Synthesis of 4-(ω-X-alkyl)benzonitriles (X = 1,3-dioxan-2-yl, CN, CO_2Et) by the reaction of terephthalonitrile dianion with ω-X-alkyl bromides in liquid ammonia

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The main products of the reaction of terephthalonitrile dianion disodium salt with ω-X-alkyl bromides (2-(2-bromoethyl)-1,3-dioxane, 5-bromovaleronitrile, ethyl 6-bromohexanoate) in liquid ammonia are the corresponding 4-(ω-X-alkyl)benzonitriles. Similar reactions of benzonitrile radical anion sodium salt lead to ω-X-alkylbenzenes. In both cases the formation of products is due to selective *ipso*-alkylation of anionic forms that indicates the nucleophilic activity of terephthalonitrile dianion and benzonitrile radical anion in these reactions and the realization of alkylation *via* S_N2 mechanism.

Key words: terephthalonitrile, benzonitrile, reductive alkylation, alkyl bromides, dianions, radical anions.

Benzonitriles, containing alkyl or ω-functionalized alkyl fragments in *para*-position, are traditionally used as universal structural blocks in fine organic synthesis of compounds with wide range of practical applications (liquid crystals,[1] pigments,[2] macrostructures,[3] repellents,[4] herbicides,[5] sound absorbents,[6] oligomer electron acceptors,[7] biologically active compounds and drugs[8]). Functionalized benzonitriles are usually obtained by Wurtz—Fittig reaction,[9] photochemical processes,[10] catalytic[11] and electrochemical[12] cross-couplings. Despite the prevalence and relatively high efficiency of these methods, their main disadvantages include the need for pre-activation of substrates (in particular, the introduction of metal and organometallic substituents), the use of expensive catalysts and ligands or specific experimental conditions. It is also important to note that such methods bring about products which can be contaminated with transition metal compounds. This requires their special purification prior to their use in pharmacy.[13] In this connection, a synthetic approach using reductive alkylation of available terephthalonitrile (**1**) in liquid ammonia looks attractive. Previously, it was shown that dianion $[\mathbf{1}]^{2-}$, generated by two-electron reduction of dinitrile **1** with alkali metal in liquid ammonia, is highly effective synthon of *para*-cyanophenylation of alkyl-, ω-alkenyl halides, and α,ω-dibromoalkanes. This reaction proceeds by the competing mechanisms of nucleophilic substitution (S_N2) and electron transfer, followed by the recombination (*ET*). On this basis, an universal access to 4-alkyl (**2**),[14] 4-(ω-alkenyl)benzonitriles (**3a—f**),[15] and α,ω-bis(*p*-cyanophenyl)alkanes (**4**),[16] which allows obtaining the products with 40—90% yields (Scheme 1), was proposed.

The aim of this work is extension of the synthetic potential of dianion $[\mathbf{1}]^{2-}$ in the production of ω-functionalized alkylbenzonitriles. Primary alkyl bromides, namely 2-(2-bromoethyl)-1,3-dioxane (**5a**), 5-bromovaleronitrile (**5b**), and ethyl 6-bromohexanoate (**5c**), differing both by the length of alkylene fragment between bromine atom and functional group and by nature of the functional group, were selected for the investigation of activity of dianion $[\mathbf{1}]^{2-}$ in respect to ω-functionalized alkyl halides. The choice of bromides as alkylation agents is supposed to be optimal as S_N2-reaction of $[\mathbf{1}]^{2-}$ with alkyl chlorides in liquid ammonia proceeds slower than with alkyl bromides. In the case of alkyl iodides *ET* process dominates in the competition between two mechanisms (S_N2 and *ET*), which leads to the 2-alkylterephtalonitriles along with 4-alkylbenzonitriles in the ratio 1/(6—2), respectively (C.f. Ref. 14a). However, it was difficult to predict before setting up the experiments that interaction of $[\mathbf{1}]^{2-}$ with alkyl bromides **5a—c** would proceed solely by the way of *ipso*-alkylation. Really, dianion $[\mathbf{1}]^{2-}$ is highly basic and thus is capable of protonation with relatively acidic

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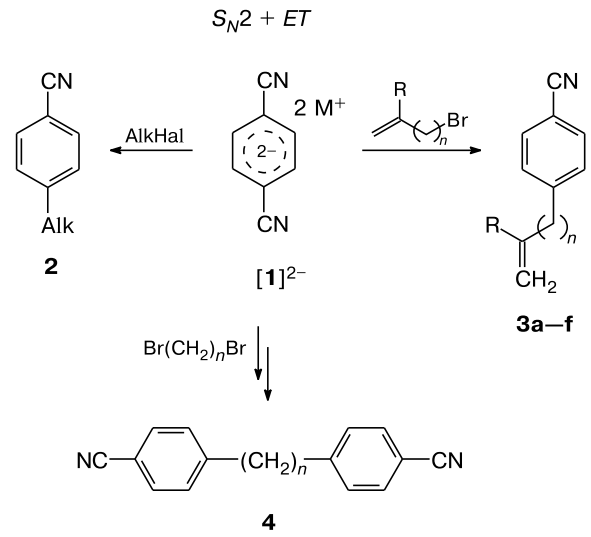
Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 10, pp. 2430—2436, October, 2016.

1066-5285/16/6510-2430

Scheme 1



2: Alk = *n*-, *i*-, *s*-, *t*-Bu; *n*-C_5H_{11}, *n*-C_8H_{17}, *c*-C_6H_{11}; Hal = Cl. Br, I

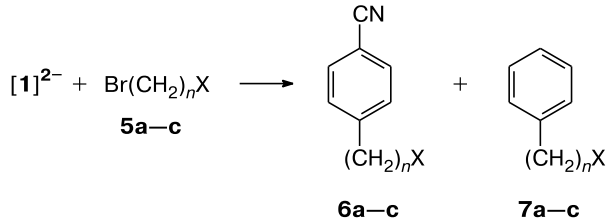
3	*n*	R	**3**	*n*	R
a	1	H	d	2	H
b	1	Me	e	3	H
c	1	F	f	4	H

4: *n* = 3, 4, 5

α-protons of ester **5b** or nitrile **5c**, which can afford benzonitrile.[14a,17] In addition, there is a possibility of reduction of reactants **5a—c** with dianion $[\mathbf{1}]^{2-}$ without the formation of alkylation products (compare Refs 18, 19). Anyway, the data on the use of such ω-modified alkyl halides in the Birch reactions of the reductive alkylation of biphenyl and benzoic acid derivatives[20] allowed one to hope for the positive results.

The dianion $[\mathbf{1}]^{2-}$ was generated by reduction of dinitrile **1** suspension in liquid ammonia with sodium metal (2.15—2.20 eq) which is more convenient compared to lithium and potassium. It was shown earlier[15] that the yields of alkylation products of alkali salt of dianion $[\mathbf{1}]^{2-}$ are weakly dependent on the nature of the metal (increase by ~3—5% in the following order $[\mathbf{1}]^{2-}[2Li^+] < [\mathbf{1}]^{2-}[2Na^+] < [\mathbf{1}]^{2-}[2K^+]$). An addition to the suspension of disodium salt of dianion $[\mathbf{1}]^{2-}$ in liquid ammonia of slight excess (1.3 eq) of bromide **5a—c** yielded the mixture of compounds mainly consisting of expected product, namely corresponding 4-(ω-X-alkyl)-benzonitrile **6a—c** (40—60% according to combined data of ^{1}H NMR and GC/MS) (Scheme 2, Table 1). However, besides compounds **6a—c** the corresponding ω-X-alkylbenzene **7a—c** (20—30%), alkylation agents **5a—c** (15—20%), and also starting dinitrile **1** (up to 20%) and some amount of minor unidentified components (total content <5%) were present in the reaction mixture. Also, according to GC/MS data the compounds with molecular ion masses corresponding to the products of *ortho*-alkylation of dianion $[\mathbf{1}]^{2-}$ were also present. The formation of these products is possible within *ET* mechanism. However, their content was very small: up to 2—3% for alkylation reagents **5b,c**, and up to 6% for bromo acetal **5a**. The products of the reductive transformations of functional groups with the reagents **5a—c** were absent. Thus, the interaction of $[\mathbf{1}]^{2-}$ with ω-X-alkyl bromides **5a—c** in ammonia proceeds predominantly as *ipso*-alkylation and results in 4-(ω-X-alkyl)benzonitriles **6a—c** in reasonable yields (see Table 1). Such orientation of the alkylation is obviously due to dominance nucleophilic component of dianion $[\mathbf{1}]^{2-}$ reactivity as in the case of unmodified primary alkyl bromides (compare Ref. 14).

Scheme 2



The most probable mechanism of the formation of the desired products **6a—c** is shown in Scheme 3. It is heterolytic (S_N2 mechanism) alkylation of the dianion by the site of maximal electron density[14,21] with the formation of cyclohexadienyl anion [**1—Alk**]$^-$, which undergoes aromatization upon rapid decyanation yielding modified benzonitriles **6a—c**.

The presence of ω-X-alkylbenzene **7** in noticeable amounts in the products can be explained as follows. First, initially formed 4-(ω-X-alkyl)benzonitriles **6** can be

Table 1. Reaction of disodium salt of dianion $[\mathbf{1}]^{2-}$ with ω-X-alkyl bromides **5a—c** in liquid ammonia[a]

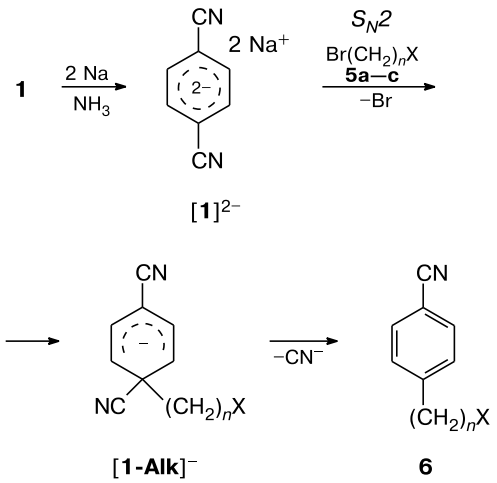
5	X	*n*	Products	Yield (%)	
				^{1}H NMR and GC/MS	TLC[c]
a	1,3-Dioxan-2-yl	2	**6a**	42	36
			7a	24	23
b	CN	4	**6b**	58	52
			7b	23	18
c	CO_2Et	5	**6c**	48	45
			7c	27	25

[a] Conditions: 2.15—2.20 eq of Na, 1.3 eq. of $Br(CH_2)_nX$ (**5a—c**), NH_3 (liquid), −33 °C, 1.5 h.

[b] Yield is presented according to joint data of ^{1}H NMR and GC/MS (by not less than two experiments, deviation of presented value not more than 5%).

[c] Separated using preparative TLC.

Scheme 3

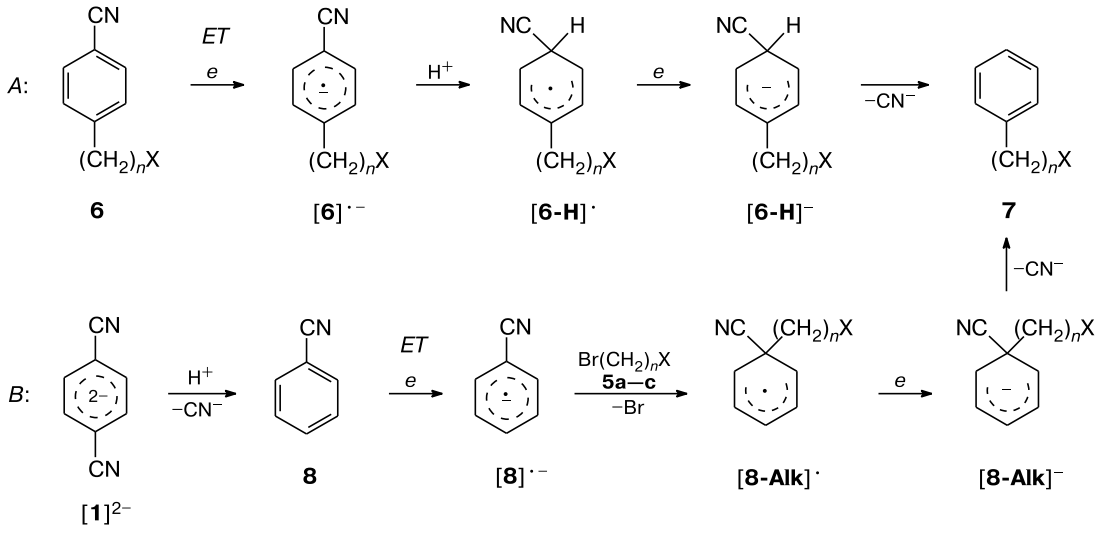


reduced by dianion $[\mathbf{1}]^{2-}$, as well as by excess alkali metal to radical anion $[\mathbf{6}]^{\bullet-}$, which upon further processing are protonated and finally transformed into alkylbenzenes **7** (Scheme 4, route *A*). This suggestion is rather probable due to described earlier results of the interaction of dianion $[\mathbf{1}]^{2-}$ with α,ω-dibromoalkanes.[16] Regardless on the ratio of the reagents, this reaction yields solely α,ω-bis(*p*-cyanophenyl)alkanes. That in turn signifies higher reaction rate of $[\mathbf{1}]^{2-}$ with initially formed 4-(ω-bromoalkyl)benzonitriles than with α,ω-dibromo-alkanes. Second, the protonation of dianion $[\mathbf{1}]^{2-}$ (by reagents **5a—c**, as well as by traces of water in reagents and solvents) could take place. This yields benzonitrile (**8**), followed by reduction and alkylation leading to alkylbenzenes **7** (compare Ref. 22, see Scheme 4, route *B*). The argument in favor of the route *B* is the presence of ethyl cyclopentanecarboxylate (~5%) among the reaction products in the case of the reagent **5c**. Ethyl cyclopentanecarboxylate is formed, apparently, as the result of intramolecular cyclization of deprotonated compound **5c**.

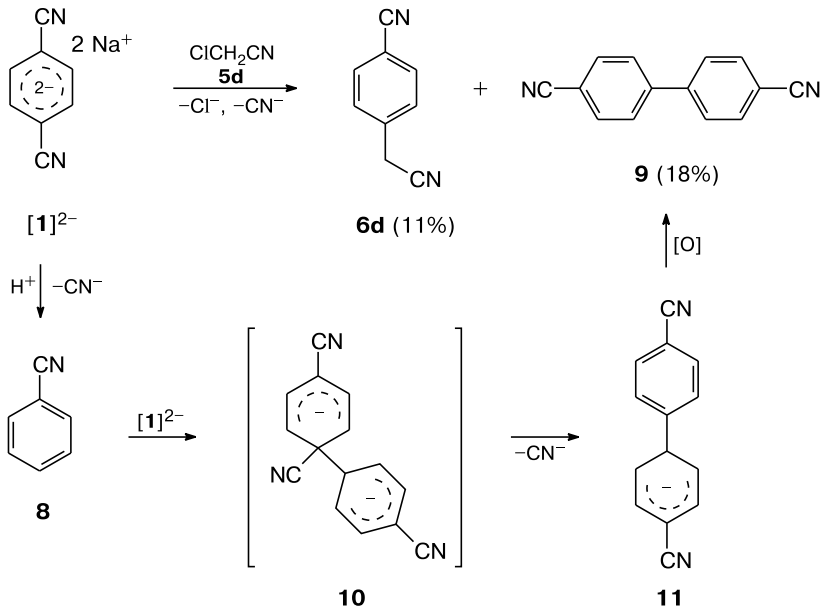
2-Chloroacetonitrile (**5d**) was involved into the reaction in order to investigate the influence of dianion $[\mathbf{1}]^{2-}$ protonation by alkylation reagent (or by products) on the synthetic result. In this case, the reaction mixture (according to ^{1}H NMR and GC/MS data) consisted of small amount of 4-cyanomethylbenzonitrile[23,24] (**6d**, 11%), 4,4′-dicyanobiphenyl (**9**, 18%), and starting dinitrile **1** (46%, Scheme 5). The formation of compound **9** signifies the protonation of dianion $[\mathbf{1}]^{2-}$ that initiates the process of its transformation into benzonitrile **8**, followed by cross-coupling[25] with dianion $[\mathbf{1}]^{2-}$. The obtained result indicates that cross-coupling of $[\mathbf{1}]^{2-}$ with nitrile **8** proceeds quicker than reductive alkylation of **8** with chloride **5d**, which should lead to phenylacetonitrile.

To confirm the assumption that protonation of dianion $[\mathbf{1}]^{2-}$ is one of the reasons for the formation of ω-X-alkylbenzenes **7a—c,** the process of single electron activation of benzonitrile **8** with sodium in liquid ammonia followed by inclusion of radical anion of benzonitrile $[\mathbf{8}]^{\bullet-}$ in the reaction with ω-X-alkyl bromides **5a—c** (Scheme 6, Table 2) was investigated. Previously, such transformation was performed using non-functionalized alkyl halides as the example. That yielded the corresponding alkylbenzenes with sufficiently high yields of 30—50% (it should be taken into account that the radical anion stoichiometry implies participation of two moles of this radical anion for the formation of one mole of prod-

Scheme 4

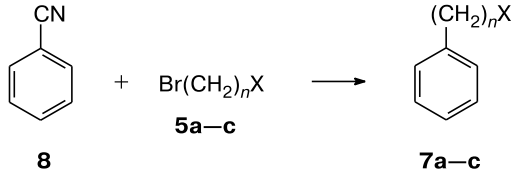


Scheme 5



uct).[21,22,26] The yields of ω-X-alkylbenzenes **7a—c** remained in the same range of 36—47% according to ^{1}H NMR and GC/MS (see Table 2) upon using of functionalized alkyl bromides **5a—c**. Besides the products **7a—c,** the starting compounds, namely nitrile **8** and alkyl bromides **5a—c,** were present in the reaction products.

Scheme 6



Reaction conditions: Na, NH_3 (liquid), -33 °C, 1.5 h.

Table 2. Reductive alkylation of benzonitrile **8** with ω-X-alkyl bromides **5a—c**[a]

Alkylation agent	Yield[b] (mol.%)
5a	**7a** (38)
5b	**7b** (36)
5c	**7c** (47)

[a] Conditions: 1 eq of **8**, 0.98 eq of Na, NH_3 (liquid), 0.6 eq of $Br(CH_2)_nX$ (**5a—c**), –33 °C, 1.5 h.
[b] Yield according to joint data of ^{1}H NMR and GLC/MS (by not less than two experiments, deviation of presented value not more than 5%).

In summary, the results obtained allow one to conclude that reductive activation of dinitrile **1** with transformation into dianion $[\mathbf{1}]^{2-}$, and also of benzonitrile **8** with transformation into radical anion $[\mathbf{8}]^{\bullet-}$, followed by treatment with ω-functionalized alkyl bromides proceeds predominantly as *ipso*-alkylation, followed by decyanation, which leads to the corresponding 4-(ω-X-alkyl)benzonitriles and 4-(ω-X-alkyl)benzenes. The alkyl bromides with more than one CH_2 unit in alkylene bridge between bromine atom and the functional group should be used to achieve good yields of the products. Otherwise, *e.g.* in the case of 2-chloroacetonitrile the protonation of dianion $[\mathbf{1}]^{2-}$ becomes the main reaction route and the yields of 4-(ω-X-alkyl)benzonitriles are decreased. In general, the proposed approach can be used as a convenient and economical method for the synthesis of α,ω-difunctionalized structural blocks, containing from one side of the chain cyanophenyl group, opening up good opportunities for further modification, [27] and from the other side containing acetal, alkoxycarbonyl or nitrile function.

Experimental

^{1}H and ^{13}C NMR spectra were registered using Bruker AV 400 and Bruker Avance III 500 spectrometers with ~5% solutions in $CDCl_3$. Internal standard was residual protonated solvent, the chemical shifts were represented in the δ scale. The assignment of signals is made based on the data of heteronuclear correlations HSQC and HMBC. For uniformity of presentation of spectral data, the numeration of atoms in structures **6a—c** and **7a—c** differs from systematic (Fig. 1). IR spectra were obtained using Vector-22 spectrometer (Bruker) in thin layer or in KBr. Exact values of the

mass of molecular ions are determined using high resolution DFS mass-spectrometer. The identification of components by GC/MS was carried out using Hewlett Packard G1081A. Analytical investigations and registrations of spectra (NMR, IR, MS, and GLC/MS) were performed by the employees of the Multi-Access Chemical Service Center SB RAS.

Liquid NH_3 was purified by dissolving of metal Na, followed by distillation into cooled to −70 °C reaction vessel. Metal Na was cleaned from oxidized surface under the layer of dry hexane. Terephthalonitrile was purified by sublimation in vacuum (m.p. 222 °C; compare Ref. 28: m.p. 222—223 °C). Benzonitrile was purified by distillation over P_2O_5. 2-(2-Bromoethyl)-1,3-dioxane, 5-bromovaleronitrile, ethyl 6-bromohexanoate, 2-chloroacetonitrile (Alfa Aesar) were passed through thin layer of silica gel just before the experiment. Diethyl ether and hexane were purified by distillation.

Generation of disodium salt of terephthalonitrile dianion ($[\mathbf{1}]^{2-}$) and its interaction with ω-functionalized alkyl halides 5a—d (general procedure). To the stirred suspension of dinitrile **1** (0.300 g, 2.34 mmol) in liquid NH_3 (30—40 mL) in the atmosphere of evaporating NH_3, at temperature −(33—50) °C sodium metal (2.15—2.20 eq) was added by portions. The obtained black-brown suspension of the disodium salt of dianion $[\mathbf{1}]^{2-}$ was stirred for additional 5 min. Then ω-X-alkyl bromide **5a—d** (1.3 eq in respect to dinitrile **1**) was added dropwise and the stirring was continued for 1—1.5 h at −33 °C in the atmosphere of evaporating NH_3. Then the reaction mixture was allowed to contact with air, Et_2O (20—30 mL) was added and the stirring was continued until complete evaporation of NH_3. Water (30 ml) was added to the residue and the organic products were extracted with Et_2O (3×25 mL). The combined ether extract was washed till neutral pH with water, then with saturated solution of NaCl, dried over $MgSO_4$, and the solvent was evaporated. The compositions of mixtures and yields of products were determined according to ^{1}H NMR (dimethyl terephthalate as standard) and GLC/MS. Individual compounds were separated by preparative thin layer chromatography (TLC) using fixed layer of absorbent (silica gel 60 PF_{254} with addition of gypsum, Merck), the eluent was hexane—Et_2O. The result of separation was controlled visually by exposure of dried plate to UV light. The fractions of products were washed from the adsorbent by Et_2O.

4-[2-(1,3-Dioxan-2-yl)ethyl]benzonitrile (6a), CAS No. 89013-02-5, was separated from the reaction mixture of $[\mathbf{1}]^{2-}$ and **5a** (0.530 g) as colorless solid (182 mg, 0.84 mmol, 36%), m.p. 67.3—67.8 °C (compare Ref. 1i: m.p. 64—65 °C), $R_f \approx 0.15$ (hexane—Et_2O, 9 : 1, fivefold eluation). IR (KBr), ν/cm^{-1}: 2226 (C≡N). ^{1}H NMR (400.13 MHz) δ Hz): 1.33 (dm, 1 H, C(5″)H, J = 13.2 Hz); 1.85—1.91 (m, 2 H, C(2′)H$_2$); 2.00—2.13 (m, H, C(5″)H); 2.76 (t, 2 H, C(1′)H$_2$, J = 7.9 Hz); 3.72 (td, 2 H, C(4″)H, and C(6″)H, J = 12.0 Hz, J = 2.2 Hz); 4.10 (ddm, 2 H, C(4″)H and C(6″)H, J = 10.7, J = 5.2 Hz); 4.48 (t, 1 H, C(2″)H, J = 5.1 Hz); 7.27 (d, 2 H, C(3)H, C(5)H, J = 8.2 Hz); 7.54 (d, 2 H, C(2)H, C(6)H, J = 8.2 Hz). ^{13}C NMR (125.77 MHz) δ: 25.5 (C(5″)); 29.9 (C(1′)); 35.8 (C(2′)); 66.7 (C(4″), C(6″)); 100.7 (C(2″)); 109.6 (C(1)); 118.8 (C(CN)); 129.0 (C(3), C(5)); 132.0 (C(2), C(6)); 147.3 (C(4)). Mass-spectrum (EI, 70 eV), m/z (I_{rel} (%)): 217 $[M]^+$ (4), 158 (9), 130 (17), 116 (20), 114 (17), 103 (9), 87 (100), 59 (15). Found: m/z 217.1018 $[M]^+$. $C_{13}H_{15}NO_2$. Calculated: M = 217.1097.

4-(4-Cyanobutyl)benzonitrile (6b),[29] CAS No. 1220102-01-1, was separated from the reaction mixture of $[\mathbf{1}]^{2-}$ and **5b** (0.432 g) as colorless oil (0.224 g, 1.22 mmol, 52%), $R_f \approx 0.25$ (hexane—Et_2O,

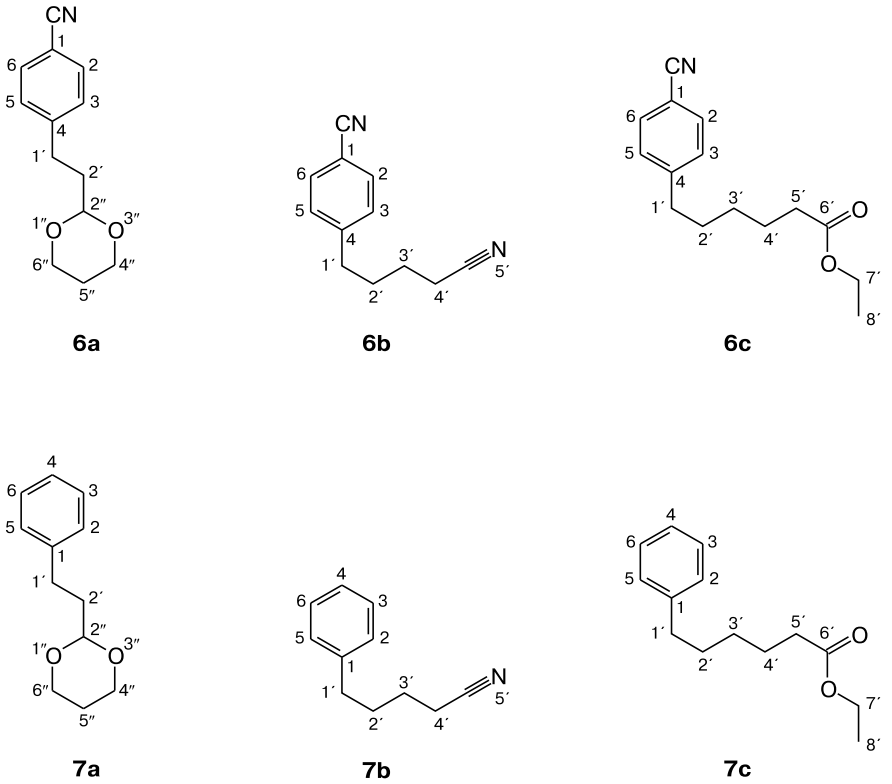


Fig. 1. Atom numeration in compounds **6a—c** and **7a—c**, used for the assignment of NMR spectra.

8 : 2, sevenfold eluation). IR (film), ν/cm^{-1}: 2227 (C≡N), 2247 (C≡N). ^{1}H NMR (500.13 MHz) δ: 1.69—1.72 (m, 2 H, C(3′)H$_2$); 1.78—1.84 (m, 2H, C(2′)H$_2$); 2.37 (t, 2 H, C(4′)H$_2$, J = 7.2 Hz); 2.72 (t, 2 H, C(1′)H$_2$, J =7.5); 7.28 (d, 2 H, C(3)H, C(5)H, J = = 8.0 Hz); 7.58 (d, 2 H, C(2)H, C(6)H, J = 8.0 Hz). ^{13}C NMR (125.77 MHz) δ: 17.9 (C(4′)); 25.7 (C(2′)); 30.6 (C(3′)); 36.0 (C(1′)); 111.0 (C(1)); 119.7 (C$_{CN}$(1)); 120.1 (C$_{CN}$(5′)); 130.0 (C(3), C(5)); 133.2 (C(2), C(6)); 147.7 (C(4)). Mass-spectrum (EI, 70 eV), m/z (I_{rel} (%)): 184 [M]$^+$ (32), 183 (28), 130 (52), 116 (100), 89 (22). Found: m/z 184.0998 [M]$^+$. $C_{12}H_{12}N_2$. Calculated: M = 184.1000.

Ethyl 6-(4-cyanophenyl)hexanoate (6c),[30] CAS No. 1888410-56-7, was separated from the reaction mixture of [**1**]$^{2-}$ and **5c** (0.593 g) as colorless oil (0.258 g, 1.05 mmol, 45%), R_f ≈ 0.42 (hexane—Et$_2$O, 8 : 2, fourfold eluation). IR (film), ν/cm^{-1}: 2227 (C≡N), 1732 (C=O). ^{1}H NMR (400.13 MHz) δ: 1.22 (t, 3 H, C(8′)H$_3$, J = 7.2 Hz); 1.33 (quint, 2 H, C(3′)H$_2$, J = 7.6 Hz); 1.58—1.66 (m, 4 H, C(2′)H$_2$, C(4′)H$_2$); 2.26 (t, 2 H, C(5′)H$_2$, J = = 7.6 Hz); 2.64 (t, 2 H, C(1′)H$_2$, J = 7.7); 4.09 (q, 2 H, C(7′)H$_2$, J = 7.2 Hz); 7.24 (d, 2 H, H(3), H(5), J = 8.2 Hz); 7.53 (d, 2 H, H(2), H(6), J = 8.2). ^{13}C NMR (125.77 MHz) δ: 14.1 (C(8′)); 24.5 (C(3′)); 28.4 (C(4′)); 30.4 (C(2′)); 34.0 (C(5′)); 35.7 (C(1′)); 60.1 (C(7′)); 109.5 (C(1)); 118.9 (C$_{CN}$); 129.0 (C(3), C(5)); 131.9 (C(2), C(6)); 148.0 (C(4)); 173.5 (C(6′)). Mass-spectrum (EI, 70 eV), m/z (I_{rel} (%)): 245 [M]$^+$ (24), 200 (24), 158 (39), 155 (54), 130 (65), 116 (100), 101 (39), 88 (52). Found: m/z 245.1410 [M]$^+$. $C_{15}H_{19}NO_2$. Calculated: M = 245.1406.

2-(2-Phenylethyl)-1,3-dioxane (7a),[31] CAS No. 5663-30-9, was separated from the reaction mixture of [**1**]$^{2-}$ and **5a** (0.530 g) as colorless oil (103 mg, 0.54 mmol, 23%), R_f ≈ 0.3 (hexane—Et$_2$O, 9 : 1, fivefold eluation). ^{1}H NMR (400.13 MHz) δ: 1.32 (dm, 1 H, C(5″)H, J = 13.4 Hz); 1.87—1.92 (m, 2 H, C(2′)H$_2$); 2.01—2.15 (m, 1 H, C(5″)H); 2.70 (t, 2 H, C(1′)H$_2$, J = 7.9 Hz); 3.74 (td, 2 H, C(4″)H and C(6″)H, J = 12.0 Hz, J = 2.4 Hz); 4.06—4.12 (m, 2 H, C(4″)H and C(6″)H); 4.49 (t, 1 H, C(2″)H, J = 5.2 Hz); 7.13—7.18 (m, 3 H, H(2), H(4), H(6)); 7.26 (t, 2 H, H(3), H(5), J = 8.1 Hz). Mass-spectrum (EI, 70 eV), m/z (I_{rel} (%)): 192 [M]$^+$ (2), 133 (15), 114 (33), 105 (17), 91 (37), 87 (100), 59 (17).

5-Phenylvaleronitrile (7b),[32] CAS No. 7726-45-6, was separated from the reaction mixture of [**1**]$^{2-}$ and **5b** (0.432 g) as colorless oil (0.060 g, 0.38 mmol, 16%), R_f ≈ 0.4 (hexane—Et$_2$O, 8 : 2, sevenfold eluation). ^{1}H NMR (400.13 MHz) δ: 1.62—1.70 (m, 2 H, C(3′)H$_2$); 1.74—1.81 (m, 2 H, C(2′)H$_2$); 2.33 (t, 2 H, C(4′)H$_2$, J = 7.1 Hz); 2.64 (t, 2 H, C(1′)H$_2$, J = 7.2 Hz); 7.14—7.20 (m, 3 H, H(2), H(6), H(4)); 7.28 (t, 2 H, H(3), H(5), J = = 7.0 Hz). Mass-spectrum (EI, 70 eV), m/z (I_{rel} (%)): 159 [M]$^+$ (24), 158 (20), 91 (100).

Ethyl 6-phenylhexanoate (7c),[33] CAS No. 52692-51-0, was separated from the reaction mixture of [**1**]$^{2-}$ and **1b** (0.593 g) as colorless oil (0.129 g, 0.58 mmol, 25%), R_f ≈ 0.7 (hexane—Et$_2$O, 8 : 2, fourfold eluation). ^{1}H NMR (400.13 MHz) δ: 1.23 (t, 3 H, C(8′)H$_3$, J = 7.1 Hz); 1.35 (quint, 2 H, C(3′)H$_2$, J = 7.4 Hz); 1.59—1.68 (m, 4 H, C(2′)H$_2$ and C(4′)H$_2$); 2.27 (t, 2 H, C(5′)H$_2$, J = 7.6 Hz); 2.59 (t, 2 H, C(1′)H$_2$, J = 7.8 Hz); 4.11 (q, 2 H, C(7′)H$_2$, J = 7.1 Hz); 7.14—7.17 (m, 3 H, H(2), H(4), H(6)); 7.25 (t, 2 H, H(3), H(5), J = 7.7). Mass-spectrum (EI, 70 eV), m/z (I_{rel} (%)): 220 [M]$^+$ (4), 174 (26), 130 (65), 101(13), 91 (100), 88 (26).

Reaction of sodium salt of benzonitrile radical anion [8]$^{\bullet-}$ with ω-functionalized alkyl bromides 5a—c in liquid ammonia (general procedure). Ammonia (30 mL) was condensed into reaction vessel, then under stirring in the atmosphere of evaporating NH_3 sequentially benzonitrile **8** (0.3 mL, 3.0 mmol) and sodium metal (0.068 g, 2.96 mmol) were added at temperature –(33—50) °C affording thus dark-red solution of benzonitrile radical anion [**8**]$^{\bullet-}$. ω-X-Alkyl bromide **5a—c** (0.6 eq in respect to nitrile **8**) was added to this solution and the stirring was continued for 1.5 h at –33 °C in the atmosphere of evaporating NH_3. Following processing was performed similarly to described above. The composition of obtained in this way reaction mixtures was analyzed by ^{1}H NMR and GC/MS methods.

The authors acknowledge the Multi-Access Chemical Service Center SB RAS for spectral and analytical measurements. The work was performed with financial support of Russian Foundation for Basic Research (Project No 14-03-00108) and Federal Agency of Scientific Organizations (Project No 0302-2016-0007).

References

1. (a) DE2456077; *Chem. Abstr.*, 1976, **85**, 114843n; (b) Jpn Kokai 77 20,985; *Chem. Abstr.*, 1977, **86**, 198027f; (c) Jpn. Kokai Tokkyo Koho JP 76126983; *Chem. Abstr.,* 1977, **86**, 131201q; (d) R. Steinstraesser, *Z. Naturforsch, Teil B.*, 1972, **27**, 774; (e) C. H. Tani, T. Veno, S. Naemura, I. T. Mimi, F. Ogawa, *NEC Res. Dev.*, 1981, **61**, 42; (f) Jpn Kokai Tokkyo Koho 74 34,488; *Chem. Abstr.*, 1974, **81**, 144290q; (g) DE3002678; *Chem. Abstr.*, 1981, **94**, P46976s; (h) GB2118934A; (i) S. M. Kelly, *Liquid Crystals*, 1991, **10**, 273.
2. Jpn. Kokai Tokkyo Koho JP 2014191000 A 20141006.
3. O. Gungor, S. Memon, M. Yilmaz, D. M. Roundhill, *Reactive Functional Polymers*, 2005, **63**, 1.
4. US Pat. 3764621; *Chem. Abstr.*, 1974, **80**, 14655f.
5. Braz. Pat. PI 78 00,095; *Chem. Abstr.*, 1979, **90**, 181580r.
6. PL 87873; *Chem. Abstr.*, 1978, **88**, 153909v.
7. Jpn. Kokai Tokkyo Koho JP 64 44,906 [86 44,926]; *Chem. Abstr.*, 1986, **105**, 153671f.
8. (a) R. Csusk, M. J. Schabel, Y. von Scholz, *Tetrahedron Asymmetry*, 1996, **7**, 3505; (b) Y. Nishii, N. Maryjama, K. Wakasugi, U. Tanabe, *Bioorg. Med. Chem.*, 2001, **1**, 33; (c) J. S. Kumar, S. Roy, A. Datta, *Bioorg. Med. Chem. Lett.*, 1999, **9**, 513; (d) T. C. Rosen, S. Yoshida, K. L. Kirk, G. Haufe, *ChemBioChem*, 2004, **5**, 1033; (e) J. A. Zablocki, J. M. Miyano, R. B. Garland, D. Pireh, L. Schretzman, S. N. Rao, R. J. Lindmark, S. G. Panzer-Knodle, N. S. Nicholson, B. B. Taite, A. K. Salyers, L. W. King, J. G. Campion, L. P. Feigen, *J. Med. Chem.*, 1993, **36**, 1811.
9. (a) P. Knochel, R. G. Singer, *Chem. Rev.*, 1993, **93**, 2117; (b) P. Knochel, G. Cahies, L. Boymond, M. Rottlander, *Angew. Chem. Int. Ed.*, 1998, **37**, 1701; (c) F. F. Kneisel, H. Leuser, P. Knochel, *Synthesis*, 2005, **15**, 2625; (d) A. Inoue, K. Kitagawa, H. Shinokubo, K. Oshima, *J. Org. Chem.*, 2001, **66**, 4333.
10. T. Itou, Y. Yoshimi, T. Morita, Y. Tokunaga, M. Hatanaka, *Tetrahedron*, **2009**, *65*, 263.
11. (a) R. F. Heck, *J. Am. Chem. Soc.,* 1968, **90**, 5531; (b) E. Negishi, H. Marsushita, M. Kobayashi, C. L. Rand, *Tetrahedron Lett.*, 1983, **24**, 3823; (c) C.-Q. Tan, X. Zheng, Z. Ma, Y. Gu, *Synth. Commun.,* 1999, **29**, 123; (d) *Metal-Catalyzed Cross-Coupling Reactions and More*, Eds A. De Meijere, S. Brase, M. Oestreich, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Ger-

many, 2014; (e) *Handbook of Organopalladium Chemistry for Organic Synthesis*, Ed. E. Negishi, Wiley Interscience, New York, 2002; (f) *Cross-Coupling reactions: A Practical Guide*, in *Topics in Current Chemistry*, Vol. **219**, Ed. N. Miyaura, Springer, Berlin, 2002; (g) R. Ikegami, A. Koresawa, T. Shibata, K. Takagi, *J. Org. Chem.*, 2003, **68**, 2195; (h) K. C. Nicolaou, P. G. Bulger, D. Sarlah, *Angew. Chem. Int. Ed.*, 2005, **44**, 4442.

12. P. Gomes, C. Gosmini, J. Perichon, *J. Org. Chem.*, 2003, **68**, 1142.
13. EMEA/CHMP/SWP/4446/2000 (final), *Guideline on the specification limits for residues of metal catalysts or metal reagents*, Committee for Medicinal Products for Human Use (CHMP), London, 21 February 2008, http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003586.pdf.
14. (a) I. I. Bilkis, E. V. Panteleeva, A. P. Tananakin, V. D. Shteingarts, *Russ. J. Org. Chem.* (*Engl. Transl.*), 1997, **33**, 652 [*Zh. Org. Khim.*, 1997, **33**, 711]; (b) Pat. USSR 1705280; *Byul. Izobret.* [*Invention Bull.*] 1992, **2**, 99 (in Rusian); *Chem. Abstrs.*, 1992, **117**, 89975.
15. E. V. Panteleeva, G. Haufe, V. D. Shteingarts, *Synlett*, 2007, 1616.
16. E. V. Panteleeva, M. Yu. Lukyanova, L. M. Pokrovsky, V. D. Shteingarts, *Russ. Chem. Bull.* (*Int. Ed.*), 2007, **56**, 1110 [*Izv. Akad. Nauk., Ser. Khim.,* 2007, 1069].
17. (a) M. Sertel, A. Yildiz, R. Gambert, H. Baumgartel, *Electrochim. Acta*, 1986, **31**, 1287; (b) A. Genaro, F. Maran, A. Maye, E. Vianello, *J. Electroanal. Chem.*, 1985, **185**, 353; (c) A. Genaro, A. Maye, F. Maran, E. Vianello, *Electrochim. Acta*, 1988, **33**, 167.
18. H. S. Sorensen, K. Daasbjerg, *Acta Chem. Scand.*, 1998, **52**, 51.
19. K. Daasbjerg, T.B. Christensen, *Acta Chem. Scand.*, 1995, **49**, 128.
20. (a) R. Lebeuf, J. Dunet, R. Beniazza, D. Ibrahim, G. Bose, M. Berlande, F. Robert, Y. Landais, *J. Org. Chem.*, 2009, **74**, 6469; (b) I. Blasco, H. Pйrez, A. Guijarro, *J. Phys. Org. Chem.*, 2015, **28**, 388; (c) P. W. Rabideau, *Tetrahedron*, 1989, **45**, 1579; (d) A. G. Schultz, *Chem. Commun.*, 1999, 1263; (e) T. Krüger, K. Vorndran, T. Linker, *Chem. Eur. J.*, 2009, **15**, 12082.
21. T. A. Vaganova, E. V. Panteleeva, V. D. Shteingarts, *Russ. Chem. Bull.* (*Int. Ed.*), 2008, **57**, 768 [*Izv. Akad. Nauk., Ser. Khim.,* 2008, 754].
22. I. I. Bilkis, T. A. Vaganova, V. I. Bobileva, V. D. Shteingarts, *J. Org. Chem. USSR* (*Engl. Transl.*), 1991, **27**, 48[*Zh. Org. Khim.*, 1991, **27**, 48].
23. J. Do, S.-G. Kim, *Tetrahedron Lett.*, 2011, **52**, 2353.
24. P. J. Lindsay-Scott, A. Clarke, J. Richardson, *Org. Lett.*, 2015, **17**, 476.
25. E. Panteleeva, L. Shchegoleva, V. Vysotsky, L. Pokrovsky, V. Shteingarts, *Eur. J. Org. Chem.*, 2005, 2558.
26. T. A. Vaganova, E. V. Panteleeva, V. D. Shteingarts, *Sinteticheskie aspekti vosstanovitelnogo alkilirovaniya arenkarbonitrilov [Synthetic aspect of reductive alkylation of arenecarbonitriles], in Panorama sovremennoi khimii Rossii [Panorama of modern chemistry in Russia], Sovremennii organicheskii sintez [Moderm organic synthesis]*, Khimia, Moscow, 2003, p. 293 (in Russian).
27. (a) *The Chemistry of the Cyano Group*, Ed. Z. Rappoport, London—New York—Sydney—Toronto, Interscience Publishers (a division of Wiley & Sons), 1970, 1046 p.; (b) F. F. Fleming, L. Yao, P. C. Ravikumar, L. Funk, B. C. Shook, *J. Med. Chem.*, 2010, **53**, 7902.
28. *Dictionary of Organic Compounds*, Eds I. Hailbron, H. M. Bunbury, Eyre&Spottiswoode, London, 1946, Vol. **3**, p. 664].
29. S. Ejiri, S. Odo, H. Takahashi, Y. Nishimura, K. Gotoh, Y. Nishihara, K. Takagi, *Org. Lett.*, 2010, **12**, 1692.
30. G. A. Price, A. R. Bogdan, A. L. Aguirre, T. Iwai, S. W. Djuric, M. G. Organ, *Catal. Sci. Technol.*, 2016, Ahead of Print. DOI:10.1039/C6CY00331A.
31. (a) J.-Y. Lee, G. C. Fu, *J. Am. Chem. Soc.*, 2003, **125**, 5616; (b) A. G. M. Barrett, W. Tam, *J. Org. Chem.*, 1997, **62**, 7673; (c) J. H. Kim, Y. K. Chung, *Chem. Commun.*, 2013, **49**, 11101; (d) T. Di Franco, N. Boutin, X. Hu, *Synthesis*, 2013, **45**, 2949; (e) Y.-S. Hon, C.-F. Lee, R.-J. Chen, Y.-F. Huang, *Synthetic Commun.*, 2003, **33**, 2829; (f) E. Ascic, R. G. Ohm, R. Petersen, M. R. Hansen, C. L. Hansen, D. Madsen, D. Tanner, T. E. Nielsen, *Chem. Eur. J.*, 2014, **20**, 3297.
32. (a) O. Vechorkin, V. Proust, X. Hu, *J. Am. Chem. Soc.*, 2009, **131**, 9756; (b) B. Anxionnat, D. G. Pardo, G. Ricci, J. Cossy, *Org. Lett.*, 2011, **13**, 4084; (c) T. Moriya, K. Shoji, S. Yoneda, R. Ikeda, T. Konakahara, N. Sakai, *Synthesis*, 2013, **45**, 3233; (d) S. Iida, R. Ohmura, H. Togo, *Tetrahedron*, 2009, **65**, 6257; (e) P. Shukla, Y.-C. Hsu, C.-H. Cheng, *J. Org. Chem.*, 2006, **71**, 655; (f) S. Huo, *Org. Lett.,* 2003, **5**, 423; (g) A. Tarrade-Matha, F. Pillon, E. Doris, *Synth. Commun.*, 2010, **40**, 1646.
33. (a) K. Nakata, C. Feng, T. Tojo, Y. Kobayashi, *Tetrahedron Lett.*, 2014, **55**, 5774; (b) T. Kawamoto, S. Uehara, H. Hirao, T. Fukuyama, H. Matsubara, I. Ryu, *J. Org. Chem.*, 2014, **79**, 3999; (c) S. Ito, Y. Fujiwara, E. Nakamura, M. Nakamura, *Org. Lett.*, 2009, **11**, 4306.

Received June 21, 2016;
in revised form July 19, 2016