Electrochemical conversions of alkyl alkylidenecyanoacetates into 3-substituted dialkyl 1,2-dicyanocyclopropane-1,2-dicarboxylates

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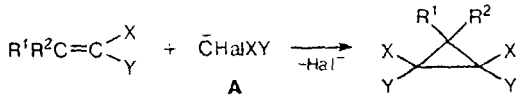
Electrolysis of alkyl alkylidenecyanoacetates in an undivided cell in the presence of alkali metal halides as mediators afforded 3-substituted dialkyl 1,2-dicyanocyclopropane-1,2-dicarboxylates in 50—85% yields.

Key words: electrolysis, alkyl alkylidenecyanoacetates, mediators, substituted dialkyl 1,2-dicyanocyclopropane-1,1-dicarboxylates.

Functionally substituted cyclopropanes belong to a class of important compounds employed in the synthesis of natural biologically active substances.[1] Functionally substituted cyclopropanes as such also exhibit a broad spectrum of physiological activities.[2] Cyclopropanecarboxylic acid derivatives are successfully used in medicine and agriculture. The best known field of their application is insecticides[2,3] based on natural and synthetic pyrethroids. In connection with the aforesaid, the development of new efficient procedures for the preparation of functionally substituted cyclopropanes attracts the attention of researchers.

A known procedure for the synthesis of functionally substituted cyclopropanes involves the addition of anions of halogenated C—H-acids (**A**), which are generated upon the action of bases on the corresponding C—H-acid (**AH**), to conjugated activated olefins. Subsequent cyclization of the anionic adducts that formed is accompanied by elimination of halide anions [4] (Scheme 1).

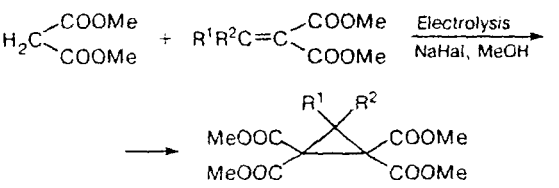
Scheme 1



X = COOR; Y = COOR, CN, or $C(O)NR_2$; Hal = Br or I

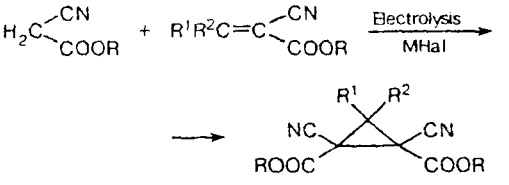
Recently,[5] a new approach to the synthesis of functionally substituted cyclopropanes was suggested. The procedure involves electrolysis of C—H-acids as such rather than their halogeno derivatives and activated olefins. Thus the electrolysis of dimethyl malonate and alkylidenemalonates in an undivided cell with the use of metal halides as mediators proceeds according to Scheme 2.

Scheme 2



With the aim of extending this approach, we synthesized functionally substituted cyclopropanes by co-electrolysis of alkyl cyanoacetates and alkyl alkylidenecyanoacetates[6] (Scheme 3).

Scheme 3



M = Li or Na; Hal = I or Br

In subsequent studies, we found that electrolysis of dimethyl ethylidenemalonate (**1**) in MeCN afforded functionally substituted cyclopropanes with different structures depending on the reaction conditions[7] (Scheme 4).

The electrochemical conversion of malonate **1** into tetramethyl 3-methylcyclopropane-1,1,2,2-tetracarboxy-

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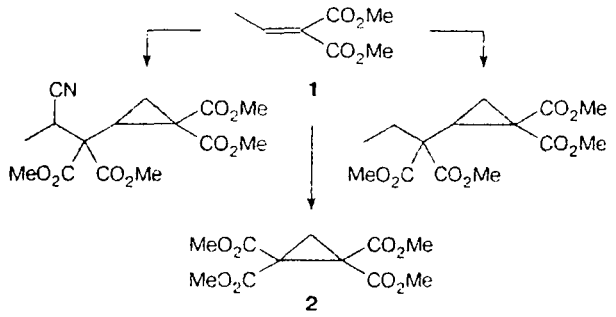
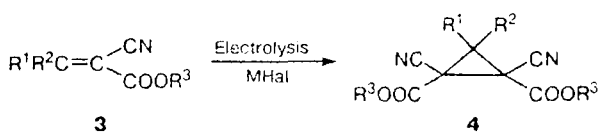
Scheme 4



late (**2**) occurs most successfully in aqueous MeCN in an undivided cell.

The principle of construction of cyclopropane structures by cyclization of malonate **1** to ester **2** served as the basis for the present work, which was devoted to direct electrochemical conversions of alkyl alkylidenecyanoacetates (**3**) into 3-substituted dialkyl 1,2-dicyanocyclopropane-1,2-dicarboxylates (**4**) (Scheme 5, Table 1).

Scheme 5



M = Li or Na; Hal = I or Br

It can be seen from the data presented in Table 1 that 5% aqueous MeOH appeared to be the solvent of choice for performing the reactions under consideration. However, similar results were obtained in the electrolysis of esters **3** in aqueous MeCN and aqueous EtOH.

A decrease in the temperature from 20 to −20 °C led to an increase in the yield of the final reaction product from 60 to 85%. The yields of cyclopropanes reached 70—80% even at 0 °C. From the practical standpoint, electrolysis at 0 °C is a much simpler experimental procedure compared to an analogous process at −20 °C. Because of this, most of the experiments were carried out at 0 °C.

As in the case of the reaction of diethyl malonate with dialkyl alkylidenemalonates[5] and of alkyl cyanoacetates with alkyl alkylidenecyanoacetates,[6] bromides rather than chlorides appeared to be the mediators of choice.

In the case where $R^1 = R^2$, functionally substituted cyclopropanes **4** exist as two isomers with *cis* and *trans* arrangement of the CN and COOR groups, respectively. Under the reaction conditions used, in the case where $R^1 = R^2$, the sterically less hindered *trans* isomer was obtained as the major reaction product.

Table 1. Electrochemical synthesis of 3-substituted dialkyl 1,2-dicyanocyclopropane-1,2-dicarboxylates (**4**)

Run	Initial olefin			Mediator	Solvent (+5% H_2O)	*T* /°C	Product	Yield (%)[a] (ratio of isomers[b])
	R^1	R^2	R^3					
1	Me	Me	Me	NaBr	MeOH	−20	**4a**	85 (5 : 1)
2	Me	Me	Me	NaBr	MeOH	0	**4a**	77 (5 : 1)
3	Me	Me	Me	NaBr	MeOH	20	**4a**	62 (2 : 1)
4	Me	Me	Me	NaI	MeOH	0	**4a**	42 (4 : 1)
5	Me	Me	Me	NaI	MeCN	0	**4a**	61 (2 : 1)
6	Me	Me	Et	NaBr	EtOH	0	**4b**	43 (1 : 1)
7	Et	Me	Me	NaBr	MeOH	0	**4c**	71 (3 : 1 : 1)
8	Pr^n	Me	Me	NaBr	MeOH	0	**4d**	67 (3 : 1 : 1)
9	Pr^n	Pr^n	Me	NaBr	MeOH	0	**4e**	53 (1 : 1)
10	$-(CH_2)_5-$		Me	NaBr	MeOH	0	**4f**	41 (1 : 1)

[a] The yield of compound **4** with respect to **3** used; the conversion of **3** was ≥ 98%.

[b] In the case where $R^1 = R^2$, functionally substituted cyclopropanes **4** exist as two isomers with the *cis* and *trans* arrangement of the CN and COOR groups, respectively. In the case where $R^1 \neq R^2$, a mixture of three isomers was obtained, namely, one isomer with the *trans* arrangement and two isomers with the *cis* arrangement of the CN and COOR groups. See the text.

In the case where $R^1 \neq R^2$, mixtures of three isomers were formed, namely, one isomer with the *trans* arrangement of the CN and COOR groups and two isomers with the *cis* arrangement of these groups. In the ^1H NMR spectra of the major isomer, the position of the singlet of the Me group at the C(3) atom corresponds to the position of the singlet of the Me group in *trans* isomers **4a,b**. Hence, it is believed that the *trans* isomer was also predominantly formed in the case where $R^1 \neq R^2$.

Previously, it was noted that the reactions of alkylidenecyanoacetates with bromomalononitrile afforded predominantly cyclopropanes with *trans* orientation of the COOEt group with respect to the bulkiest substituent.[8] An analogous situation was also observed in the case of electrochemical condensation of alkyl cyanoacetates with alkyl alkylidenecyanoacetates to form 3-substituted dialkyl 1,2-dicyanocyclopropane-1,2-dicarboxylates.[6]

When electrolysis was performed under conditions of run *10* (see Table 1) with the use of NaOAc as the electrolyte by passing 1 *F* of electricity per mole of the initial **3** through the reaction mixture, cyclohexanone and methyl cyanoacetate were formed in 24 and 33% yields, respectively (GLC data). It thus follows that electrolysis of alkyl alkylidenecyanoacetates in aqueous MeOH in the absence of metal halides resulted in their decomposition according to the Knoevenagel retroreaction.

Based on the results obtained, the following mechanism of electrochemical conversions of alkyl alkylidenecyanoacetates can be proposed (Scheme 6).

Scheme 6

Anode: $2\ Hal^- - 2e \longrightarrow Hal_2$ (Hal = I, Br).
Cathode: $2\ H_2O + 2e \longrightarrow 2\ HO^- + H_2$.

In a solution:

$$R^1R^2C{=}C(CN)COOR + HO^- \longrightarrow R^1R^2C{=}O + NCCHCOOR, \quad (1)$$

$$NCCHCOOR + Hal_2 \longrightarrow NCCH(Hal)COOR + Hal^-, \quad (2)$$

$$NCCH(Hal)COOR + HO^- \longrightarrow NCC(Hal)COOR + H_2O, \quad (3)$$

$$NCC(Hal)COOR + \underset{\mathbf{3}}{R^1R^2C{=}C(CN)COOR} \longrightarrow \quad (4)$$

Stage (1) involves the Knoevenagel retro-reaction. This electrolysis-induced process has been observed previously in the case of decomposition of dialkyl ethylidenemalonates.[7] Other electrolysis-induced retro-reactions, *viz.*, decomposition of tetraalkyl propane-1,1,3,3-tetracarboxylates[9] and 2-substituted and 2,2-disubstituted tetraalkyl 1,1,3,3-propanetetracarboxylates[10] according to the Michael retro-reaction, were also reported.

In alcoholic solutions, alkoxyl anions, which are generated on a cathode, along with HO^- anions act as a base in stage (3).

The higher efficiency of NaBr as a mediator compared to that of NaI is apparently due to the fact that the alkyl bromocyanoacetate formed as an intermediate is a stronger C—H-acid than iodocyanoacetate and thus the stage of deprotonation (3) proceeds more rapidly. It is also probable that the rate of addition of the alkyl bromocyanoacetate anion to activated olefin **3** in stage (4) is substantially higher than that in the case of the analogous addition of alkyl iodocyanoacetate.

Experimental

The ^1H and ^{13}C NMR spectra of solutions of the compounds under study in $CDCl_3$ were recorded on Bruker WM-250 (250 MHz) and Bruker AM-300 (300 MHz) instruments. The chemical shifts are given in the δ scale relative to Me_4Si as the internal standard.

The GLC analysis was performed on an LKhM-8MD chromatograph equipped with a flame ionization detector (nitrogen as the carrier gas; the flow rate 30 mL min^{-1}; 2500×3-mm glass column with 5% SE-Superphase on Inerton Super (0.16—0.20 mm)).

Synthesis of cyclopropanes 4 (general procedure). Ester **2** (14 mmol), an electrolyte (mediator) (7 mmol), and a solvent (20 mL) (see Table 1) were placed in an undivided cell with external cooling equipped with an Fe cathode, a C anode (the distance between the electrodes was ~5 mm), a magnetic stirrer, a thermometer, and a reflux condenser. Electrolysis was performed in the constant current mode (the current density was 100 mA cm^{-2}) by passing 2.2 *F* mol^{-1} of electricity. The solvent was evaporated, the residue was washed with water (20 mL), and the products were extracted with chloroform (50 mL). The organic layer was separated and dried with Na_2SO_4. The solvent was evaporated and esters **4a—f** were isolated by vacuum distillation.

Dimethyl *trans*-1,2-dicyano-3,3-dimethylcyclopropane-1,2-dicarboxylate (*trans*-4a)[10] was isolated by crystallization from the reaction mixture (run *1*), m.p. 151—152 °C. ^1H NMR, δ: 1.65 (s, 6 H, Me); 3.93 (s, 6 H, MeO). ^{13}C NMR, δ: 19.4 (q); 37.2 (s); 40.0 (s); 54.9 (q); 113.3 (s); 162.9 (s).

Dimethyl *cis*-1,2-dicyano-3,3-dimethylcyclopropane-1,2-dicarboxylate (4a) was distilled from the reaction mixture (run *3*) (a 2 : 1 mixture of *trans* and *cis* isomers), b.p. 125—127 °C (0.5 Torr). ^1H NMR, δ: *cis*-**4a**: 1.55 (s, 3 H, Me); 1.71 (s, 3 H, Me); 3.87 (s, 6 H, MeO). Found (%): C, 55.75; H, 5.13; N, 11.63. $C_{11}H_{12}N_2O_4$. Calculated (%): C, 55.93; H, 5.08; N, 11.86.

Diethyl 1,2-dicyano-3,3-dimethylcyclopropane-1,2-dicarboxylate (4b)[10] (a 1 : 1 mixture of *trans* and *cis* isomers), b.p. 139—142 °C (0.5 Torr). ^1H NMR, δ: *trans*-**4b**: 1.34 (t, 6 H, Me); 1.62 (s, 6 H, Me); 4.33 (m, 4 H, CH_2O); *cis*-**4b**: 1.29 (t, 6 H, Me); 1.58 (s, 3 H, Me); 1.69 (s, 3 H, Me); 4.30 (m, 4 H, CH_2O). Found (%): C, 58.91; H, 6.15; N, 10.28. $C_{13}H_{16}N_2O_4$. Calculated (%): C, 59.09; H, 6.06; N, 10.61.

Dimethyl 1,2-dicyano-3-ethyl-3-methylcyclopropane-1,2-dicarboxylate (4c) (a 3 : 1 : 1 mixture of isomers), b.p. 132—134 °C (0.5 Torr). ^1H NMR, δ: 1.02, 1.05, and 1.17 (all t, 3 H, $CH_2\underline{CH_3}$); 1.52, 1.58 (*trans* isomer), and 1.68 (all s, 3 H, Me); 1.85—2.05 (m, 2 H, CH_2); 3.86, 3.87, 3.89, and 3.90 (all s, 6 H, MeO). Found (%): C, 57.42; H, 5.73; N, 10.89. $C_{12}H_{14}N_2O_4$. Calculated (%): C, 57.61; H, 5.60; N, 11.21.

Dimethyl 1,2-dicyano-3-methyl-3-propylcyclopropane-1,2-dicarboxylate (4d) (a 3 : 1 : 1 mixture of isomers), b.p. 131—133 °C (0.3 Torr). ^1H NMR, δ: 0.91, 0.98, and 1.05 (all t, 3 H, $CH_2\underline{CH_2}$); 1.20—1.40 (m, 2 H, $\underline{CH_2}CH_3$); 1.49, 1.58 (*trans* isomer), and 1.68 (all s, 3 H, Me); 1.83—1.95 (m, 2 H, CH_2); 3.80, 3.84, 3.90, and 3.91 (all s, 6 H, MeO). Found (%): C, 58.91; H, 5.88; N, 10.33. $C_{13}H_{16}N_2O_4$. Calculated (%): C, 59.09; H, 6.06; N, 10.61.

Dimethyl 1,2-dicyano-3,3-dipropylcyclopropane-1,2-dicarboxylate (4e) (a 1 : 1 mixture of *trans* and *cis* isomers), b.p. 140—143 °C (0.3 Torr). ^1H NMR, δ: 0.88, 0.97, and 1.07 (all t, 6 H, Me); 1.45—1.55 (m, 4 H, CH_2); 1.75—1.93 (m, 4 H, CH_2); 3.89 and 3.90 (both s, 6 H, MeO). Found (%): C, 61.38; H, 6.57; N, 9.37. $C_{15}H_{20}N_2O_4$. Calculated (%): C, 61.64; H, 6.85; N, 9.59.

Dimethyl 1,2-dicyanospiro[2.5]octane-1,2-dicarboxylate (4f) (a 1 : 1 mixture of *trans* and *cis* isomers,), b.p. 137—140 °C (0.2 Torr). ^1H NMR, δ: 1.52—1.79 (m, 6 H, CH_2); 1.90—2.05 (m, 4 H, CH_2); 3.88 and 3.91 (both s, 6 H, MeO). ^{13}C NMR, δ: 24.8 (t); 28.9 (t); 33.0 (t); 34.1 (s); 35.0 (s); 43.7 (s); 44.5 (s); 54.5 (q); 54.9 (q); 112.1 (s); 113.0 (s); 160.4 (s); 160.8 (s). Found (%): C, 60.56; H, 5.49; N, 9.87. $C_{14}H_{16}N_2O_4$. Calculated (%): C, 60.87; H, 5.80; N, 10.14.

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References

1. T. Tsuji and S. Nishida, *The Chemistry of the Cyclopropyl Group*, J. Wiley and Sons, New York, 1987.
2. L. A. Yanovskaya, V. A. Dombrovskii, and A. Kh. Khusid, *Tsiklopropany s funktsional'nymi gruppami. Sintez i primenenie* [*Cyclopropanes with Functional Groups. Synthesis and Application*], Nauka, Moscow, 1980 (in Russian).
3. J. Crosby, *Tetrahedron*, 1991, **47**, 4789.
4. G. Bonavent, M. Causse, M. Guittard, and R. Fraisse-Julien, *Bull. Soc. Chim. Fr.*, 1964, 2462.
5. M. N. Elinson, S. K. Feducovich, S. G. Bushuev, A. A. Zakharenkov, D. V. Pashchenko, and G. I. Nikishin, *Mendeleev Commun.*, 1998, 15.
6. M. N. Elinson, S. K. Feducovich, S. G. Bushuev, D. V. Pashchenko, and G. I. Nikishin, *Izv. Akad. Nauk, Ser. Khim.*, 1998, 1165 [*Russ. Chem. Bull.*, 1998, **47**, 1133 (Engl. Transl.)].
7. M. N. Elinson, S. K. Feducovich, A. A. Zakharenkov, and G. I. Nikishin, *Mendeleev Commun.*, 1999, 20.
8. J. C. Kim and H. Hart, *J. Chem. Soc., C*, 1969, 2409.
9. M. N. Elinson, S. K. Feducovich, S. V. Lindeman, M. S. Aleksanyan, Yu. T. Struchkov, and G. I. Nikishin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1989, 1603 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1989, **38**, 1467 (Engl. Transl.)].
10. M. N. Elinson, S. K. Feducovich, and G. I. Nikishin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1990, 2783 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1990, **39**, 2523 (Engl. Transl.)].

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