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Formation of polysubstituted chlorocyclopropanes from electrophilic olefins and activated trichloromethyl compounds

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Abstract—Chlorocyclopropanes and bicyclic chlorocyclopropanes are prepared in non basic conditions by electroreductive or Mg-promoted Barbier activation of $PhCCl_3$ or Cl_3CCO_2Me in the presence of acyclic or cyclic α,β-unsaturated carbonyl compounds.

1. Introduction

Cyclopropane containing molecules usually display interesting specific structural and physico-chemical properties. The presence of substituents on the C3 ring enables further transformations such as functional group interconversions or couplings with other molecules. Thus, 1-chlorocyclopropanecarboxylic acids are precursors of various aminocyclopropanecarboxylic acids[1a,b] known for their biological activity[2] whereas 2-chlorocyclopropanecarboxylic acids are precursors of agrochemicals,[3] and have also been used recently in the synthesis of Callipeltoside A, a novel antitumor agent, with the aim of elucidating its structure and notably the C-20 and C-21 configurations.[4]

The formation of polysubstituted chlorocyclopropanes from the coupling of acyclic α,β-unsaturated esters or cyclic α,β-unsaturated ketones with α,α-dichlorocarbanions, or equivalent nucleophilic organometallic species stabilized by an electron withdrawing group such as CO_2R or Ph, has already been reported in the literature. These nucleophilic intermediates are generated either by basic treatments (i.e., sodium hydride,[5] LDA,[6] electrogenerated bases,[7] two-phase-solid–liquid system[8] or LiHMDS-DBU[9]) of alkyl dichloroacetates and α,α-dichlorotoluene, or by an oxidative addition of a carbon–chlorine bond of the corresponding trichloromethyl compounds (Cl_3C–Y: Y = CO_2R, Ph) onto a soluble Cu(0)–isonitrile complex.[10] These preparations of chlorocylopropanes involve either a conjugate nucleophilic addition followed by subsequent ring closure (MIRC reaction[11a,b]) or carbenoid intermediates. Cyclocondensation to olefins is also mentioned with the ambiphilic chloroaryl carbenes photolytically generated from 3-chloro-3-aryldiazirines.[12] Moreover it must be noted that substituted 1-chlorocyclopropanecarboxaldehydes, precursors of methyl 1-chlorocyclopropanecarboxylates are synthesized via a semi-benzilic Favorski rearrangement of substituted 2,2-dichlorocyclobutanols obtained by reduction of the corresponding cyclobutanones.[13]

We have already investigated the synthesis of methyl 2,2-diphenylcyclopropanecarboxylates and of 2-acyl-1,1-diphenylcyclopropanes.[14a–c] We have notably reported two methods: one is an indirect electroreductive coupling between dichlorodiphenylmethane and cyclic or acyclic α,β-unsaturated carbonyl compounds (referred to below as process A),[14a,b] whereas the other one is a Mg-mediated Barbier type reaction in DMF (referred to below as process B).[14c] This last route uses the same couples of reagents as those involved in process A, but it does not apply to α,β-unsaturated methyl ketones.

2. Results and discussion

In this paper, we report the preparation of polysubstituted chlorocyclopropanes from α,β-unsaturated acyclic esters or

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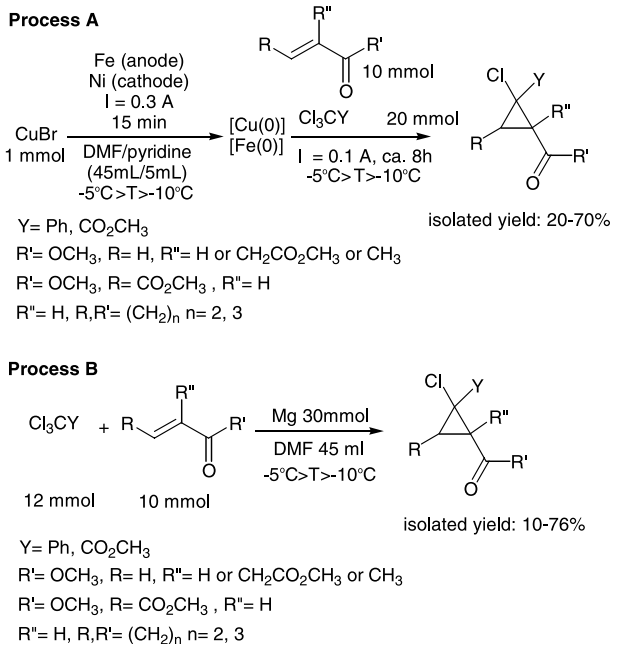


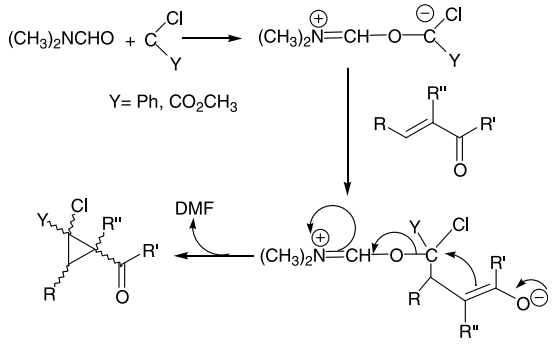
Scheme 1.

from cyclic α,β-unsaturated ketones and methyl trichloroacetate or α,α,α-trichlorotoluene (Scheme 1). It offers the opportunity to use and study both methods (processes A and B) and to compare their respective advantages and limitations, which proved to be rather complementary. The results are listed in Table 1.

These results first show that both methods generate nucleophilic intermediates, which add more or less efficiently to the olefin depending on its nature. More interestingly, these two methods are complementary. Thus, methacrylic acid esters show low reactivity in the electrochemical process (A) while yields obtained from the chemical method (B) are high (Table 1, entries 5 and 6). Such behaviour has already been observed with crotonic and methacrylic acids esters in other electrochemical reactions.[16] On the contrary, yields are higher from the electrochemical method than from the chemical one when maleic or fumaric acid esters are involved (Table 1, entries 7–10). This may indicate the occurrence, in process B, of side reactions at the olefins due to their reducibility, whereas in the electrochemical process, the cathode potential is self-controlled according to the most easily reduced species, in this case the copper salts. All the other cases studied gave similar results from both methods.

The mechanisms involved in either process have not been fully elucidated so far. The occurrence of a non complexed carbene species can, however, be ruled out in both cases, due notably to the absence of stereocontrol in the ring formation (Table 1, entries 7, 9 and 8, 10). In addition, would the carben be formed (chlorophenylcarbene and chloromethoxycarbonylcarbene) it would be rather electrophilic, as described in the literature,[12a,b,17,18] and should therefore react with electron-rich olefins like tetramethylethylene, or cyclohexene, which has never been observed.

In the Mg-Barbier type process (B), a route via α,α-dichloromagnesium compounds, which are known to lose



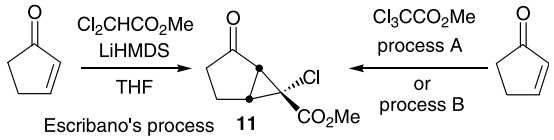
Scheme 2.

rapidly MgX_2 to form carbene intermediates,[19] is not likely since no reaction was observed in the presence of nucleophilic olefins. So, we think that a first formed carben species reacts with DMF to form a nucleophilic intermediate in a process similar to the formation of the DMF–$SOCl_2$ complex described by Newman[20] (Scheme 2). The role of DMF is even crucial in this process. Indeed, very surprisingly, no reaction occurred in diethylether or in THF instead of DMF as solvent. On the contrary, addition of an equal amount of DMF to an ether solution of $PhCCl_3$ and methyl acrylate induced the cyclopropanation to start.

With reference to the complementarity of both processes (A and B), it is clear that they do not involve the same type of nucleophilic species derived from the trichloromethyl compounds. In the electrochemical process (A), the reactive intermediate could be a copper–iron bi-metallic nucleophilic complex, which is not yet identified.

In the presence of acyclic α,β-unsaturated esters, chlorocyclopropanes are prepared, according to both methods, with a low to moderate diastereoselectivity (Table 1, entries 1–6) but, when cyclic enones are used as electrophilic olefins, the diastereoselectivity of the cyclopropanation becomes very high (Table 1, entries 11–14): only one of the two possible structures (*endo*-chlorine or *exo*-chlorine adduct) is obtained.

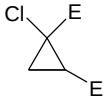
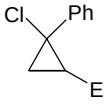
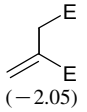
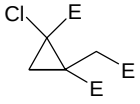
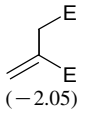
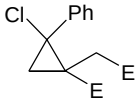
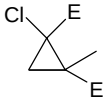
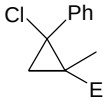
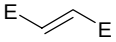
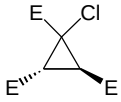
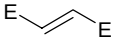
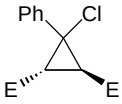
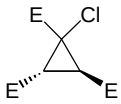
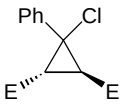
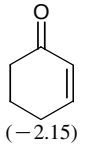
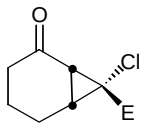
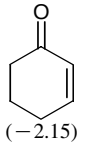
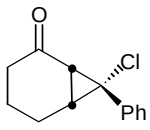
We have assigned to the compound **11** an *endo*-chlorine structure by comparison with the results obtained by Escribano et al.[9] Actually, whatever the route used (process A or B, or Escribano's process[9]) (Scheme 3), the same bicyclic compound is formed, as determined by GC-analysis, and from the ^1H and ^{13}C NMR spectra.



Scheme 3.

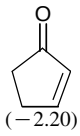
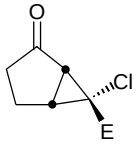
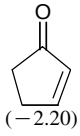
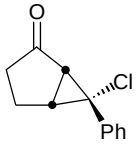
The *endo*-chlorine structure was established by Escribano[9] from X-ray diffraction experiments. Our 1D ^1H NOE-Difference NMR experiments, using selective excitation with a shaped pulse (gradient version) on the methoxy group, are consistent with the assignment given by Escribano. Indeed, the NOE effect (Fig. 1) is mainly seen at the H-1 and H-5 bridge-head protons. However, our measurement of the ^3J (^1H–^{13}C) coupling constant between

Table 1. Formation of polysubstituted chlorocyclopropanes by electroreductive or Mg-promoted coupling of α,β-unsaturated carbonyl compounds and α,α,α-trichloromethyl derivatives (Cl_3C–Y)

Entry	α,β-Unsaturated carbonyl compound[a] E_{red} (V/sce)[b]	Cl_3CY	Polysubstituted chlorocyclopropane[a]	*n*	Process A electrochemical process isolated yield (%)	Process B chemical process isolated yield (%)
1	 (−2.15)	$Cl_3CCO_2CH_3$		**1**	70 *R*S*/R*R** 17/83	76 *R*S*/R*R** 7/93
2	 (−2.15)	$PhCCl_3$		**2**	35 *R*S*/R*R** 60/40	68 *R*S*/R*R** 57/43
3	 (−2.05)	$Cl_3CCO_2CH_3$		**3**	57 *R*S*/R*R** 30/70	65 *R*S*/R*R** 28/72
4	 (−2.05)	$PhCCl_3$		**4**	41 *R*S*/R*R** 35/65	57 *R*S*/R*R** 36/64
5	 (−2.30)	$Cl_3CCO_2CH_3$		**5**	<10[c]	70 *R*S*/R*R** 45/55
6	 (−2.30)	$PhCCl_3$		**6**	<10[c]	73 *R*S*/R*R** 25/75
7	 (−1.60)	$Cl_3CCO_2CH_3$		**7**	67 *R*R**	33 *R*R**
8	 (−1.60)	$PhCCl_3$		**8**	52 *R*R**	23 *R*R**
9	 (−1.45)	$Cl_3CCO_2CH_3$		**7**	40 *R*R**	24 *R*R**
10	 (−1.45)	$PhCCl_3$		**8**	46 *R*R**	10 *R*R**
11	 (−2.15)	$Cl_3CCO_2CH_3$		**9**	58 1*RS*,6*RS*,7*RS*	53 1*RS*,6*RS*,7*RS*
12	 (−2.15)	$PhCCl_3$		**10**	30 1*RS*,6*RS*,7*RS*	50[d] 1*RS*,6*RS*,7*RS*

(*continued on next page*)

Table 1 (*continued*)

Entry	α,β-Unsaturated carbonyl compound[a] E_{red} (V/sce)[b]	Cl_3CY	Polysubstituted chlorocyclopropane[a]	*n*	Process A electrochemical process isolated yield (%)	Process B chemical process isolated yield (%)
13	 (−2.20)	$Cl_3CCO_2CH_3$		**11**	30 1*RS*,5*RS*,6*RS*	40[d] 1*RS*,5*RS*,6*RS*
14	 (−2.20)	$PhCCl_3$		**12**	20 1*RS*,5*RS*,6*RS*	40[d] 1*RS*,5*RS*,6*RS*

[a] E=CO_2CH_3.
[b] See Ref. 15.
[c] Determined by GC without internal standart.
[d] Reagents ratio: activated olefin/α,α,α-trichlorotoluene, 20 mmol/10 mmol.

the bridge-head protons and the carbon of the carbonyl of the C-6 methyl ester substituent gives a value of 3.7 Hz, and not 7.2 Hz as reported by Escribano.[9] This result was obtained by using a simple pulse sequence, which selectively decouples protons from the CH_3 of the methyl ester (Fig. 2), and was confirmed by 2D ^{13}C/JCH NMR experiment (Fig. 3). Our idea on the discrepancy between Escribano's work and our NMR measurements is that the Karplus relationship used by Escribano is convenient for a ^3J (^{1}H–Csp^3–Csp^3–^{13}Csp^3) like in the propane[19] but not for a ^3J (^{1}H–Csp^3–Csp^3–^{13}Csp^2) like in the compound **11**. So, we agree with the structure proposed by Escribano, but not with the NMR data. Now, regarding the other bicyclic compounds **9**, **10**, and **12** (see Table 1) we prepared, they all have ^3J (^{1}H–Csp^3–Csp^3–^{13}Csp^2) values close to 4 Hz, as for the compound **11** and by using the same NMR methods. So we think that we can reasonably assign an *endo*-Cl structure to these four bicyclic compounds.

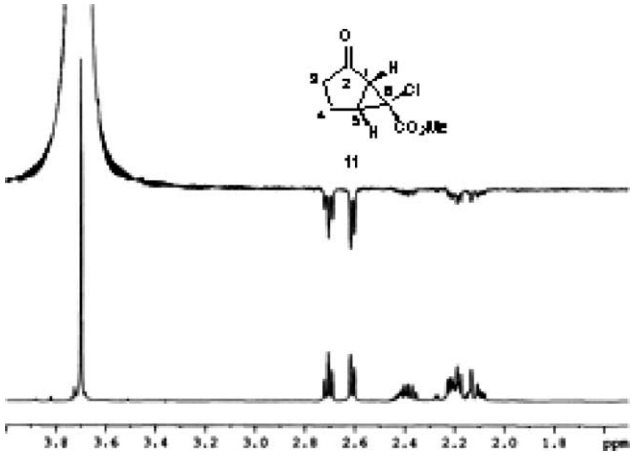


Figure 1. 1D ^{1}H NOE-Difference NMR of **11**.

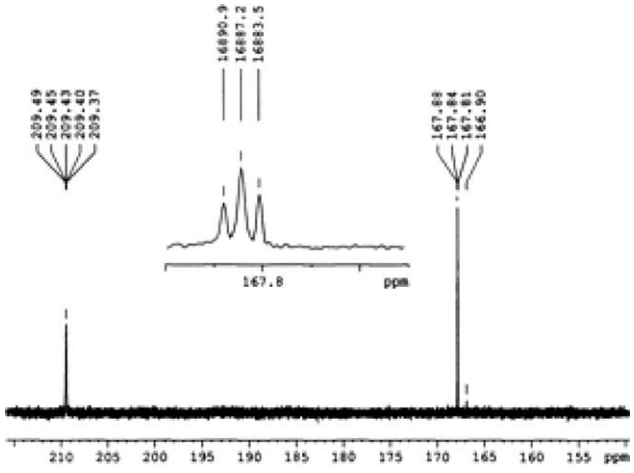


Figure 2. ^{13}C NMR decoupled –OCH_3 of **11**,^3J ^{1}H–^{13}C: H-1 and H-5/CO_2R=3.7 Hz.

The cyclopropanations described here are regiospecific. Indeed, no addition onto the carbonyls of the activated olefins

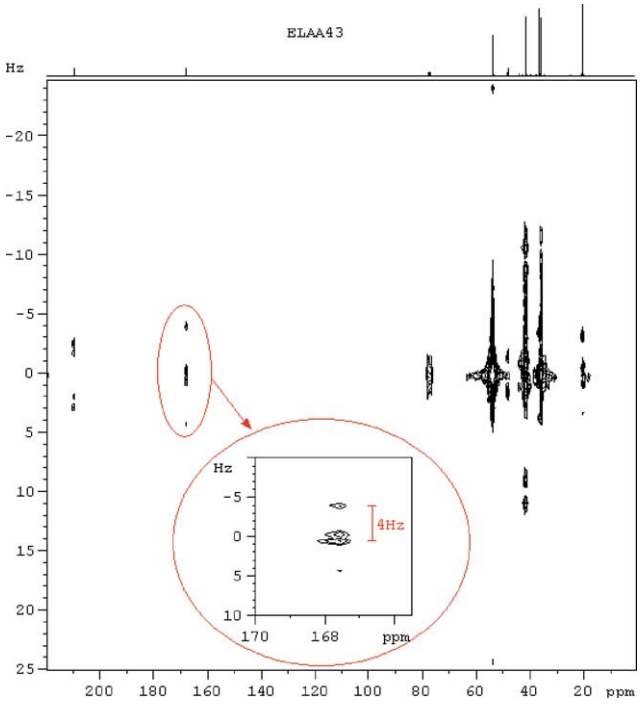
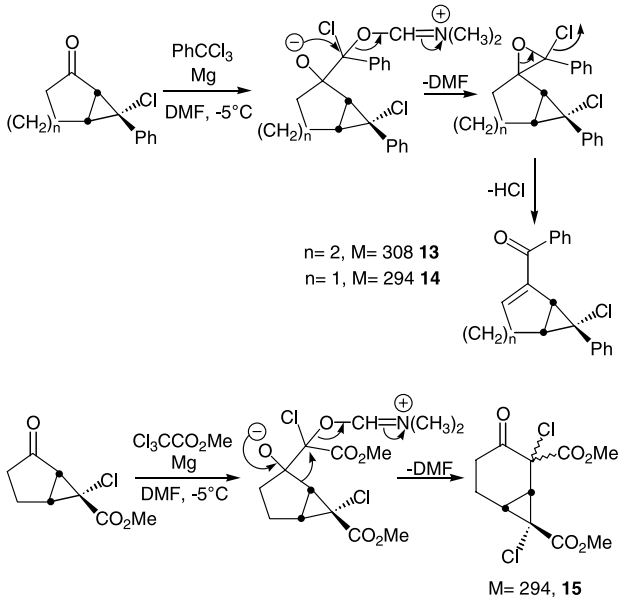


Figure 3. 2D ^{13}C/JCH NMR of **11**: ^3J ^{1}H–^{13}C: H-1 and H-5/CO_2R ~ 4 Hz.

was observed during or at the near end of the reaction, though the trichloromethyl compound is used in excess. Side products coming from the halocompounds are their reduced forms and traces of the dimers (YCCl=CClY). However, with process B, and in the case of cyclic enones and Cl_3C–Y (Table 1, entries 12, 13 and 14), we could observe, at the near end of the reaction, the formation of three by-products showing parent ions at *m/e* = 308, 294, 294, respectively, in their mass spectra. We thus made the assumption that the nucleophilic species generated in situ could react on the carbonyl of the bicyclic products, according to reactions described by Larson[6] and by Schäfer.[21,22] The structures **13**, **14**, **15** have been postulated for these by-products (Scheme 4). To prevent this side reaction in the preparation of the compounds **10**, **11**, **12** (see Table 1), we modified process B in a way to keep the electrophilic olefins in excess vs the *gem*-polyhalocompound all over the reaction. However, surprisingly, in the preparation of the bicyclic compound **9** (Table 1, entry 11), no 1,2-addition was observed. Up to now, we have no explanation for this result.



Scheme 4.

3. Conclusions

We have described in this paper two simple, efficient and complementary methods (processes A and B) for the preparation of polysubstituted chlorocyclopropanes using electrophilic olefins and activated trichloromethyl compounds as starting materials. These new routes do not make use of strong bases or very expensive copper carbenoid *tert*-butyl isocyanides. Also, we have noticed that, in DMF, the nucleophilic species resulting from the Mg reduction of α,α,α-trichlorotoluene were able to react with ketones leading to benzoylated olefins. So far, the only other reductive route reported involves an electrochemical reduction of α,α,α-trichlorotoluene in a double-walled glass cell with a mercury pool cathode.[22a,c] We are now extending this Mg-Barbier reaction in DMF to the preparation of cycloalk-1-en-1-yl and alk-1-en-1-ylphenyl ketones.

4. Experimental

Melting points were determined with an Electrothermal IA 9100 digital melting point apparatus. ^1H, ^{13}C NMR spectra were recorded on a Bruker AC-200 (200, 50 MHz, respectively) or Bruker Avance 300 (300, 75 MHz, respectively) or Bruker DRX-400 (400, 100 MHz, respectively) spectrometers. Mass spectra (electron impact) were obtained on a GCQ Thermoquest spectrometer equipped with a DB 5MS capillary column. Infrared spectra were recorded on a Perkin Elmer Spectrum BX FT-IR spectrometer. 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. The XC10 Fe rod (iron with 0.1% of carbon) and Mg grits (50–150 mesh) were purchased, respectively, from Weber Métaux and Fluka.

4.1. General procedure

Process A, indirect electrochemical process with Fe anode in the presence of CuBr. The reactions are conducted in an undivided cell fitted with an Fe rod as the anode and a nickel foam as the cathode (area: ca. 40 cm^2). A solution of CuBr (144 mg, 1 mmol) and Bu_4NBr (300 mg) in DMF (45 mL) and pyridine (5 mL) is electrolysed at constant current intensity (0.3 A) during 15 min at $-5\,°C > T > -10\,°C$. Then, the activated olefin (10 mmol) and the α,α,α-trichloromethyl compound (20 mmol) are added and electrolysed (0.1 A) until the complete consumption of the olefin (about 8 h). The DMF is evaporated under reduced pressure. The reaction mixture is poured into a cold mixture of 1 M HCl (50 mL) and diethyl ether (50 mL). The layers are separated and extracted with diethyl ether (three portions of 25 mL). The combined ethereal extracts are washed with a saturated solution of ammonium chloride and brine, dried over $MgSO_4$. Products are isolated either by column chromatography on silica gel (230–400 mesh) or aluminium oxide (70–230 mesh) using pentane–ether as eluent.

Process B, Mg-promoted Barbier type reaction in the presence of DMF. Magnesium grits (50–100 mesh) (30 mmol) are suspended in DMF (40 mL) in a three-neck flask fitted with a thermometer and a dropping funnel, and cooled at $-5\,°C$. Half of the solution containing olefin (10 mmol), α,α,α-trichloromethyl compound (12 mmol) and DMF (5 mL) is rapidly introduced in the flask. The beginning of the reaction is clearly indicated by the temperature rising up to $+5\,°C$, and the mixture turning yellow. The remaining of the reactants was then added within 5 min, and the reaction is allowed to proceed up to complete consumption of the olefin. After the usual work-up, the product is isolated by column chromatography on silica gel (230–400 mesh) using pentane–ether as eluent.

4.2. Isolated products

4.2.1. Dimethyl 1-chlorocyclopropane-1,2-dicarboxylate (1).[14a] CAS RN: 39822-02-1 (*R**,*S**), 39822-01-0 (*R**,*R**).

4.2.2. Methyl 2-chloro-2-phenylcyclopropane-1-carboxylate (2).[14a] CAS RN: 39822-09-8 (*R**,*S**), 39822-10-1 (*R**,*R**).

4.2.3. Dimethyl 2-chloro-1-methoxycarbonylmethylcyclopropane-1,2-dicarboxylate (3).[14a] CAS RN: 424790-89-6 (*R**,*S**), 424790-88-5 (*R**,*R**).

4.2.4. Methyl 2-chloro-1-methoxycarbonylmethyl-2-phenylcyclopropane-1-carboxylate (4) (new compound). ($C_{14}H_{15}ClO_4$); MW: 282.723. Anal. Calcd for $C_{14}H_{15}ClO_4$: C, 59.48; H, 5.35; O, 22.63; Cl, 12.54. Found: C, 59.28; H, 5.33; O, 22.63; Cl, 12.66. Pentane–ether (95/5) to (90/10); obtained: 1.16 g (yield: 41%, (*R**,*S**)/(*R**,*R**): 35:65, process A), 1.61 g (yield: 57%, (*R**,*S**)/(*R**,*R**): 36:64, process B); (*R**,*S**): oil, (*R**,*R**): mp=76–78 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ (*R**,*S**): 7.3–7.2 (Ph, 5H, m); 3.75 (OCH_3, 3H, s); 3.5 (OCH_3, 3H, s); 3.1 (CH_2, 1H, d, J=17.6 Hz); 2.35 (H-3 or H-3′, 1H, d, J=7.4 Hz); 1.65 (H-3 or H-3′, 1H, d, J=7.4 Hz); 1.3 (CH_2, 1H, d, J=17.6 Hz); for the couple H-3/H-3′ ($\Delta\nu/J$=19.0 AX system); for the methylene group ($\Delta\nu/J$=21.0 AX system). (*R**,*R**): 7.4–7.2 (Ph, 5H, m); 3.7 (OCH_3, 3H, s); 3.4 (CH_2, 1H, d, J=17.6 Hz); 3.2 (OCH_3, 3H, s); 2.9 (CH_2, 1H, d, J=17.6 Hz); 2.5 (H-3 or H-3′, 1H, d, J=6.9 Hz); 1.5 (H-3 or H-3′, 1H, d, J=6.9 Hz); for the couple H-3/H-3′ ($\Delta\nu/J$=29.0 AX system); for the methylene group ($\Delta\nu/J$=5.5 AB system). ^{13}C NMR (50 MHz, $CDCl_3$) δ (*R**,*S**): CO: 170.9, 169.9; C(Ph): 138.5, 128.5; C-2: 53.3; OCH_3: 52.0, 51.9; CH_2: 37.3; C-1: 33.3; C-3: 25.6. (*R**,*R**): CO: 171.7, 169.7; C(Ph): 137.8, 128.7; C-2: 53.4; OCH_3: 51.7, 49.7; CH_2: 37.5; C-1: 34.3; C-3: 23.7. EI-MS *m*/*z* (*R**,*S**): 282 (M, 1), 220 (32), 219 (13), 218 (base peak), 192 (14), 191 (20), 190 (46), 187 (13), 165 (26), 164 (16), 163 (78), 162 (17), 159 (20), 155 (11), 149 (24), 145 (20), 129 (17), 128 (56), 127 (30), 115 (11). (*R**,*R**): 282 (M, 1), 220 (30), 219 (12), 218 (base peak), 192 (16), 191 (19), 190 (41), 187 (14), 165 (26), 164 (13), 163 (71), 162 (15), 159 (21), 155 (10), 149 (22), 145 (20), 129 (20), 128 (64), 127 (30), 115 (11). IR ν (cm^{-1}) ($CDCl_3$) 3080, 3030, 2990, 2970, 2900, 1735, 1600, 1570, 1470.

4.2.5. Dimethyl 1-chloro-2-methylcyclopropane-1,2-dicarboxylate (5). ($C_8H_{11}ClO_4$); MW: 206.625; CAS RN: 42392-04-1 (*R**,*S**), 132785-43-4 (*R**,*R**). Pentane (100) to pentane–ether (95/5); obtained: 1.45 g (yield: 70%, (*R**,*S**)/(*R**,*R**): 45:55, process B; (*R**,*S**) and (*R**,*R**): oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ (*R**,*S**): 3.5 (OCH_3, 3H, s); 3.4 (OCH_3, 3H, s); 2.0 (H-3 or H-3′, 1H, d, J=6.5 Hz); 1.3 (CH_3, 3H, s); 1.0 (H-3 or H-3′, 1H, d, J_{gem}=6.5 Hz); for the couple H-3/H-3′ ($\Delta\nu/J$=31.4 AX system). (*R**,*R**): 3.65 (OCH_3, 3H, s); 3.6 (OCH_3, 3H, s); 1.85 (H-3 or H-3′, 1H, d, J=6.6 Hz); 1.7 (H-3 or H-3′, 1H, d, J=6.6 Hz); 1.2 (CH_3, 3H, s); for the couple H-3/H-3′ ($\Delta\nu/J$=5.6 AB system). ^{13}C NMR (50 MHz, $CDCl_3$) δ (*R**,*S**): CO: 170.8, 167.8; OCH_3: 53.1, 52.4; C-1: 48.5; C-2: 33.7; C-3: 27.9; CH_3: 17.3. (*R**,*R**): CO: 169.0, 166.9; OCH_3: 53.0, 52.1; C-1: 45.2; C-2: 35.1; C-3: 25.5; CH_3: 14.8. EI-MS *m*/*z* (*R**,*S**): 206 (M, <1), 177 (13), 176 (15), 175 (37), 174 (32), 171 (22), 170 (51), 148 (35), 147 (17), 146 (base peak), 139 (16), 133 (12), 131 (31), 127 (11), 119 (18), 115 (20), 111 (12), 87 (15), 83 (15). (*R**,*R**): 206 (M, 1), 176 (11), 175 (22), 174 (26), 171 (13), 170 (36), 148 (34), 147 (17), 146 (base peak), 139 (18), 131 (26), 119 (18), 115 (15), 111 (15), 83 (13), 55 (10). IR ν (cm^{-1}) (film) 3100, 2990, 2970, 1750, 1730, 1440.

4.2.6. Methyl 2-chloro-1-methyl-2-phenylcyclopropane-1-carboxylate (6). ($C_{12}H_{13}ClO_2$); MW: 224.687; CAS RN: 91433-96-4 (*R**,*S**), 91434-02-5 (*R**,*R**). Pentane (100) to pentane–ether (95/5); obtained: 1.64 g (yield: 73%, (*R**,*S**)/(*R**,*R**): 25:75, process B; (*R**,*S**) and (*R**,*R**): oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ (*R**,*S**): 7.4–7.6 (Ph, 5H, m); 4.0 (OCH_3, 3H, s); 2.4 (H-3 or H-3′, 1H, d, J=6.8 Hz); 1.7 (H-3 or H-3′, 1H, d, J=6.8 Hz); 1.2 (CH_3, 3H, s); for the couple H-3/H-3′ ($\Delta\nu/J$=20.0 AX system). (*R**,*R**): 7.5–7.45 (Ph, 5H, m); 3.5 (OCH_3, 3H, s); 2.6 (H-3 ou H-3′, 1H, d, J=6.5 Hz); 1.95 (CH_3, 3H, s); 1.6 (H-3 or H-3′, 1H, d, J=6.5 Hz); for the couple H-3/H-3′ ($\Delta\nu/J$=32.3 AX system). ^{13}C NMR (50 MHz, $CDCl_3$) δ (*R**,*S**): CO: 171.0; C(Ph): 137.9, 128.8, C-2: 52.1; OCH_3: 49.9; C-1: 33.1; C-3: 24.5; CH_3: 17.6. (*R**,*R**): C-4: 171.4; C-7: 139.6; other aromatic C: 128.4; C-2: 53.9; C-5: 51.8; C-1: 32.4; C-3: 26.0; C-6: 18.0. EI-MS *m*/*z* (*R**,*S**): 225 (M, 6), 189 (35), 167 (12), 165 (34), 161 (8), 157 (8), 131 (15), 130 (12), 129 (base peak), 128 (28), 105 (10). (*R**,*R**): 225 (M, 9), 189 (35), 167 (10), 165 (35), 161 (10), 157 (10), 131 (16), 130 (15), 129 (base peak), 128 (27), 105 (10). IR ν (cm^{-1}) (film) 3030, 2920, 1720, 1580, 1500, 1450.

4.2.7. *trans*-Trimethyl 1-chlorocyclopropane-1,2,3-tricarboxylate (7).[14d] CAS RN: 205320-46-3.

4.2.8. *trans*-Dimethyl 3-chloro-3-phenylcyclopropane-1,2-dicarboxylate (8).[14d] CAS RN: 205320-44-1.

4.2.9. (1*RS*,6*RS*,7*RS*)-Methyl 7-chloro-2-oxobicyclo[4.1.0]heptane-7-carboxylate (9). ($C_9H_{11}ClO_3$); MW: 202.637; CAS RN: 406217-16-1. Pentane–ether (90/10) to (80/20); obtained: 1.17 g (yield: 58%, process A), 1.07 g (yield: 53%, process B); oil. ^{1}H NMR (200 MHz, $CDCl_3$) 3.5 (OCH_3, 3H, s); 2.3–2.1 (2H, m); 2.1–1.8 (3H, m); 1.7–1.5 (3H, m). ^{13}C NMR (50 MHz, $CDCl_3$) δ COR: 202.5; COOR: 168.7; OCH_3: 53.5; C-7: 48.7; C-3: 38.9; C-1: 34.1; C-6: 30.1; C-4 and C-5: 23.9, 17.6. EI-MS *m*/*z* 202 (M, 10), 176 (23), 174 (73), 172 (28), 171 (13), 170 (88), 148 (10), 147 (31), 146 (14), 145 (34), 144 (36), 143 (51), 142 (base peak), 139 (13), 135 (32), 117 (12), 116 (10), 115 (21), 111 (11), 107 (41), 106 (10), 87 (13), 81 (14), 80 (11), 79 (99), 78 (15), 77 (43), 53 (11), 51 (40). IR ν (cm^{-1}) ($CDCl_3$) 1750, 1720.

4.2.10. (1*RS*,6*RS*,7*RS*)-7-Chloro-7-phenylbicyclo[4.1.0]-heptane-2-one (10). ($C_{13}H_{13}ClO$); MW: 220.699; CAS RN: 126252-39-9. Pentane (100) to pentane–ether (95/5); obtained: 0.662 g (yield: 30%, process A), 1.10 g (yield: 50%, process B); mp=69–70 °C. ^{1}H NMR (200 MHz, $CDCl_3$) 7.6–7.2 (Ph, 5H, m); 2.3–1.6 (H-1 to H-6, 8H, m). ^{13}C NMR (50 MHz, $CDCl_3$) δ CO: 204.9; C(Ph): 141.9, 128.3, 127.5; C-7: 54.9; C-3: 39.1; C-1: 33.6; C-6: 29.0; C-4 and C-5: 24.9, 18.6. EI-MS *m*/*z* 220 (M, 8), 192 (15), 185 (10), 157 (28), 141 (8), 130 (12), 129 (base peak), 128 (27), 127 (9), 115 (15). IR ν (cm^{-1}) ($CDCl_3$) 3080, 3020, 2980, 1700, 1600, 1580, 1500.

4.2.11. (1*RS*,5*RS*,6*RS*)-Methyl 6-chloro-2-oxobicyclo[3.1.0]hexane-6-carboxylate (11). ($C_8H_9ClO_3$); MW:

188.610; CAS RN: 2158-08-1. Pentane (100) to pentane–ether (85/15); obtained: 0.566 g (yield: 30%, process A), 0.754 g (yield: 40%, process B); mp = 41–42 °C. ^{1}H NMR (300 MHz, $CDCl_3$) 3.7 (OCH_3, 3H, s); 2.7 (H-5, 1H, t, ^3J = 6.3 Hz); 2.6 (H-1, 1H, d, ^3J = 6.3 Hz); 2.5–2.05 (H-3 and H-4, 4H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ COR: 209.4; CO_2R: 167.8; OCH_3: 53.8; C-6: 48.3; C-1: 41.6; C-3: 36.6; C-5: 36.0; C-4: 20.4. EI-MS *m/z* 162 (15), 160 (38), 156 (37), 149 (11), 148 (23), 147 (48), 146 (65), 145 (44), 134 (35), 133 (20), 132 (base peak), 131 (49), 129 (13), 128 (11), 125 (31), 124 (12), 118 (14), 117 (25), 116 (26), 115 (19), 111 (23), 109 (11), 101 (15), 100 (13), 93 (30), 87 (14), 80 (14), 79 (17), 73 (11), 69 (14), 65 (61), 51 (16). IR ν (cm^{-1}) ($CDCl_3$) 3068, 3050, 3010, 2956, 2873, 1730, 1703, 1440.

4.2.12. (1*RS*,5*RS*,6*RS*)-6-Chloro-6-phenylbicyclo[3.1.0] hexane-2-one (12) (new compound). ($C_{12}H_{11}ClO$); MW: 206.672. ES-HR-MS calcd for $C_{12}H_{11}ONaCl$ *m/z* 229.0396, found 229.0399. Pentane (100) to pentane–ether (95/5); obtained: 0.413 g (yield: 20%, process A), 0.811 g (yield: 40%, process B); mp = 86–87 °C. ^{1}H NMR (200 MHz, $CDCl_3$) 7.4–7.15 (Ph, 5H, m); 2.6–2.15 (H-1 to H-5, 6H, m). ^{13}C NMR (50 MHz, $CDCl_3$) δ O: 211.1; C(Ph): 140.8, 128.9, 128.6, 127.6; C-6: 54.5; C-1: 41.4; C-3: 37.4; C-5: 34.7; C-4: 21.1. EI-MS *m/z* 164 (20), 143 (10), 130 (11), 129 (base peak), 128 (31), 127 (8), 115 (15). IR ν (cm^{-1}) ($CDCl_3$) 3150, 3040, 2980, 2940, 1730, 1600, 1580, 1500.

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References and notes

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