3, 1H, d, ^2J=5 Hz), 1.00–0.96 (H-4 and H-5, 6H, 2s), 0.4 (H-3, 1H, d, ^2J=5 Hz); ^{13}C NMR[2] (50 MHz, CDCl$_3$) δ *C*O: 172.7, 171.9; O*C*H$_3$: 51.1, 51; C-6: 35.7; C-1: 30; C-3: 25.5; C-2: 24.5; C-4, C-5: 22, 20; EI-MS[2] *m/z* 200, 169, 168, 140, 125, 109, 81 (base peak), 79, 53; IR[2] ν cm^{-1} (CCl$_4$) 1735.

4.3.8. Dimethyl 3-methylcyclopropane-1α,2β-dicarboxylate 16. ($C_8H_{12}O_4$); MW: 172; CAS RN: 28363-79-3. Pentane/ether: 95/5; obtained: 0.85 g (50% yield, method b2); liquid. ^{1}H NMR[5b] (200 MHz, CDCl$_3$) δ 3.63 (OCH$_3$, 3H, s), 3.62 (OCH$_3$, 3H, s), 2.25 (H-1, 1H, dd, ^3J=9.5, 4.8 Hz), 2.04 (H-2, 1H, dd, ^3J=5.8, 4.8 Hz), 1.79 (H-3, 1H, m), 1.20 (H-4, 3H, d, ^3J=6 Hz); ^{13}C NMR[5b] (50 MHz, CDCl$_3$) δ *C*O: 172.3, 170.3; O*C*H$_3$: 51.9, 51.6; C-1, C-2: 28.2, 27.7; C-3: 23.7; C-4: 11; EI-MS *m/z* 141, 113 (base peak), 81, 59, 53; IR ν cm^{-1} (CCl$_4$) 1735.

4.3.9. Dimethyl 3β-methylcyclopropane-1α,2α-dicarboxylate 17a. ($C_8H_{12}O_4$); MW: 172; CAS RN: 14661-79-1. Pentane/ether: 90/10; obtained: 0.172 g (10% yield, method b2); liquid. ^{1}H NMR[10b] (200 MHz, CDCl$_3$) δ 3.60 (OCH$_3$, 6H, s), 1.95 (H-3, 1H, m), 1.76 (H-1, H-2, 2H, d, ^3J=6.1 Hz), 1.1 (H-4, 3H, d, ^3J=6 Hz); ^{13}C NMR[10b] (50 MHz, CDCl$_3$) δ *C*O: 169.9; O*C*H$_3$: 51.7; C-1, C-2: 28.9; C-3: 20.3; C-4: 16.4; EI-MS[10b] *m/z* 172, 141, 113 (base peak), 85, 81, 71, 59, 53; IR[10b] ν cm^{-1} (CCl$_4$) 1735.

4.3.10. Dimethyl 3α-methylcyclopropane-1α,2α-dicarboxylate 17b. ($C_8H_{12}O_4$); MW: 172; CAS RN:

87421-39-4. Pentane/ether: 90/10; obtained: 0.345 g (20% yield, method b2); liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.38 (OCH_3, 6H, s), 1.80 (H-1, H-2, 2H, d, ^3J=8.8 Hz), 1.35 (H-3, 1H, m), 1.06 (H-4, 3H, d, ^3J=6.5 Hz); ^{13}C NMR[5b] (50 MHz, $CDCl_3$) δ *C*O: 169.1; O*C*H_3: 51.3; C-1, C-2: 23.7, 23.6; C-3: 18.7; C-4: 8.1; EI-MS *m/z* 172, 141, 140, 113 (base peak), 112, 85, 81, 71, 53; IR ν cm^{-1} (CCl_4) 1735.

4.3.11. Methyl 2-methyl-1-methoxycarbonylmethyl-cyclopropane-1-carboxylate 18 (new compound). ($C_9H_{14}O_4$); MW: 186; FAB-HR-MS calcd for $C_9H_{14}O_4$ $(M+Li)^+$ *m/z* 193.1052, found 193.1038. Pentane/ether: 90/10; obtained: 0,84 g (two diastereoisomers R^*R^* and R^*S^*: 50–50; 45% yield, method b1); liquid.

^{1}H NMR (200 MHz, $CDCl_3$) δ 3.67 (OCH_3, 6H, s), 2.90 (H-4, 1H, d, ^2J=17 Hz), 2.20 (H-4, 1H, d, ^2J=17 Hz), 1.30-0.90 (H-2 and H-3, 3H, m), 1.2 (CH_3, 3H, d, J=1.6 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ *C*O: 172.2, 172; O*C*H_3: 51.5, 51.3, C-4: 40, C-1: 25.6, C-2: 23.1, C-3: 20.7; C-5: 12.3; EI-MS *m/z* 186, 155, 154, 127, 126, 111, 95, 94, 67 (base peak), 66, 65, 59, 53; IR ν cm^{-1} (CCl_4) 1735.

^{1}H NMR (200 MHz, $CDCl_3$) δ 3.69 (OCH_3, 3H, s), 3.64 (OCH_3, 3H, s) 2.70 (H-4, 1H, d, ^2J=17 Hz), 2.5 (H-4, 1H, d, ^2J=17 Hz), 1.65 (H-2, 1H, m), 1.45 (H-3, 1H, dd, ^2J=4 Hz, ^3J=9 Hz) 1.1 (CH_3, 3H, d, ^3J=6 Hz), 0.5 (H-3, 1H, dd, ^2J=4 Hz, ^3J=7 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ *C*O: 174.8, 172.6; O*C*H_3: 51.7, 51.4, C-4: 33.4, C-1: 24.2, C-3: 22.4, C-2: 20.7; *C*H_3: 13.6; EI-MS *m/z* 186, 171, 155, 154, 127, 126, 111, 95, 94, 85, 68, 67 (base peak), 66, 65, 59, 55, 54, 53; IR ν cm^{-1} (CCl_4) 1735.

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