Electrochemical transformations of alkylidenemalonates into substituted cyclopropanecarboxylates

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Electrolysis of alkylidenemalonates in acetonitrile in the presence of sodium iodide as a mediator in an undivided cell leads to various substituted cyclopropanetetracarboxylates depending on the conditions of the electrolysis and on the structure of the starting alkylidenemalonate.

Alkylidenemalonates are well-known intermediates used in organic synthesis primarily owing to reactions of their activated double bond conjugated with two carboxyl groups.[1]

The known electrochemical transformations of alkylidenemalonates are associated with two types of the reactivity of the activated double bond: reductive hydrodimerisation[2,3] and addition of electrochemically generated anions to the double bond.[4,5]

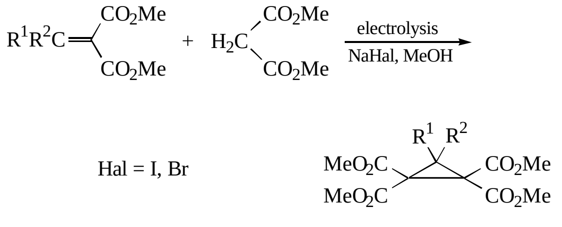
Nevertheless, to our knowledge, direct transformations of alkylidenemalonates into cyclopropanetetracarboxylates are unknown.

In the last few years, mediators were widely used for the electrooxidation and electroreduction of organic compounds.[6] Among a variety of mediators, the halide anion–halogen redox system is one of the most useful from the viewpoint of organic synthesis and large-scale industrial processes.[7]

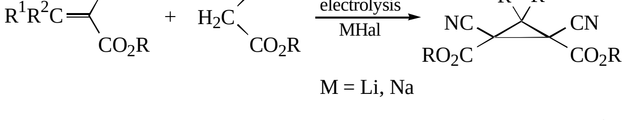
Recently, in studies of the electrochemical oxidation of organic compounds in the presence of alkali metal halides, we have performed electrochemical cyclodimerisation of alkylidenemalonates into 3,4-disubstituted cyclobutane-1,1,2,2-tetracarboxylates[3,8] and electrocatalytic transformation of alkylidenemalonates into 2-alkyl-3,3-dimethoxyalkane-1,1-dicarboxylates *via* an electrochemically induced oxidative rearrangement.[9,10]

Cyclopropane derivatives occupy a significant place in synthetic organic chemistry.[11] Their structure and reactivity are responsible for the widespread use in the synthesis of naturally occurring products. Cyclopropanecarboxylic acid derivatives play an important role as effective agents in agriculture and medicine.[12] Insecticidal pyrethrins (cyclopropanoid chrysanthemic acid derivatives) are perhaps the best known examples of their use.[13]

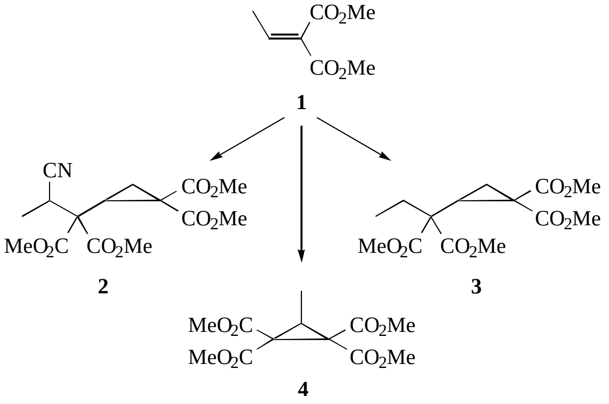
We have already used an electrochemical approach to the synthesis of substituted cyclopropanes by electrolysis of alkylidenemalonates and a malonate in methanol in the presence of halides as mediators in an undivided cell:[14]



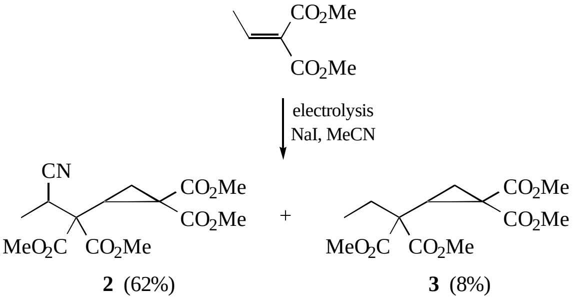
Recently we have also synthesised substituted cyclopropanes by co-electrolysis of alkylidenecyanoacetates and cyanoacetic ester:[15]



Here we report a new unusual direct electrochemical transformation of alkylidenemalonates into functionally substituted cyclopropanes. We found that electrochemical transformation of ethylidenemalonate **1** in acetonitrile in the presence of NaI in an undivided cell depends on the conditions and gives rise to three types of substituted cyclopropanetetracarboxylates **2**–**4**.† One of these compounds is formed as the main product of the reaction (Table 1). Note that the reactions described below are the first example of direct transformations of the alkylidenemalonates into functionally substituted cyclopropanes:



Electrolysis of ethylidenemalonate in acetonitrile in the presence of only NaI leads mainly to the formation of cyclopropanetetracarboxylate **2** accompanied by a small amount of cyclopropanetetracarboxylate **3**:



Addition of ethylmalonate to the reaction mixture causes an increase in the cyclopropanetetracarboxylate **3** yield up to 57% (Table 1, experiment nos. 2–4).

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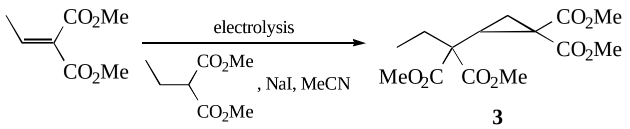
† All new compounds exhibited expected NMR spectra and data of elemental analysis or exact mass measurements.

For **2**: ^{1}H NMR (CDCl$_3$) δ: 1.43 (d, 3H, Me), 1.57 (m, 1H, CH), 1.82 (m, 1H, CH), 2.43 (m, 1H, CH), 3.51 (m, 1H, CH), 3.71 (s, 6H, OMe), 3.73 (s, 6H, OMe). ^{13}C NMR (CDCl$_3$) δ: 14.47 (t), 18.37 (q), 28.25 (d), 31.36 (d), 33.39 (s), 53.10 (q), 53.20 (q), 53.26 (q), 58.40 (s), 120.03 (s), 166.97 (s), 168.07 (s), 169.74 (s).

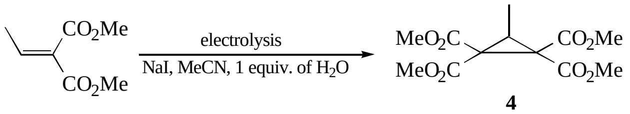
For **3**: ^{1}H NMR (CDCl$_3$) δ: 0.92 (t, 3H, Me), 1.51 (dd, 1H, CH_aH_b–CH_c, J_{ab} –5.3 Hz, J_{ac} 10.2 Hz), 1.81 (dd, 1H, CH_aH_b–CH_c, J_{ab} –5.3 Hz, J_{ac} 8.9 Hz), 2.01 (m, 2H, CH$_2$), 2.51 (dd, 1H, CH_aH_b–CH_c, J_{ac} 10.2 Hz, J_{bc} 8.9 Hz), 3.71 (s, 6H, OMe), 3.73 (s, 6H, OMe). ^{13}C NMR (CDCl$_3$) δ: 8.96 (q), 18.44 (t), 27.94 (t), 27.96 (d), 32.76 (s), 52.26 (q), 52.42 (q), 57.14 (s), 167.97 (s), 168.32 (s), 169.56 (s), 170.23 (s).

For **4**: ^{1}H NMR (CDCl$_3$) δ: 1.39 (d, 3H, Me), 2.46 (q, 1H, CH), 3.71 (s, 6H, OMe), 3.72 (s, 6H, OMe). ^{13}C NMR (CDCl$_3$) δ: 8.32 (q), 31.41 (d), 43.94 (s), 52.72 (q), 53.13 (q), 165.02 (s), 167.01.



3

Small amounts of a protogenic solvent such as methanol or water also influence the ethylidenemalonate electrolysis (Table 1). Thus, in the presence of water, cyclopropanetetracarboxylate **4** was obtained in 60% yield.



4

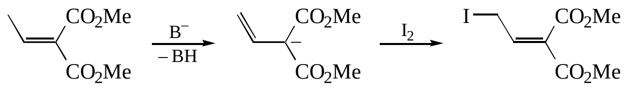
Electrolysis of ethylidenemalonate under the same conditions in the presence of malonate resulted in the formation of cyclopropane **4** in 92% yield (Table 1, experiment no. 7).

Taking into consideration the data obtained, the following scheme of the formation of cyclopropanes **2**–**4** is proposed. Electrochemical reactions occur at both the anode and the cathode to generate intermediates which determine the overall course of the process. In all reactions studied, the anodic process is the oxidation of iodide anions into iodine:

$$2I^- - 2e^- \longrightarrow I_2$$

The formation of iodine at the anode is observed by a corresponding colour change when electrolysis is conducted without stirring of the reaction mixture.

Electrolysis of ethylidenemalonate in acetonitrile in an undivided cell in the presence of NaI and in the absence of other additives leads to the formation of anion **A** from ethylidenemalonate by the action of the base electrogenerated at the cathode under the conditions of the electrolysis. The reaction of anion **A** with iodine generated at the anode gives rise to iodopropylidenemalonate **5**:



A **5**

As it has been found previously, under the specified conditions, acetonitile reacts with Na generated at the cathode with the formation of methane and the cyanide anion:[16,17]

$$MeCN + 2Na + H^+ \longrightarrow CH_4 + CN^- + 2Na^+$$

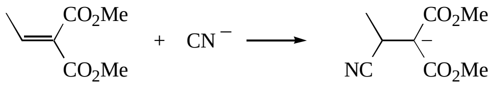
Thus, in this case, ethylidenemalonate can serve as a proton donor for the methylide anion generated in the last reaction.

Table 1 Electrolysis of ethylidenemalonate **1**.[a]

Experiment no.	Additives	Electricity passed/ F mol^{-1}	Cyclopropane yield (%)[b] 2	3	4
1	—	2.1	62 (54)	8	—
2	Ethylmalonate (2 mmol)	2.1	33	22	—
3	Ethylmalonate (7 mmol)	2.1	9	57 (48)	—
4	Ethylmalonate (14 mmol)	2.1	6	52	—
5	MeOH (14 mmol)	2.1	19	30	13
6	H_2O (14 mmol)	2.1	—	—	60 (47)
7	Malonate (1 mmol)	2.1	—	—	92 (88)

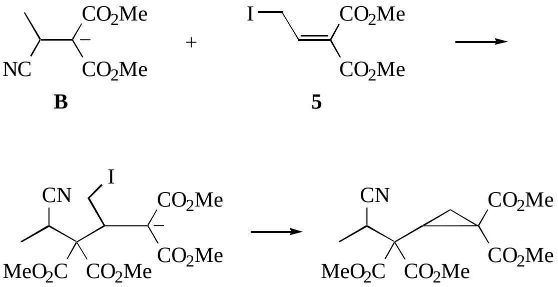
[a] 14 mmol of ethylidenemalonate; 7 mmol of NaI; 20 ml of acetonitrile; glassy carbon cathode; C-anode; current density 100 mA cm^{-2}; 40 °C. [b] Determined by gas chromatography and NMR spectroscopy, yields of the isolated compounds are given in parentheses.

The cyanide anion formed adds to the double bond of ethylidenemalonate to produce anion **B**:



B

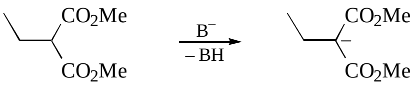
The addition of the latter to the double bond of malonate **5** followed by cyclisation analogous to that reported previously,[9] gives rise to cyclopropane **2** as the end product:



B **5**

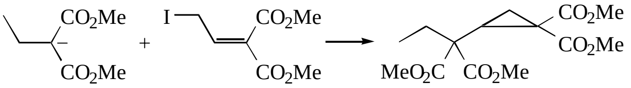
2

The addition of ethylmalonate to the electrolytic system leads to the formation of anion **C** in the system (this ion is more stable than anion **A**) due to the interaction of ethylmalonate with any electrogenerated base that exists in the system. Among them, anion **A** can act as an electrogenerated base for ethylmalonate:



C

The addition of anion **C** to the double bond of intermediate iodomalonate **5** and the following intermolecular cyclisation gives cyclopropane **3**:

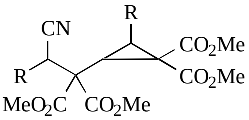


C **5** **3**

The formation of small quantities of cyclopropane **3** in the absence of ethylmalonate takes place because of partial hydrogenation of ethylidenemalonate into ethylmalonate at the cathode under conditions of the electrolysis.

The addition of protogenic solvents causes an additional route of the electrolytic process. Under these conditions, an electrochemically induced Knoevenagel retro-reaction takes place with the formation of a malonate ester which adds to the double bond of ethylidenemalonate with subsequent cyclisation to cyclopropane ester **4**. In the presence of water, the above retro-reaction becomes the main route of the process. The presence of small quantities of methanol also facilitates the hydrogenation of the double bond of ethylidenemalonate and thus increases the yield of cyclopropane ester **3**.

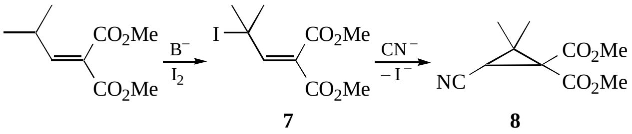
Electrolysis of propylidene- and butylidenemalonates in acetonitrile in the presence of NaI under conditions of experiment no. 1 (Table 1) leads to a more complex mixture of products in which cyclopropanes **6a**,**b** were identified and isolated by column chromatography in 33 and 25% yields, respectively.



6a,**b**

a R = Me
b R = Et

Under the conditions studied, isobutylidene malonate is unable to form dimeric products apparently because of steric hindrances in the addition of anions **B** and **C** to the double bond owing to a bulky isopropyl substituent. In this case, the electrogenerated cyanide ion attacks the double bond of γ-iodoisobutylidenemalonate **7**, which is formed in a way analogous to the formation of intermediate **5** in the solution. The following cyclisation leads to 3,3-dimethyl-2-cyanocyclopropane-1,1-dicarboxylate **8** in 73% yield.



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