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Intramolecular electrophilic rearrangements in saturated acyclic systems. Reactions of bis-carbanions with isocyanates

Yu. G. Gololobov,* T. I. Guseva, N. G. Senchenya, and P. V. Petrovskii

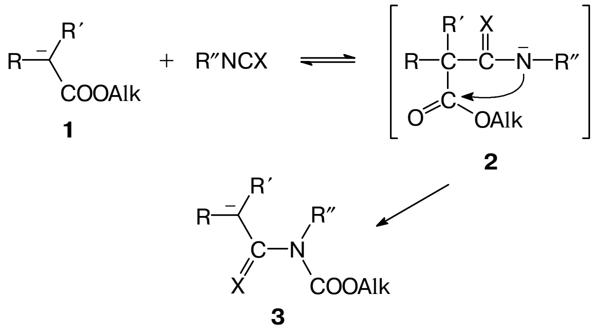
A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences,
28 ul. Vavilova, 119991 Moscow, Russian Federation.
Fax: +7 (095) 135 5085. E-mail: yugol@ineos.ac.ru

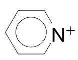
The reactions of mono- and bis-isocyanates with bis-carbanions whose COOAlk groups at the anionic centers do not contain acidic hydrogen atoms proceed unusually to form bis-carbamates (including oligomeric carbamates) due to migration of the alkoxycarbonyl groups from the carbon to the nitrogen atom.

Key words: isocyanates, carbanions, bis-carbanions, electrophilic rearrangements, insertion reactions, carbamates, bis-carbamates, phenylcyanoacetic esters, bis-CH-acids.

Recently,[1—4] a new electrophilic rearrangement has been discovered in the reactions of monocarbanions **1** with monoisocyanates. This rearrangement occurs through intramolecular migration of the alkoxycarbonyl group from the carbon atom to the N-anionic center in the initially formed intermediate **2** (Scheme 1).

Scheme 1



$\mathrm{R = Pr^i{}_3P^+CH_2}$, Ph,  $\mathrm{N^+}$; R′ = CN, COOEt;

R″ = Me or Ar = Ph, *o*-Tol, *m*-Tol, 1-naphthyl, *p*-$\mathrm{ClC_6H_4}$, 3,4-$\mathrm{Cl_2C_6H_3}$, $\mathrm{C_6H_4}$-*p*-$\mathrm{NO_2}$;

Alk = Me, Et; X = O, S

Previously, the reactions of isocyanates with carbanions **1** containing a substituted aliphatic, aromatic, or pyridinium fragment along with one or two alkoxycarbonyl groups at the carbanionic center have been studied (see Scheme 1). At the second stage of conversions, an unusual intramolecular nucleophilic substitution occurs in which the carbanion serves as the leaving group. Therefore, the process as a whole (see Scheme 1) can be characterized as the insertion of isocyanates (including isothiocyanates[2]) at the C—C bond giving rise to new types of carbamates.

In the present study, we extended the above-mentioned conversions to more complicated compounds. On the one hand, we introduced the bis-carbanion, which was prepared by deprotonation of bis-CH-acid, into the reactions with phenylisothiocyanate. On the other hand, mono- and bis-carbanions derived from bis-CH-acids were introduced into the reactions with bis-isocyanates.

Results and Discussion

Transesterification of methyl phenylcyanoacetate (**1a**) with the corresponding diol in the presence of TsOH afforded phenylcyanoacetic esters of diols **4** (Scheme 2).

Scheme 2

$$\underset{\mathbf{1a}}{\mathrm{PhCH(CN)COOMe}} + \mathrm{HO{-}R{-}OH} \xrightarrow{\mathrm{TsOH}}$$

$$\longrightarrow \underset{\mathbf{4a{-}d}}{\mathrm{PhCH(CN)COO{-}R{-}OOC(CN)CHPh}}$$

R = $\mathrm{(CH_2)_4}$ (**a**), $\mathrm{(CH_2)_6}$ (**b**), $\mathrm{(CH_2)_{10}}$ (**c**), 1,4-$\mathrm{CH_2C_6H_4CH_2}$ (**d**)

The yields, data from elemental analysis, and spectral characteristics of the resulting bis-CH-acids **4** are given in Table 1.

Bis-CH-acid **4b** was converted into the corresponding bis-carbanion **5b** by treatment with sodium hydride in dry THF. Apparently, bis-N-anion **6b** was formed at the first stage of the reaction of compound **5b** with two

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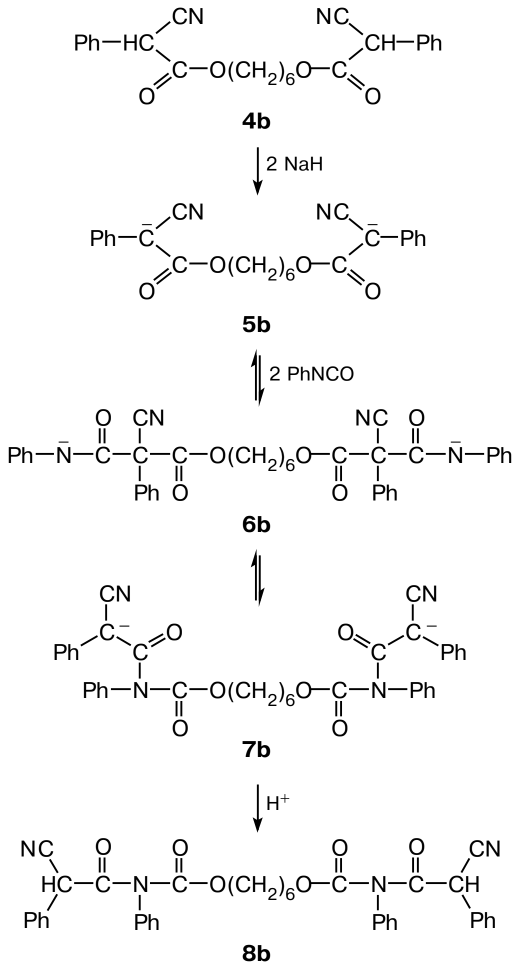
Table 1. Yields, melting points, data from elemental analysis, and spectral characteristics of bis-CH-acids **4**

Compound	R	Yield (%)	M.p. /°C	Found/Calculated (%)			Molecular formula	^{1}H NMR (CDCl$_3$), δ, *J*/Hz
				C	H	N		
4a	$(CH_2)_4$	46	81—82	$\underline{70.24}$ 70.20	$\underline{5.27}$ 5.36	$\underline{7.46}$ 7.44	$C_{22}H_{20}N_2O_4$	1.54—1.66 (m, 4 H, $OCH_2C\underline{H}_2$); 4.15 (t, 4 H, $OC\underline{H}_2CH_2$, *J* = 6.8); 4.71 (s, 2 H, $NC—C\underline{H}$); 7.25—7.42 (m, 10 H, H arom.)
4b	$(CH_2)_6$	65	68—69	$\underline{71.48}$ 71.27	$\underline{5.96}$ 5.98	$\underline{6.89}$ 6.93	$C_{24}H_{24}N_2O_4$	1.19—1.27 (m, 4 H, $OCH_2CH_2C\underline{H}_2$); 1.54—1.60 (m, 4 H, $OCH_2C\underline{H}_2CH_2$); 4.14 (t, 4 H, $OC\underline{H}_2CH_2CH_2$, *J* = 6.8); 4.71 (s, 2 H, $NC—C\underline{H}$); 7.25—7.42 (m, 10 H, H arom.)
4c	$(CH_2)_{10}$	35	50—51	$\underline{73.03}$ 73.02	$\underline{6.99}$ 7.00	$\underline{5.95}$ 6.08	$C_{28}H_{32}N_2O_4$	1.08—1.16 (m, 12 H, $OCH_2CH_2(C\underline{H}_2)_3$); 1.54—1.61 (m, 4 H, $OCH_2C\underline{H}_2(CH_2)_3$); 4.13 (t, 4 H, $OC\underline{H}_2(CH_2)_4$, *J* = 6.8); 4.68 (s, 2 H, $NC—C\underline{H}$); 7.22—7.46 (m, 10 H, H arom.)
4d	$CH_2Ar^*CH_2$	25	115—116	$\underline{74.07}$ 73.58	$\underline{4.90}$ 4.75	$\underline{6.28}$ 6.60	$C_{26}H_{20}N_2O_4$	4.71 (s, 2 H, $NC—C\underline{H}$); 5.18 (s, 4H, CH_2); 7.21—7.25 (m, 4 H, H arom.); 7.33—7.46 (m, 10 H, H arom.)

* Ar = 1,4-C_6H_4.

Scheme 3



moles of phenylisocyanate at ~20 °C [5] (Scheme 3) followed by the intramolecular attack of the negatively charged nitrogen atom on the carbon atom of the ester group, which led to the cleavage of the weakened C—C bond to form carbanion **7b**. Acidification of the reaction mixture afforded bis-carbamate **8b**.

Scheme 4

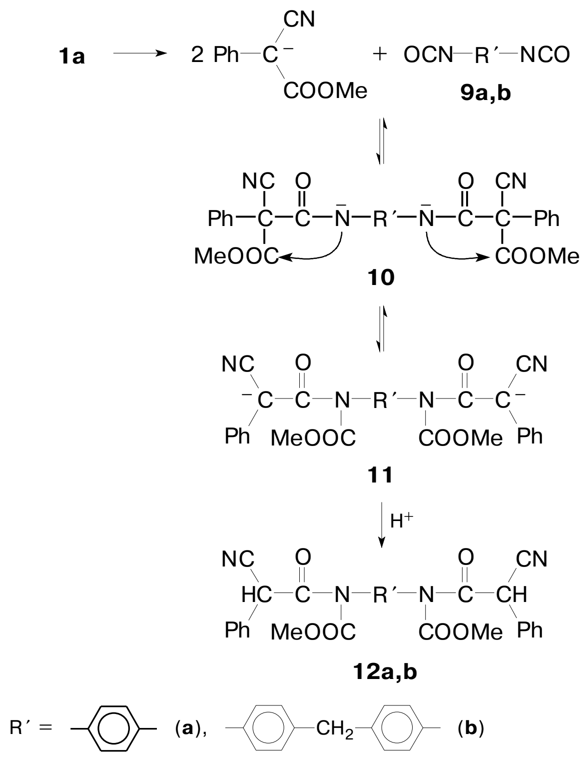
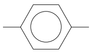
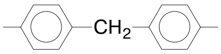


Table 2. Yields, melting points, data from elemental analysis, and spectral characteristics of bis-carbamates **12**

Compound	R′	Yield (%)	M.p. /°C	Found/Calculated (%)			Molecular formula	^{1}H NMR (CDCl$_3$), δ
				C	H	N		
12a		45	181—182	65.88 65.88	4.25 4.34	10.85 10.97	$C_{28}H_{22}N_4O_6$	3.70 (s, 6 H, MeO); 6.28 (s, 2 H, NC—C<u>H</u>); 7.00 (s, 4 H, ArN); 7.25—7.47 (m, 10 H, Ph)
12b		50	91—92	70.00 69.99	4.72 4.70	9.21 9.33	$C_{35}H_{28}N_4O_6$	3.70 (s, 6 H, MeO); 3.97 (s, 2 H, CH$_2$); 6.36 (s, 1 H, NC—C<u>H</u>); 6.88—6.90 (d, 4 H, Ar (2,6)); 7.17—7.19 (d, 4 H, Ar (3,5)); 7.37—7.48 (m, 10 H, Ph)

Therefore, Scheme 3 provides a unique example of intramolecular and, apparently, stepwise C→N migration of two ester groups. Here the main chain of bis-carbamates **8** is formed through the insertion of the ester group between the nitrogen atoms of the amide fragments.

The extension of the C→N rearrangement to monocarbanions and bis-isocyanates gave rise to bis-carbamates **12**. The characteristic structural feature of the latter is the construction of the main chain of the molecule through the bis-isocyanate fragment (Scheme 4).

The formation of bis-carbamates **12** resulted from C→N migration of the methoxycarbonyl group in the initially formed bis-N-anion **10**. The characteristics of bis-carbamates **12** are given in Table 2.

The ^{1}H NMR spectra have low-field singlets corresponding to two methine protons, which is characteristic of the reaction products shown in Schemes 3 and 4 (*cf.* Refs. 2 and 3). It should be noted that if the reactions of the carbanions under consideration with isocyanates proceeded according to a standard scheme[5] without C→N migration of the alkoxycarbonyl groups, the corresponding amides would be formed after acidification of the reaction mixture. However, these amides were not detected by NMR spectroscopy.

The reactions proceeding according to Schemes 3 and 4 provide the basis for the extension of the range of compounds in which C→N migrations occur as well as for the use of these rearrangements in the chemistry of high-molecular-weight compounds. Apparently, this requires introduction of the bis-carbanions under study into reactions with bis-isocyanates. These reactions may lead either to the polymer-chain growth (Scheme 5) or to the formation of cyclic structures with different molecular weights.

The reactions of the reagents in a solution in THF according to Scheme 5 afforded predominantly oligomeric compounds with low molecular weights (Table 3). Unlike the narrow signals for the methine (and other) protons observed in the ^{1}H NMR spectra of dimeric products **8b** and **12**, analogous signals in the ^{1}H NMR spectra of oligomers **15** are broadened. This seems to be quite reasonable because the latter signals belong to the single-type protons in the oligomeric chain.

Therefore, the reactions of bis-carbanions with bis-isocyanates are accompanied by intramolecular rearrangements to give oligomeric carbamates.

Scheme 5

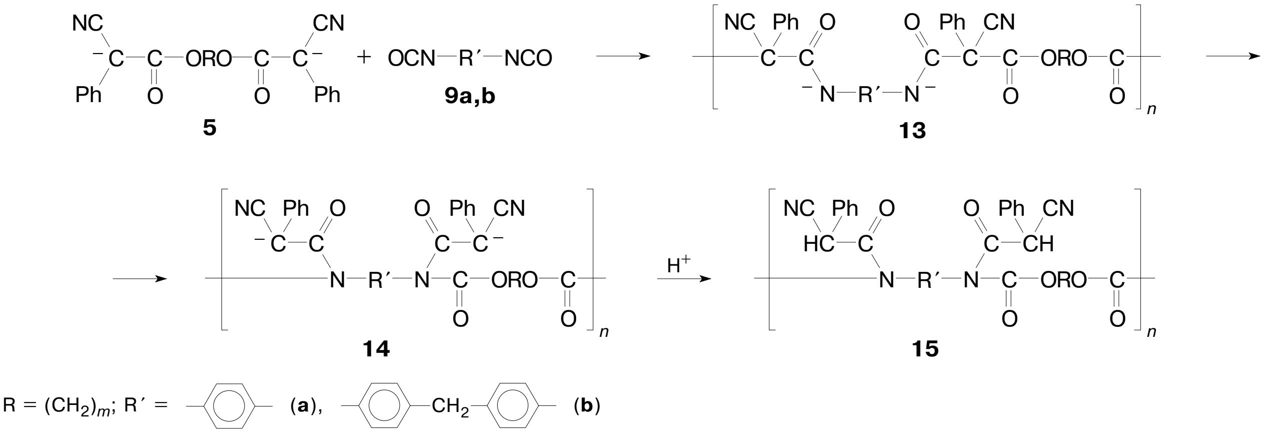


Table 3. Yields, softening points, and spectral characteristics of oligomers **15**

Compound	R	R′	Yield (%)	T_{soft} /°C	M_w*	^1H NMR ($CDCl_3$), δ
15a	$(CH_2)_4$	Ar**	70	75	1400	1.18—1.40 (m, 4 H, CH_2); 3.85—4.15 (m, 4 H, OCH_2); 6.20—6.30 (m, 2 H, CH); 6.75—6.90 (m, 4 H, ArN); 7.15—7.43 (m, 10 H, Ph)
15b	$(CH_2)_6$	Ar	66	60	1776	1.15—1.37 (m, 4 H, $OCH_2CH_2C\underline{H}_2$); 1.53—1.74 (m, 4 H, $OCH_2C\underline{H}_2CH_2$); 3.93—4.15 (m, 4 H, OCH_2); 6.30—6.42 (m, 2 H, CH); 7.00—7.10 (m, 4 H, ArN); 7.25—7.48 (m, 10 H, Ph)
15c	$(CH_2)_{10}$	Ar	48	50	1455	0.98—1.23 (m, 12 H, $OCH_2CH_2(C\underline{H}_2)_6$); 1.42—1.61 (m, 4 H, $OCH_2C\underline{H}_2$); 4.00—4.20 (m, 4 H, OCH_2); 6.34—6.42 (m, 2 H, CH); 6.95—7.15 (m, 4 H, ArN); 7.35—7.64 (m, 10 H, Ph)
15d	CH_2ArCH_2	Ar	42	95	1551	5.00—5.15 (m, 4 H, OCH_2); 6.30—6.40 (m, 2 H, CH); 6.87—7.05 (m, 4 H, ArN); 7.20—7.27 (m, 4 H, $ArCH_2$); 7.43—7.62 (m, 10 H, Ph)
15e	$(CH_2)_6$	$ArCH_2$ Ar	60	70	2028	0.98—1.15 (m, 12 H, $OCH_2CH_2C\underline{H}_2$); 1.35—1.53 (m, 4 H, $OCH_2C\underline{H}_2$); 3.55—3.70 (m, 2 H, $ArC\underline{H}_2Ar$); 3.84—4.10 (m, 4 H, OCH_2); 6.25—6.33 (m, 2 H, CH); 6.85—7.00 (m, 4 H, NAr(2,6)); 7.10—7.25 (m, 4 H, NAr(3,5)); 7.40—7.59 (m, 10 H, Ph)

* M_w is the weight-average molecular weight.

** Ar = 1,4-C_6H_4.

Experimental

The molecular weights of oligomers **15** were determined by gel permeation chromatography on a Bruker LC21 chromatograph equipped with a Knauer refractometric detector and an IBM column (7.7×300 mm) calibrated against poly(styrene) standards with a narrow molecular weight distribution. Polystyrene-divinylbenzene gel was used as the stationary phase; THF was used as the solvent; the flow rate was 1 mL min^{-1}; the temperature was 40 °C. The softening points were determined from thermomechanical curves. Thermomechanical tests were carried out on Tsetlin's instrument according to a procedure reported previously[6] using pellets 4 mm in diameter and 2 mm in thickness. The pressure of 0.5 MPa was applied to a 4-mm die. The rate of heating was 1.6 °C mm^{-1}.

The ^1H and ^{13}C NMR spectra were recorded on a Bruker AMX-400 spectrometer (400.26 MHz). The IR spectra were measured on a Karl Zeiss M-82 instrument (KBr). The Raman spectra were recorded on a Ramanor-HG-2S spectrometer (Ar laser).

The reagents were purchased from Aldrich; THF was dried over KOH and distilled over NaOH.

Butane-1,4-diyl bis(phenylcyanoacetate) (4a). Methyl phenylcyanoacetate (**1a**) (17.5 g, 0.1 mol), 1,4-butylene glycol (4.5 g, 0.05 mol), $TsOH \cdot H_2O$ (0.2 g), and toluene (50 mL) were placed in a three-neck flask equipped with a stirrer, a dropping funnel, and a direct condenser, and the reaction mixture was brought to boiling. Once distillation of the toluene—methanol azeotrope started, dry toluene (100 mL) was added to the reaction mixture using the dropping funnel during 3 h with continuous stirring and distillation of the solvent. When the temperature of the vapor reached 110 °C, the reaction was terminated. Then the reaction mixture was cooled and washed with water (6×50 mL) until it became neutral. The aqueous layer was twice extracted with ether and the combined organic layers were dried with $MgSO_4$. The solvent was distilled off and the crystals (15.4 g) that formed were twice recrystallized from 95% EtOH. Compound **4a** was obtained as colorless crystals in a yield of 8.7 g (46.2%), m.p. 81—82 °C.

Compounds **4b—d** were prepared according to an analogous procedure (see Table 1).

Hexane-1,6-diyl bis(*N*-phenyl-*N*-phenylcyanoacetylcarbamate) (8b). Powdered NaH (0.25 g, 0.011 mol) was added with stirring and cooling with ice to a solution of bisphenylcyanoacetate **4b** (2.02 g, 0.005 mol) in dry THF (20 mL) under an atmosphere of dry N_2. The reaction mixture was stirred at 20 °C for 15 min and then a solution of phenyl isocyanate (1.19 g, 0.01 mol) in THF (10 mL) was added dropwise. The mixture was stirred at ~20 °C for 2.5 h and then TFA (0.74 mL, 0.01 mmol) was added at 4 °C. Sodium trifluoroacetate that precipitated was filtered off and the solvent was removed *in vacuo*. The residue was washed with hot Et_2O and recrystallized from 95% EtOH. A white crystalline compound was obtained in a yield of 1.3 g (40.5%), m.p. 148—150 °C. Found (%): C, 71.05; H, 5.27; N, 8.76. $C_{38}H_{34}N_4O_6$. Calculated (%): C, 71.03; H, 5.29; N, 8.72. ^1H NMR ($CDCl_3$), δ: 1.20—1.28 (m, 4 H, $OCH_2CH_2C\underline{H}_2$); 1.31—1.40 (m, 4 H, $OCH_2C\underline{H}_2CH_2$); 4.01—4.08 (m, 4 H, $OC\underline{H}_2CH_2CH_2$); 6.36 (s, 2 H, $C\underline{H}CN$); 7.22—7.40 (m, 20 H, H arom.).

Dimethyl *N,N′*-bis(phenylcyanoacetyl)-*N,N′*-(1,4-phenylene)dicarbamate (12a) and dimethyl *N,N′*-bis(phenylcyanoacetyl)-*N,N′*-[methylenebis(1,4-phenylene)]dicarbamate (12b). A powder of NaH (0.25 g, 0.011 mol) was added with stirring and cooling to 4 °C to a solution of ester **1a** (1.75 g, 0.01 mmol) in THF (20 mL). After 15 min, a solution of the corresponding diisocyanate **9a** or **9b** (0.005 mol, see Table 2) in THF (10 mL) was added dropwise and the reaction mixture was stirred for 2.5 h. Then a solution of TFA (0.74 mL) in dry Et_2O (10 mL) was added at 4 °C. The mixture was filtered and the solvent was removed *in vacuo*. The residue was washed with Et_2O and recrystallized from 95% EtOH.

Compound **12a**. ^{13}C NMR ($CDCl_3$), δ: 44.7 ($\underline{C}HCN$); 54.7 (Me); 116.1 (CN); 128.6—137.0 (Ph); 153.5 (COOMe); 167.2 (C(O)N). IR (KBr), ν/cm^{-1}: 2959 (H—CCN); 2252 (CN);

1747 (COOMe); 1715 (C(O)N). Raman spectrum, ν/cm^{-1}: 3084 (—CHPh); 3060 (C—HPh); 2250 (CN); 1786 (COOMe); 1708 (C(O)N); 1601 (Ph).

The characteristics of compounds **12a,b** are given in Table 2.

Reactions of bis-carbanions 5 with diisocyanates 9. Sodium hydride (5 mmol) was added to a solution of acid **4** (2.5 mmol) in dry THF (40 mL) with cooling to 5 °C under an atmosphere of Ar. After completion of H_2 evolution, the solution of bis-carbanion **5** was filtered at ~20 °C and a solution of the corresponding diisocyanate **9** in THF (40 mL) was added to the filtrate with stirring using a magnetic stirrer. The mixture was kept at ~20 °C for one day and then a solution of TFA (5 mmol) in dry Et_2O (10 mL) was added with stirring. The solvent was concentrated *in vacuo* to one-half of the initial volume. The residue was cooled, filtered, and mixed with a tenfold excess of hexane. The precipitate that formed was reprecipitated from THF with hexane to a constant weight. The characteristics of oligomers **15a—e** are given in Table 3.

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