

Electrochemical transformation of malonate and alkylidenemalonates into 3-substituted cyclopropane-1,1,2,2-tetracarboxylates

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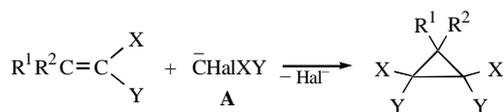
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Electrolysis of malonate and alkylidenemalonates in an undivided cell in methanol in the presence of sodium bromide or sodium iodide as mediators leads to substituted 1,1,2,2-cyclopropanetetracarboxylates in 80–95% substance and 60–75% current yield.

Cyclopropane derivatives occupy a significant place in synthetic organic chemistry.¹ Their structural and reactivity features have found widespread applications in the synthesis of natural products. Cyclopropanecarboxylic acid derivatives play an important role as effective agents in agriculture and medicine.² Insecticidal pyrethrins (derivatives of cyclopropanoid chrysanthemic acid) are perhaps the best known example of their use.³

A well-known method of synthesis of cyclopropanes involves addition of halogenosubstituted C-H acid anions **A**, generated by the action of base on the corresponding C-H acid **AH**, to the conjugated activated olefin followed by cyclization with elimination of halogen anion:⁴



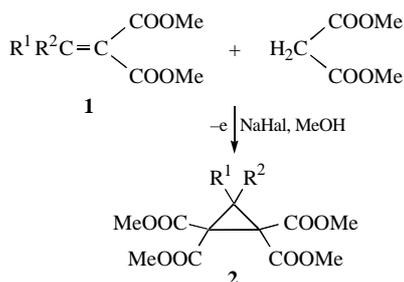
X = COOR

Y = COOR, CN, C(O)NR₂

Hal = Br, I

In recent years the method of anion **A** generation and its reactions with activated olefins have been achieved in double-phase systems in the presence of phase-transfer catalysts.⁵ Electrochemical reduction of dihalogeno-substituted malonates and further successful addition of anion (**A** X = Y = COOR) to the activated double bond was the next step in the development of this reaction scheme.⁶

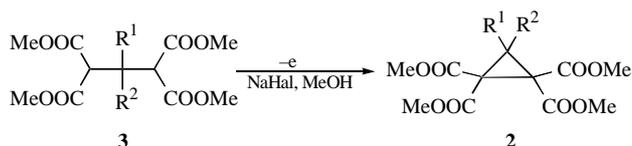
We now wish to report a new approach to the substituted cyclopropanes by the electrolysis of malonate (but not halogeno-substituted malonate) and alkylidenemalonates in an undivided cell in the presence of halides as mediators (Table 1).



Special experiments have been used to check the mechanism of the process. Decreasing the quantity of electricity passed from 2.5 F mol⁻¹ to 1.0 and 0.5 F mol⁻¹ (experiments 3 and 4) resulted in a decreasing yield of **2a** from 95% (experiment 2) to 36% and 19%, respectively. Under these conditions 2-methyl-1,1,3,3-propanetetracarboxylate **3a** was obtained as the main product in 56% and 77% yield, respectively.

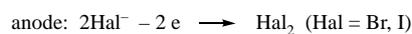
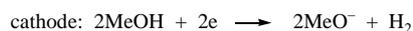
Electrochemical cyclization of 2-substituted-1,1,3,3-propanetetracarboxylates **3** have already been observed under conditions of indirect electrochemical oxidation mediated by halides:⁷

Thus, the first step in the process of indirect electrochemical transformation of alkylidenemalonates and malonates into substituted cyclopropanes **2** involves the electrochemically-

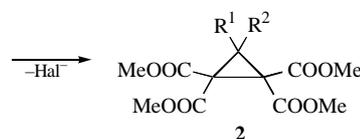
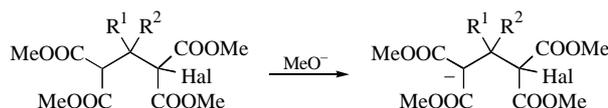
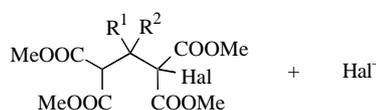
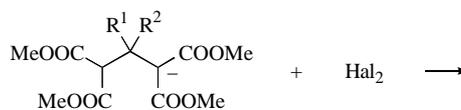
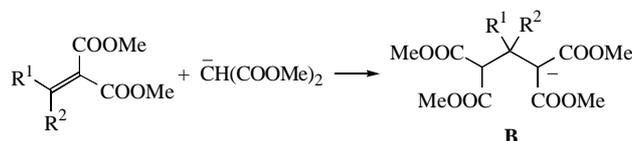
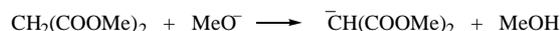


induced addition of malonate anion **A** to the activated double bond of alkylidenemalonate with the formation of anion **B**. Further halogenation of anion **B** with halogen generated at the anode and cyclization induced by interaction with MeO⁻ anion result in the formation of the end product of the process, cyclopropane **2** (Scheme 1).

It has been found previously that sodium iodide is a more effective mediator for the indirect electrochemical cyclization of 2-substituted-1,1,3,3-propanetetracarboxylates **3**.⁷ This is connected with the higher selectivity of iodine as an oxidant of anion **B** in the presence of MeO⁻ anions compared to bromine.



in solution:



Scheme 1

Table 1 Electrochemical synthesis of 3-substituted cyclopropane-1,1,2,2-tetracarboxylates.^a

| N | Alkylidenemalonate | R ¹ | R ² | Mediator | Electricity passed/ F mol ⁻¹ | Product, yield (%) ^b |
|----------------|--------------------|----------------------------------|----------------|----------|--|---------------------------------|
| 1 | 1a | Me | H | NaI | 3.0 | 2a , 92 (61) |
| 2 | 1a | Me | H | NaBr | 2.5 | 2a , 95 (76) |
| 3 | 1a | Me | H | NaBr | 1.0 | 2a , 39; 3a , 56 |
| 4 | 1a | Me | H | NaBr | 0.5 | 2a , 16; 3a , 77 |
| 5 | 1b | Pr | H | NaI | 4.0 | 2b , 83 (42) |
| 6 | 1b | Pr | H | NaBr | 3.0 | 2b , 94 (63) |
| 7 | 1c | n-C ₅ H ₁₁ | H | NaBr | 4.0 | 2c , 83 |
| 8 | 1d | Ph | H | NaBr | 4.0 | 2d , 75 |
| 9 ^c | 1e | COOMe | COOMe | NaBr | 4.0 | 2e , 58 |

^aAlkylidenemalonate 14 mmol, malonate 14 mmol, mediator 7 mmol, 20 ml of methanol, Fe-cathode, C-anode, current density 100 mA cm⁻², 30 °C.

^bCurrent yield in parentheses. ^cTemperature 50 °C.

In the present investigation we have found that sodium bromide is more effective as a mediator for the process of indirect electrochemical transformation of alkylidenemalonates and malonate into substituted cyclopropanes **2**. Thus, when using NaBr as a mediator the best substrate and current yields of substituted cyclopropanes **2** were obtained.

This unusual result is most likely associated with the opening up of a new pathway for the process when using NaBr as a mediator (Scheme 2).

The higher efficiency of NaBr as a mediator (Scheme 2) is directly related to the fact that bromomalonate is a stronger C-H acid compared to iodomalonate. That is why the stage of proton abstraction (2) by MeO⁻ anion in the case of bromomalonate is faster than in the case of iodomalonate. Another reason may be that addition of bromomalonate to alkylidenemalonates is more rapid than the analogous addition of iodomalonate anion.

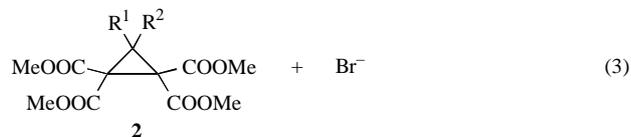
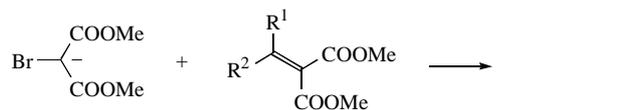
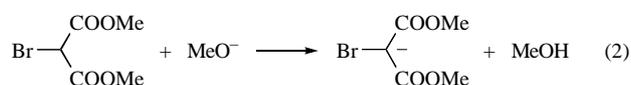
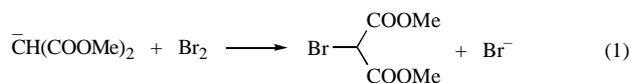
The main side reactions of the process are cathodic hydrogenation and cathodic hydrodimerisation of alkylidene-

malonates. Nevertheless, in all experiments the total yield of these two by-products was less than 10%. For the reaction of benzylidenemalonate the corresponding hydrodimer, 2,3-diphenyl-1,1,4,4-butanetetracarboxylate **4**, was isolated in 9% yield. The process of alkylidenemalonate hydrodimerization becomes the main reaction pathway on cathodes with a high hydrogen overvoltage (lead, glassy carbon, graphite).⁸ The sufficient yield of **4** when using benzylidenemalonate as the activated olefin is connected with the higher stability of the intermediate anion-radical because of conjugation in the anion-radical centre with the electrons of the aromatic ring.

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**Scheme 2**

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