Electrochemical transformation of cyanoacetic ester and alkylidenecyanoacetic esters into 3-substituted 1,2-dicyanocyclopropane-1,2-dicarboxylates

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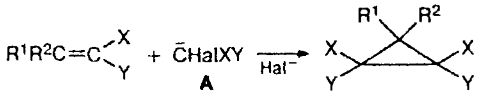
Electrolysis of cyanoacetic ester and alkylidenecyanoacetic esters in an undivided cell in the presence of mediators (alkali metal halides) gives rise to 3-substituted 1,2-dicyanocyclopropane-1,2-dicarboxylates in 60—95% yields.

Key words: electrolysis, cyanoacetic ester, alkylidenecyanoacetic esters, mediators, 3-substituted 1,2-dicyanocyclopropane-1,2-dicarboxylates.

Functionally substituted cyclopropanes constitute an important class of compounds used in the synthesis of natural biologically active substances.[1] In addition, functionally substituted cyclopropanes by themselves also manifest a broad range of biological activities.[2] Derivatives of cyclopropanecarboxylic acids are successfully employed in medicine and agriculture. The best known application of this type of compounds is the use of natural and synthetic pyrethroids as insecticides.[2,3] Therefore, development of simple and efficient methods for the synthesis of functionally substituted cyclopropanes still remains an important problem.

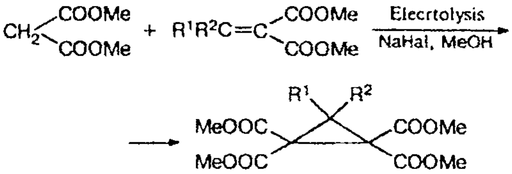
A known method for the preparation of functionally substituted cyclopropanes is based on the addition of anions of halogen-substituted C—H acids (**A**), prepared by treatment of the corresponding C—H acids (**AH**) with bases, to conjugated activated olefins followed by cyclization of the adduct anion accompanied by elimination of a halide ion:[4]



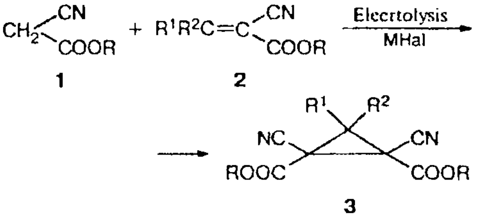
X = COOR, Hal = Br, I
Y = COOR, CN, C(O)NR$_2$

Later, generation of type **A** anions from halo-substituted C—H acids and the reactions of these anions with activated olefins were carried out using two-phase systems and phase transfer catalysts.[5,6] In recent years, functionally substituted cyclopropanes have been obtained by electroreduction of ethyl dihalomalonate to the corresponsding anions (**A**, X = Y = COOR) in the presence of activated olefins.[7,8]

Recently, we proposed a new approach to the synthesis of functionally substituted cyclopropanes. This appoach was based on the electrolysis of C—H acids themselves (rather than halo-substituted C—H acids) together with activated olefins; more precisely, malonic ester and alkylidenemalonates were subjected to joint electrolysis in an undivided cell in the presence of metal halides as mediators:[9]



This work deals with the further development of the method for the synthesis of functionally substituted cyclopropanes directly from C—H acids and conjugated activated olefins; for this purpose, we prepared functionally substituted cyclopropanes by electrolysis of alkyl cyanoacetates (**1**) with alkylidenecyanoacetates (**2**) in an undivided cell in the presence of metal halides as mediators (Table 1):



M = Li, Na; Hal = I, Br

The joint electrolysis of methyl (**1a**) or ethyl (**1b**) cyanoacetate and alkylidenecyanoacetates in methanol or ethanol, respectively, was carried out in an undivided

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Table 1. Electrosynthesis of 3-substituted 1,2-dicyanocyclopropane-1,2-dicarboxylates[a]

Entry	Starting ester	Starting olefin		Mediator	Solvent	Quantity of electricity /F mol^{-1}	Yield of cyclopropane (%)[b] (Isomer ratio[c])
	R	R^1	R^2				
1	Et	Me	Me	NaI	EtOH	2.2	**3a**, 78 (3 : 1)
2	Et	Me	Me	NaBr	EtOH	2.2	**3a**, 95 (3 : 1)
3	Me	Me	Me	NaBr	MeOH	2.2	**3b**, 56 (4 : 1)
4	Et	Me	Me	LiBr	Acetone	2.2	**3a**, 80 (2 : 1)
5	Et	Me	Me	LiBr	MeCN	2.2	**3a**, 66 (3 : 2)
6	Et	Me	Et	NaBr	EtOH	2.2	**3c**, 88 (2 : 1 : 1)
7	Me	Me	Et	NaBr	MeOH	2.2	**3d**, 65 (2 : 1 : 1)
8	Et	Me	Pr^n	NaBr	EtOH	2.4	**3e**, 86 (2 : 1 : 1)
9	Me	Me	Pr^n	NaBr	MeOH	2.4	**3f**, 70 (2 : 1 : 1)
10	Et	Me	*cyclo*-Pr	NaBr	EtOH	2.5	**3g**, 67 (3 : 1 : 1)
11	Me	Me	*cyclo*-Pr	NaBr	MeOH	2.5	**3h**, 62 (4 : 1 : 1)
12	Me	Pr^n	Pr^n	NaBr	EtOH	2.5	**3i**, 78 (3 : 1)
13	Et	$-(CH_2)_5-$		NaBr	EtOH	2.4	**3j**, 95 (1 : 1)
14	Et	$-(CH_2)_6-$		NaBr	EtOH	2.4	**3k**, 84 (1 : 1)

[a] *Conditions:* 14 mmol of ester **1**, 14 mmol of olefin **2**, and 7 mmol of a mediator in 20 mL of a solvent, Fe cathode, C anode, current density 100 mA cm^{-2}, temperature 10 °C.

[b] The isolated yield of cyclopropane **3** based on the taken ester **1**; the degree of conversion of **1** and **2** was ≥98%.

[c] At R^1 = R^2, functionally substituted cyclopropanes **3** exist as two isomers with *cis*- and *trans*-arrangements of the CN and COOR groups. At R^1 ≠ R^2, a mixture of three isomers is formed: an isomer with *trans*-arranged CN and COOR groups and two isomers with the *cis*-arrangement of these groups (see the relevant discussion in the text).

cell, equipped with a graphite anode and an iron cathode, with constant current density until the cyanoacetate and alkylidenecyanoacetate were completely consumed.

The optimum temperature for the electrolysis is +10 °C. An increase in the temperature to +30 °C (which is the optimum temperature for the electrolysis of ethyl malonate in the presence of alkylidenemalonates[9]) decreases the yield of the corresponding cyclopropane derivative by 20—30%.

When the temperature is lowered to 0 °C or −10 °C, the yield of the final reaction product does not increase.

As in the case of the similar reaction of ethyl malonate with alkylidenemalonates,[9] bromides proved to be better mediators than iodides.

The reactions carried out in ethanol normally result in better yields of functionally substituted cyclopropanes **3**. The process can also be accomplished in acetone or acetonitrile; however, the yields of cyclopropane derivatives **3** in these solvents are lower. Lower yields of cyclic products have also been obtained when electrolysis was carried out in methanol.

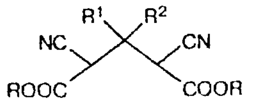
The difference between ethanol and methanol is especially pronounced for the initial compounds of the series in which substituents R^1 and R^2 are small. For instance, for R^1 = R^2 = Me, the yield of **3a** in ethanol is 95%, and the yield of **3b** in methanol is 56% (Table 1, entries 2 and 3). This is due to the fact that dimerization of alkylidenecyanoacetate catalyzed by an electrically generated base and resulting in the formation of several dimeric and oligomeric by-products proceeds more efficiently in methanol.[10]

In the case where R^1 = R^2, functionally substituted cyclopropanes can exist as two isomers with the *cis*- and *trans*-arrangements of the CN and COOR groups. In the reaction studied here at R^1 = R^2, the *trans*-isomer, which is sterically less hindered, is formed predominantly.

When R^1 ≠ R^2, the reaction yields a mixture of three isomers, one of which contains *trans*-arranged CN and COOR groups and two of which contain these groups in *cis*-positions. The ^{1}H NMR chemical shift of the singlet due to the Me group attached to C(3) in the major isomer is close to that of the signal for the Me group in *trans*-**3a**,**b**. This fact implies that at R^1 ≠ R^2, the *trans*-isomer is also the major product.

In a previous study it has been noted that the reaction of alkylidenecyanoacetates with bromomalononitriles yields predominantly isomers with the *trans*-arrangement of the COOEt group in relation to the bulkiest substituent.[11]

When the quantity of electricity passed decreased to 0.5 and 1.0 F per mole of cyanoacetate **1**, ester **1** and activated olefin **2** were not completely converted, and cyclopropane **3** formed in a lower yield. No compounds of type **4** were detected in the reaction mixture.



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Based on the results obtained, we propose the following mechanism for the process in question:

$$\text{anode: } 2\,\text{Hal}^- - 2\,e \longrightarrow \text{Hal}_2 \qquad (\text{Hal} = \text{I, Br})$$

cathode: $2\ NCCH_2COOR + 2\ e \longrightarrow 2\ NC\bar{C}HCOOR + H_2$

in alcohols:

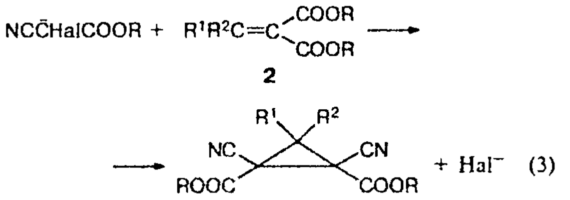
cathode: $2\ ROH + 2\ e \longrightarrow 2\ RO^- + H_2$

$2\ NCCH_2COOR + 2\ RO^- \longrightarrow 2\ NC\bar{C}HCOOR + H_2$

in solution:

$NC\bar{C}HCOOR + Hal_2 \longrightarrow NCCHHalCOOR + Hal^- \quad (1)$

$NCCHHalCOOR + NC\bar{C}HCOOR \longrightarrow$
$\longrightarrow NC\bar{C}HalCOOR + NCCH_2COOR \quad (2)$



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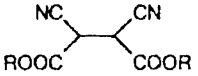
It is known that electrolysis of ethyl cyanoacetate in an undivided cell in the presence of metal halides as mediators does not give a dimer (ester 5), but gives a cyclic trimer, *trans*-1,2,3-tricyanocyclopropane-1,2,3-tricarboxylate,[12] which is produced *via* the intermediate formation of the anion of halocyanoacetic ester. This fact is in full agreement with steps (1) and (2) of the mechanism that we propose in this study.



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The higher efficiency of NaBr as mediator compared to NaI is due to the fact that the intermediate alkyl bromocyanoacetate is a stronger C—H acid than alkyl iodocyanoacetate, and so the proton transfer step (2) occurs faster in the former case. It is also possible that the rate of addition of the ion derived from alkyl bromocyanoacetate to activated alkene 2 in step (3) is also markedly higher than the rate of the similar addition in the case of iodomalonate.

Experimental

The ^{1}H and ^{13}C NMR spectra of solutions of substances in $CDCl_3$ were recorded on Bruker WM-250 (250 MHz) and Bruker AM-300 (300 MHz) instruments; the chemical shifts are presented in the δ scale and referred to tetramethylsilane as the internal standard.

GLC analysis was carried out on an LKh-8MD chromatograph equipped with a flame ionization detector and a 2500×3 mm glass column with 5% SE-Superphase on Inerton Super (0.16—0.20 mm); nitrogen passed at a rate of 30 mL min^{-1} was used as the carrier gas.

Electrosynthesis of 3-substituted 1,2-dicyanocyclopropane-1,2-dicarboxylates (general procedure). Ester **1** (14 mmol), activated olefin **2** (14 mmol), an electrolyte (mediator) (7 mmol), and a solvent (20 mL) were placed in an undivided electrolytic 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. Then the mixture was electrolyzed with constant current density (100 mA cm^{-2}); the quantities of electricity passed are presented in Table 1. The reaction mixture was concentrated, washed with 20 mL of water, and extracted with 50 mL of chloroform. The organic layer was separated, dried with Na_2SO_4, and concentrated. Vacuum distillation of the residue gave esters **3a—k**.

Diethyl 1,2-dicyano-3,3-dimethylcyclopropane-1,2-dicarboxylate (3a) (ratio *trans/cis* = 3 : 1), b.p. 139—142 °C (0.5 Torr). ^{1}H NMR, *trans*-**3a**, δ: 1.34 (t, 6 H, CH_3); 1.62 (s, 6 H, CH_3); 4.33 (m, 4 H, CH_2O). ^{1}H NMR, *cis*-**3a**, δ: 1.29 (t, 6 H, CH_3); 1.58 (t, 3 H, CH_3); 1.69 (s, 3 H, CH_3); 4.30 (m, 4 H, CH_2O). ^{13}C NMR, *trans*-**3a**, δ: 13.76 q, 19.16 q, 35.14 s, 38.30 s, 64.12 t, 112.11 s, 160.80 s. ^{13}C NMR, *cis*-**3a**, δ: 13.81 q, 23.09 q, 24.77 q, 35.56 s, 37.55 s, 63.71 t, 113.05 s, 160.45 s. Found (%): C, 58.85; H, 6.11; N, 10.37. $C_{13}H_{16}N_2O_4$. Calculated (%): C, 59.09; H, 6.06; N, 10.61.

Dimethyl 1,2-dicyano-3,3-dimethylcyclopropane-1,2-dicarboxylate (3b) (*trans/cis* ratio = 2 : 1), b.p. 125—127 °C (0.5 Torr). ^{1}H NMR, *cis*-**3b**, δ: 1.55 (s, 3 H, CH_3); 1.71 (s, 3 H, CH_3); 3.87 (s, 6 H, CH_3O). 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.

Dimethyl *trans*-1,2-dicyano-3,3-dimethylcyclopropane-1,2-dicarboxylate (*trans*-3b) was isolated from the reaction mixture by crystallization (entry 3), m.p. 151—152 °C. ^{1}H NMR, δ: 1.65 (s, 6 H, CH_3); 3.93 (s, 6 H, CH_3O). ^{13}C NMR, δ: 19.38 q, 37.20 s, 39.95 s, 54.86 q, 113.30 s, 162.86 s. Found (%): C, 55.81; H, 5.11; N, 11.69. $C_{11}H_{12}N_2O_4$. Calculated (%): C, 55.93; H, 5.08; N, 11.86.

Diethyl 1,2-dicyano-3-ethyl-3-methylcyclopropane-1,2-dicarboxylate (3c) (isomer ratio = 2 : 1 : 1), b.p. 133—135 °C (0.3 Torr). ^{1}H NMR, δ: 0.95 t, 1.05 t, 1.15 t (3 H, $CH_2\underline{CH}_3$); 1.30 t, 1.33 t (6 H, $OCH_2\underline{CH}_3$); 1.48 s, 1.57 s (*trans*-isomer); 1.66 s (3 H, CH_3); 1.80—2.00 (m, 2 H, $\underline{CH}_2CH_3$), 4.25 and 4.33 (both m, 4 H, CH_2O). Found (%): C, 60.25; H, 6.36; N, 9.83. $C_{14}H_{18}N_2O_4$. Calculated (%): C, 60.43; H, 6.47; N, 10.07.

Dimethyl 1,2-dicyano-3-ethyl-3-methylcyclopropane-1,2-dicarboxylate (3d) (isomer ratio = 2 : 1 : 1), b.p. 132—134 °C (0.5 Torr). ^{1}H NMR, δ: 1.02, 1.05, 1.17 (all t, 3 H, $CH_2\underline{CH}_3$); 1.52, 1.58 (*trans*-isomer), 1.68 (all s, 3 H, CH_3); 1.85—2.05 (m, 2 H, CH_2); 3.86, 3.87, 3.89, 3.90 (all s, 6 H, CH_3O). Found (%): C, 57.33; H, 5.67; N, 10.97. $C_{12}H_{14}N_2O_4$. Calculated: C, 57.61; H, 5.60; N, 11.21.

Diethyl 1,2-dicyano-3-methyl-3-propylcyclopropane-1,2-dicarboxylate (3e) (isomer ratio = 2 : 1 : 1), b.p. 138—142 °C (0.3 Torr). ^{1}H NMR, δ: 0.91, 0.95, 1.02 (all t, 3 H, $CH_2\underline{CH}_3$); 1.20—1.38 (m, 8 H, $\underline{CH}_2CH_3$ and $OCH_2\underline{CH}_3$); 1.52, 1.58 (*trans*-isomer), 1.68 (all s, 3 H, CH_3); 1.85—2.00 (m, 2 H, CH_2); 4.25—4.40 (m, 4 H, CH_2O). Found (%): C, 61.37; H, 6.91; N, 9.27. $C_{15}H_{20}N_2O_4$. Calculated (%): C, 61.64; H, 6.85, N, 9.59.

Dimethyl 1,2-dicyano-3-methyl-3-propylcyclopropane-1,2-dicarboxylate (3f) (isomer ratio = 2 : 1 : 1), b.p. 131—133 °C (0.3 Torr). ^{1}H NMR, δ: 0.91, 0.98, 1.05 (all t, 3 H, $CH_2\underline{CH}_3$); 1.20—1.40 (m, 2 H, $\underline{CH}_2CH_3$); 1.49, 1.58 (*trans*-isomer), 1.68 (all s, 3 H, CH_3); 1.83—1.95 (m, 2 H, CH_2); 3.80, 3.84, 3.90, 3.91 (all s, 6 H, CH_3O). Found (%): C, 58.83; H, 5.97; N, 10.29. $C_{13}H_{16}N_2O_4$. Calculated (%): C, 59.09; H, 6.06; N, 10.61.

Diethyl 1,2-dicyano-3-cyclopropyl-3-methylcyclopropane-1,2-dicarboxylate (3g) (isomer ratio = 3 : 1 : 1), b.p. 148—151 °C (0.3 Torr). ^{1}H NMR, δ: 0.58—0.90 (m, 5 H, CH and CH_2); 1.12, 1.22, 1.32 (all s, 3 H, CH_3); 1.34—1.36 (m, 6 H, CH_3); 4.22—4.40 (m, 4 H, CH_2O). Found (%): C, 61.93; H, 6.07; N, 9.47. $C_{15}H_{18}N_2O_4$. Calculated (%): C, 62.07; H, 6.21; N, 9.66.

Dimethyl 1,2-dicyano-3-cyclopropyl-3-methylcyclopropane-1,2-dicarboxylate (3h) (isomer ratio = 4 : 1 : 1), b.p. 154—156 °C (0.6 Torr). ^{1}H NMR, δ: 0.60—0.90 (m, 5 H, CH and CH_2); 1.14, 1.23, 1.34 (all s, 3 H, CH_3); 3.85, 3.87, 3.93, 3.94 (all s, 6 H, OCH_3). Found (%): C, 59.33; H, 5.37; N, 10.37. $C_{13}H_{14}N_2O_4$. Calculated (%): C, 59.54; H, 5.34; N, 10.69.

Diethyl 1,2-dicyano-3,3-dipropylcyclopropane-1,2-dicarboxylate (3i) (*trans/cis* ratio = 1 : 1), b.p. 154—158 °C (0.3 Torr). ^{1}H NMR, δ: 0.88, 0.97, 1,07 (all t, 6 H, $CH_2\underline{CH_3}$); 1.33, 1.37 (all t, 6 H, $OCH_2\underline{CH_3}$); 1.45—1.55 (m, 4 H, CH_2); 1.75—1.93 (m, 4 H, CH_2); 4.29 and 4.38 (both m, 4 H, CH_2O). Found (%): C, 63.38; H, 7.57; N, 8.39. $C_{17}H_{24}N_2O_4$. Calculated (%): C, 63.75; H, 7.51; N, 8.75.

Diethyl 1,2-dicyanospiro[2.5]octane-1,2-dicarboxylate (3j) (*trans/cis* ratio = 1 : 1), b.p. 157—160 °C (0.2 Torr). ^{1}H NMR, δ: 1.32 (t, 3 H, CH_3); 1.36 (t, 3 H, CH_3); 1.52—1.79 (m, 6 H, CH_2); 1.90—2.05 (m, 4 H, CH_2); 4.29 (m, 2 H, CH_2O); 4.37 (m, 2 H, CH_2O). ^{13}C NMR, δ: 13.76 q, 13.81 q, 24.75 t, 28.86 t, 32.95 t, 34.11 s, 34.97 s, 43.70 s, 44.48 s, 63.77 t, 64.11 t, 112.06 s, 112.99 s, 160.40 s, 160.76 s. Found (%): C, 62.83; H, 6.67; N, 8.97. $C_{16}H_{20}N_2O_4$. Calculated (%): C, 63.16; H, 6.58; N, 9.21.

Diethyl 1,2-dicyanospiro[2.6]nonane-1,2-dicarboxylate (3k) (*trans/cis* ratio = 1 : 1), b.p. 168—173 °C (0.2 Torr). ^{1}H NMR, δ: 1.31 (t, 3 H, CH_3); 1.35 (t, 3 H, CH_3); 1.50—1.85 (m, 8 H, CH_2); 1.93—2.09 (m, 4 H, CH_2); 4.28 (m, 2 H, CH_2O); 4,35 (m, 2 H, CH_2O). Found (%): C, 63.83; H, 6.87; N, 8.53. $C_{17}H_{22}N_2O_4$. Calculated (%): C, 64.15; H, 6.92; N, 8.81.

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References

1. T. Tsuji and S. Nishida, *The Chemistry of the Cyclopropyl Group*, Wiley, 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. A. Jonczyk and M. Makosza, *Synthesis*, 1976, 387.
6. G. V. Kryshtal', N. I. Shtemenko, and L. A. Yanovskaya, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1980, 2420 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1980, **29** (Engl. Transl.)].
7. J.-C. Le Menn, J. Sarrazin, and A. Talles, *Electrochim. Acta*, 1990, **35**, 563.
8. J.-C. Le Menn, J. Sarrazin, and A. Talles, *Can. J. Chem.*, 1991, **69**, 761.
9. M. N. Elinson, S. K. Feducovich, S. G. Bushuev, A. A. Zakharenkov, D. V. Pashchenko, and G. I. Nikishin, *Mendelev Commun.*, 1998, 15.
10. S. F. Birch and G. A. R. Kon, *J. Chem. Soc.*, 1923, **123**, 2440.
11. J. C. Kim and H. Hart, *J. Chem. Soc., C*, 1969, 2409.
12. M. N. Elinson, T. L. Lizunova, M. O. Dekaprilevich, Yu. T. Struchkov, and G. I. Nikishin, *Mendeleev Commun.*, 1993, 191.

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