

# Electrocatalytic multicomponent cyclization of an aldehyde, malonitrile and a malonate into 3-substituted-2,2-dicyanocyclopropane-1,1-dicarboxylate—the first one-pot synthesis of a cyclopropane ring from three different molecules

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**Abstract**—Electrolysis of an aldehyde, malonitrile and a malonate in an alcohol in an undivided cell in the presence of sodium acetate–sodium halide as a double mediatory system results in the formation of 3-substituted-2,2-dicyanocyclopropane-1,1-dicarboxylates in 40–60% yields.

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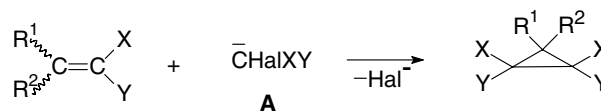
Cyclopropane is a basic structural element in a wide range of natural compounds and occupies a significant place in synthetic organic chemistry.<sup>1</sup> The cyclopropyl group is also a vital structural unit in many synthetic and naturally occurring compounds, exhibiting a wide spectrum of biological properties ranging from enzyme inhibition to herbicidal, antibiotic, antitumour and antiviral activities.<sup>2,3</sup> Insecticidal pyrethrins (derivatives of chrysanthemic acid) are perhaps the best known example of their use.<sup>1</sup> Thus, the prevalence of cyclopropane-containing compounds with biological activity, whether isolated from natural sources or rationally designed pharmaceutical agents, has inspired chemists to find novel and diverse approaches to their synthesis.

Although the synthetic methods for cyclopropanes have long been documented, so far, all consist of two main groups: (1) intramolecular cyclization or, (2) interaction of two different molecules (addition of carbenes to olefins or Michael initiated ring closure (MIRC) are the best known examples of this type).<sup>1,3</sup> MIRC plays an important role in organic chemistry and many synthetic applications are described in the literature.<sup>4</sup>

The well-known MIRC leading to substituted cyclopropanes involves the addition of halogenosubstituted C–H acid anions (**A**), generated by the action of a base on the corresponding C–H acid (**AH**), to the conjugated activated olefins followed by cyclization with elimination of halide<sup>5</sup> (Scheme 1).

Anion (**A**) generation and its reactions with activated olefins have been accomplished in biphasic systems in the presence of a phase transfer catalyst.<sup>6</sup> The electrochemical reduction of dihalogeno substituted malonates followed by the addition of anion **A** ( $X=Y=COOR$ ) to activated double bonds provides an improvement of this reaction scheme.<sup>7</sup>

The next essential step was to exclude halogen-containing organic compounds as initial reagents. Hence a novel electrochemical approach to functionally substituted cyclopropanes was performed by the electrolysis



X = COOR

Y = COOR, CN, C(O)NR<sub>2</sub>

Hal = Br, I

**Scheme 1.**

**Keywords:** Electrolysis, Electrocatalytic transformation; Mediators; Aldehydes; Malonitrile; Malonate; Cyclopropanes.

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of alkylidenemalonates and malonate in an undivided cell in methanol in the presence of halides as mediators.<sup>8</sup>

The co-electrolysis of alkylidencyanoacetic and malonic esters resulted in the stereoselective syntheses of (*E*)-isomers of trialkyl 3-substituted-2-cyanocyclopropane-1,1,2-tricarboxylates<sup>9</sup> (Scheme 2).

Recently, we accomplished the electrocatalytic transformation of alkylidenemalononitriles and malonate into dialkyl 3-substituted-2,2-dicyanocyclopropane-1,1-dicarboxylates<sup>10</sup> (Scheme 3).

It has also been found that tetracyanocyclopropanes, on electrolysis in alcohols in an undivided cell, were very easily attacked by alkoxide anions generated at the cathode to afford substituted 2-amino-4,4-dialkoxy-1,5-dicyano-3-azabicyclo[3.1.0]hex-2-enes<sup>11</sup> (Scheme 4).

Combining these two methods, we accomplished the stereoselective electrocatalytic transformation of alkylidenemalononitriles and malononitrile into bicyclic pyrrolines containing a cyclopropane ring<sup>12</sup> (Scheme 5).

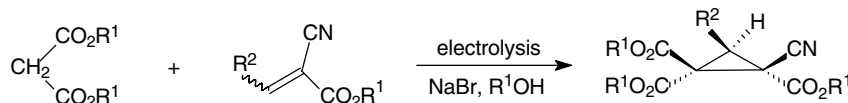
The next step of our research was a one-pot stereoselective electrocatalytic transformation of an aromatic alde-

hyde and malononitrile into bicyclic pyrrolines in the presence of the new double mediatory system NaOAc–NaBr<sup>13</sup> (Scheme 6).

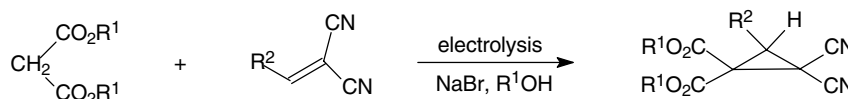
In the present study, we report our results on the one-pot, multicomponent electrocatalytic transformation of aldehydes **1a–i**, malononitrile and malonate into 3-substituted-2,2-dicyanocyclopropane-1,1-dicarboxylates **2a–i** in methanol in the presence of the double mediatory system sodium acetate–sodium bromide in an undivided cell, which to our knowledge is the first example of cyclopropane ring formation from three different molecules (Scheme 7, Table 1).

In the mediatory system, NaOAc acts as a catalyst for the Knoevenagel condensation of the aldehyde and malononitrile. When electricity was not passed, the aldehyde and malononitrile, in the presence of NaOAc, were condensed into alkylidenemalononitriles in a time less than half of that of the electrochemical reaction (30 min). Earlier NaOAc was used as a catalyst in the Perkin condensation<sup>15</sup> and in the Knoevenagel reaction.<sup>13</sup>

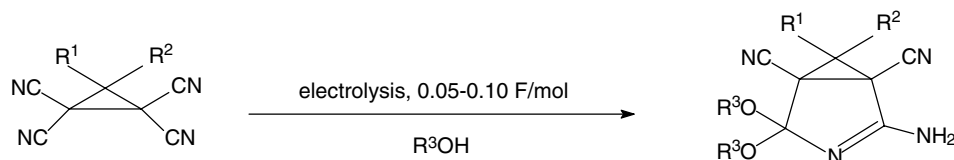
Taking into consideration the above results, the data on the mechanism of the electrocatalytic variant of the



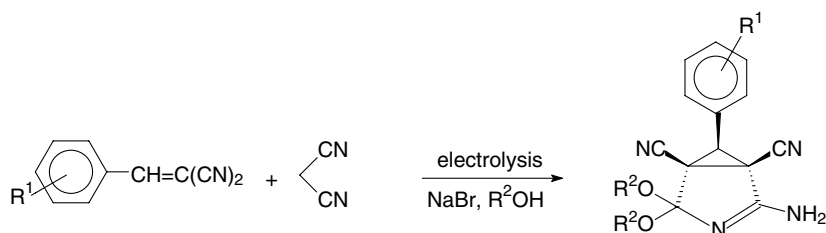
Scheme 2.



Scheme 3.



Scheme 4.



Scheme 5.

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