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Brief Communications

Novel reactions of arylmalonate carbanions. The reaction with phenyl isocyanate resulting in carbamates by 1,3-C→N migration of the ethoxycarbonyl group*

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The reactions of carbanions of diethyl phenyl and 4-nitrophenylmalonates with phenyl isocyanate occur with 1,3-C→N migration of the ethoxycarbonyl group to form the corresponding adducts. The introduction of NO_2 groups into the benzene ring of arylmalonates inhibits the reaction.

Key words: substituted carbamates; phenyl isocyanate; phenyl, 4-nitrophenyl, and 2,4-dinitrophenylmalonates; C→N migration of ethoxycarbonyl group; X-ray diffraction analysis.

We have earlier described the processes of 1,3-C→N migration of the alkoxycarbonyl groups occurring during the interaction of isocyanates with the carbanions based on phosphorus-containing zwitterions,[1,2] esters of phenylcyanoacetic acid,[3] and pyridinium ylides.[4] The study of the mechanism of these transformations (Scheme 1) showed[5] that the reaction proceeds in two steps, and the introduction of the electron-withdrawing substituents into the arylisocyanate ring accelerates the formation of carbamates.

It can be assumed that the introduction of electron acceptors into the substituent R bound to the carbanion center would decrease the nucleophilicity of carbanion **1** and thus decrease the reaction rate. To check experimentally this assumption, we introduced the carbanions of phenyl, 4-nitrophenyl, and 2,4-dinitrophenylmalonates **5** into the reaction with phenyl isocyanate (Scheme 2).

Sodium salts **5** soluble in THF were synthesized by the reactions of arylmalonates with NaH in THF. The synthesized salts were introduced into the reactions without isolation in the same solvent with the doubled amount of phenyl isocyanate. The Na salts that formed were separated from phenyl isocyanate excess. The completion of formation of carbamate **7a** requires 3—4 h, whereas the formation of carbamate **7b** takes 5—6 h. Then carbamate sodium salts were transformed into CH acids **8a**,**b** by the treatment with dilute hydrochloric acid. According to the

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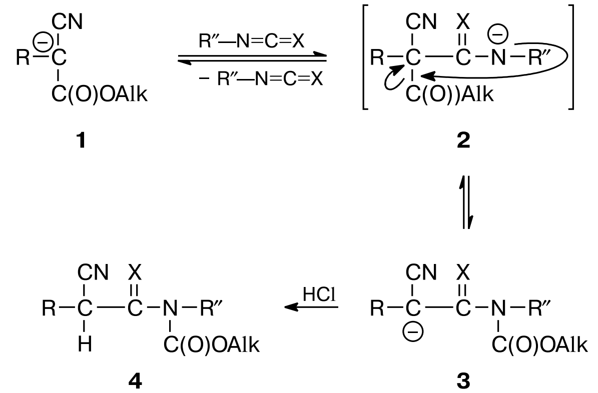
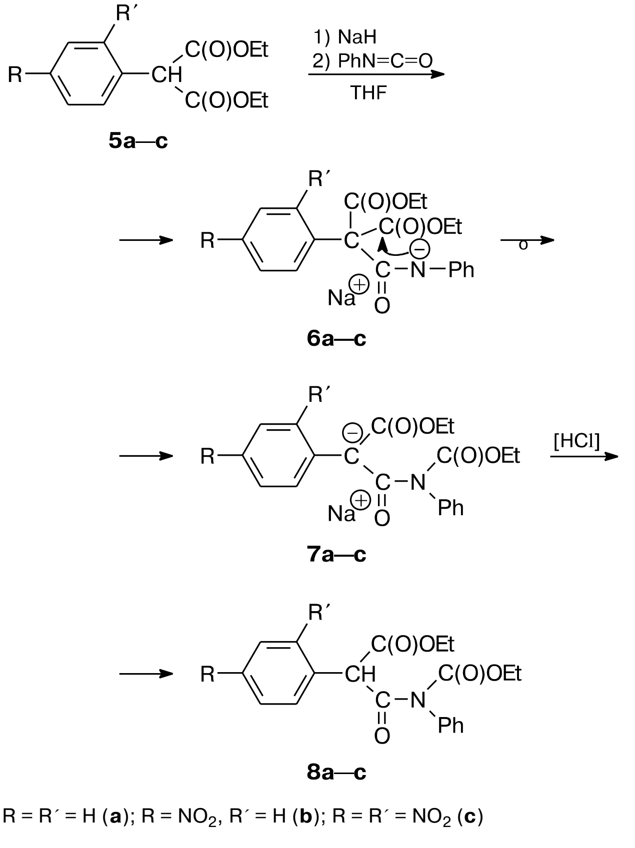
Scheme 1



R = Ph, Py$^{(+)}$, 1-isoquinolyl; R′$_3$P$^{(+)}$CH$_2$, where R′ = Pr^n, Pr^i, Bu^n, Et$_2$N;
X = O, S; Alk = Me, Et, Allyl, propargyl; R″ = Me, *cyclo*-C$_6$H$_{11}$, Ar

Scheme 2



R = R′ = H (**a**); R = NO$_2$, R′ = H (**b**); R = R′ = NO$_2$ (**c**)

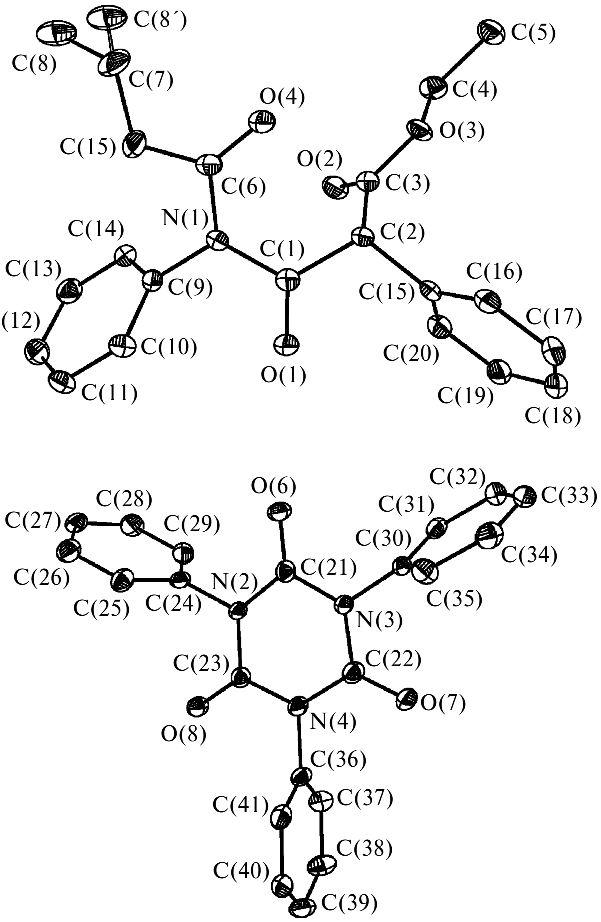


Fig. 1. Spatial structure of the 1 : 1 adduct of carbamate **8a** with the phenyl isocyanate trimer.

spectral data, the resulting reaction mixture mainly consisted of compounds **8a**,**b**. The major admixture (~10%) was the isocyanate trimer. Repeated crystallizations gave crystalline individual compounds **8a**,**b** and their complexes with the isocyanate trimer. The adduct of compound **8a** with the phenyl isocyanate trimer obtained after the first crystallization was studied by X-ray diffraction analysis (Fig. 1). The detailed description of X-ray diffraction analysis of the adduct of compound **8a** with 1,3,5-triphenylhexahydro-1,3,5-triazine-2,4,6-trione will be published elsewhere. The structures of compounds **8a**,**b** were confirmed by the data of elemental analysis and ^{1}H NMR and IR spectra. The IR spectra exhibit the characteristic absorption bands of the alkoxycarboxyl groups at the carbon atoms (1748 cm^{-1}) and the nitrogen atom of the carbamate group (1728 cm^{-1}). The ^{1}H NMR spectra contain signals from the diastereotopic CHHO protons of the ethoxycarbonyl groups. We failed to isolate carbamate **8c** in the individual state. Its formation in the reaction mixture was detected spectroscopically: the ^{1}H NMR spectrum (acetone-d) contains the singlet from the methinic proton at 6.55 ppm, and the IR spectrum exhibits the band at 1713 cm^{-1}. According to the data of ^{1}H NMR spectroscopy, the reaction mixture also contained the starting CH acid **5c** and isocyanate polymer. In the competitive reaction of the carbanions of CH acids **5a**,**b** with phenyl isocyanate, the ratio of formed compounds **8a**/**8b** is equal to 2.3/1.0 (determined from the intensity ratio of the methinic protons: δ_{CH} 5.82 (**8a**) and 5.98 (**8b**)). Thus, as we assumed, the introduction of electron acceptors into the benzene ring of phenylmalonate inhibits the formation of carbamates in the reactions of anions of the corresponding CH acids with phenyl isocyanate, most likely, due to a decrease in the rate of the first step of the reaction (see Scheme 2).

Experimental

^{1}H NMR spectra were obtained on a Bruker AMX-400 spectrometer in $CDCl_3$. IR spectra were recorded on a Magna-IR-750 FT-IR spectrometer (Nicolet) in Nujol. Diethyl phenylmalonate and phenyl isocyanate were purchased from ACROS Organics. Diethyl 4-nitrophenylmalonate was synthesized by the reaction of malonic ester, NaH, and 4-nitrofluorobenzene in THF. The yield was 23%, m.p. 58—59 °C (*cf.* Ref. 6: m.p. 56—57 °C).

Phenyl(ethoxycarbonyl)acetic acid (*N*-ethoxycarbonyl-*N*-phenyl)amide (8a). Diethyl phenylmalonate (4.72 g, 20.0 mmol) was added dropwise to a suspension of sodium hydride (0.80 g, 20.0 mmol) in THF (30 mL), The reaction mixture was stirred for 10 min, and phenyl isocyanate (4.3 mL, 40.0 mmol) was added dropwise to the transparent reaction solution. After 4 h, the solvent was distilled off *in vacuo*, and the residue was washed with diethyl ether and treated in benzene with dilute (1 : 10) hydrochloric acid. The organic layer was separated and dried over sodium sulfate for 12 h. Benzene was removed *in vacuo*, and the residue was twice crystallized from a petroleum ether—diethyl ether (1 : 1) mixture. The white precipitate was obtained in a yield of 1.21 g (20%), m.p. 68—69 °C. Found (%): C, 67.58; H, 5.81; N, 4.36. $C_{20}H_{21}NO_5$. Calculated (%): C, 67.60; H, 5.91; N, 3.94. ^{1}H NMR, δ: 1.14 (t, 3 H, $C\underline{H}_3CH_2{}^N$, $^3J_{H,H}$ = 7.1 Hz); 1.27 (t, 3 H, $C\underline{H}_3CH_2{}^C$, $^3J_{H,H}$ = 7.2 Hz); 4.15 (dq, 1 H, $CH_3C\underline{H}_aH_b{}^N$, $^2J_{H,H}$ = 8.0 Hz, $^3J_{H,H}$ = 7.1 Hz); 4.18 (dq, 1 H, $CH_3CH_a\underline{H}_b{}^N$, $^2J_{H,H}$ = 8.0 Hz, $^3J_{H,H}$ = 7.1 Hz); 4.23 (dq, 1 H, $CH_3C\underline{H}_aH_b{}^C$, $^2J_{H,H}$ = 8.4 Hz, $^3J_{H,H}$ = 7.2 Hz); 4.26 (dq, 1 H, $CH_3CH_a\underline{H}_b{}^C$, $^2J_{H,H}$ = 8.4 Hz, $^3J_{H,H}$ = 7.2 Hz); 5.86 (s, 1 H, CH); 7.11—7.12 (m, 1 H, $H_o{}^C$); 7.30—7.42 (m, 8 H, H_{Ph}). IR, ν/cm^{-1}: 2980 (CH), 1748 (^{C}COOEt), 1728 (^{N}COOEt), 1708 (C(O)N).

4-Nitrophenyl(ethoxycarbonyl)acetic acid (*N*-ethoxycarbonyl-*N*-phenyl)amide (8b). Diethyl 4-nitrophenylmalonate (1.41 g, 5.0 mmol) in THF (10 mL) was added dropwise to a suspension of sodium hydride (0.20 g, 5.0 mmol) in THF (10 mL). The reaction mixture was stirred for 30 min, and a solution of phenyl isocyanate (1.1 mL, 10.0 mmol) in THF (10 mL) was added dropwise to the transparent reaction solution. After 5 h, the solvent was distilled off *in vacuo*, and the residue was washed with a mixture of petroleum ether, diethyl ether, and benzene. The filtered-off powder was treated in benzene with dilute (1 : 10) hydrochloric acid. The organic layer was separated and dried over sodium sulfate for 12 h. The solvent was removed *in vacuo*, and the residue was twice crystallized from a petroleum ether—diethyl ether (1 : 1) mixture. The white precipitate was obtained in a yield of 0.60 g (30%), m.p. 111—114 °C. Found (%): C, 60.28; H, 4.81; N, 6.91. $C_{20}H_{20}N_2O_7$. Calculated (%): C, 60.00; H, 5.00; N, 7.00. ^{1}H NMR, δ: 1.40 (t, 3 H, $C\underline{H}_3CH_2{}^N$, $^3J_{H,H}$ = 7.1 Hz); 1.26 (t, 3 H, $C\underline{H}_3CH_2{}^C$, $^3J_{H,H}$ = 7.1 Hz); 4.15 (dq, 1 H, $CH_3C\underline{H}_aH_b{}^N$, $^2J_{H,H}$ = 7.6 Hz, $^3J_{H,H}$ = 7.1 Hz); 4.18 (dq, 1 H, $CH_3CH_a\underline{H}_b{}^N$, $^2J_{H,H}$ = 7.6 Hz, $^3J_{H,H}$ = 7.1 Hz); 4.22 (dq, 1 H, $CH_3C\underline{H}_aH_b{}^C$, $^2J_{H,H}$ = 8.4 Hz, $^3J_{H,H}$ = 7.2 Hz); 4.26 (dq, 1 H, $CH_3CH_a\underline{H}_b{}^C$, $^2J_{H,H}$ = 8.4 Hz, $^3J_{H,H}$ = 7.2 Hz); 5.98 (s, 1 H, CH); 7.10 (dq, 2 H, $H_o{}^{Ph}$, $^3J_{H,H}$ = 6.7 Hz, $^4J_{H,H}$ = 1.9 Hz): 7.34—7.43 (m, 3 H, H^{Ph}); 7.55 (dq, 2 H, $H_o{}^{Ar}$, $^3J_{H,H}$ = 8.8 Hz, $^4J_{H,H}$ = 2.2 Hz); 8.55 (dt, 2 H, $H_o{}^{Ar}$, $^3J_{H,H}$ = 8.8 Hz, $^4J_{H,H}$ = 2.2 Hz). IR, ν/cm^{-1}: 2932 (CH), 1739 (^{C}COOEt), 1714 (^{N}COOEt), 1708 (C(O)N), 1597 (C=C_{Ph}), 1527, 1374 (NO_2).

Competitive reaction of the carbanions obtained from CH acids 5a and 5b with phenyl isocyanate. Sodium hydride (28 mg, 7.0 mmol) was added to a solution of a mixture of **5a** (0.2 g, 3.5 mmol) and **5b** (0.16 g, 3.5 mmol) in THF (3 mL). Phenyl isocyanate (47 mg, 4.0 mmol) was added to the resulting mixture. After 1 h, the mixture was poured into diethyl ether (30 mL), and the precipitate was filtered off and treated with a solution of hydrochloric acid (1 : 10) in the presence of diethyl ether. After drying the solvent was distilled off *in vacuo*. The ^{1}H NMR spectrum contains, along with the signals from the starting CH acids **5a**,**b**, the signals δ_H = 5.82 (**8a**) and 5.98 (**8b**).

X-ray diffraction study of the 1 : 1 adduct of compound 8a with the phenyl isocyanate trimer. The crystals of zwitterion **8a**$\cdot C_{21}H_{15}N_3O_3$ ($C_{41}H_{36}N_4O_8$, M = 712.74) are triclinic, space group $P\bar{1}$, at T = 100 K a = 9.6517(12), b = 11.0568(13), c = 18.281(3) Å, α = 100.044(5), β = 97.607(5), γ = 108.732(5)°, V = 1781.7(4) Å^3, Z = 2, F(000) = 748, d_{calc} = 1.329 g/cm^3, μ = 0.093 mm^{-1}. The unit cell parameters and intensities of 15 607 reflections were measured on a Bruker SMART Apex II CCD automated diffractometer (T = 100 K, λMo-Kα radiation, graphite monochromator, φ and ω scan modes, θ_{max} = 26.2°). X-ray absorption correction was applied to the obtained data by the SADABS program.[7] The structure was determined by a direct method and refined by the full-matrix least-squares method in the anisotropic approximation for non-hydrogen atoms. In the crystal, one of the ethyl groups is disordered over two positions with site occupancies of 0.7 : 0.3. The positions of the hydrogen atoms were geometrically calculated and refined in the isotropic approximation with the fixed positional (riding model) and thermal parameters (U_{iso}(H) = 1.5U_{eq}(C) for the CH_3 groups and U_{iso}(H) = 1.2U_{eq}(C) for all other groups). The final R factors are R_1 = 0.0543 for 3817 independent reflections with $I > 2\sigma(I)$ and wR_2 = 0.0870 for all 7058 independent reflections. All calculations were performed using the SHELXTL PLUS (Version 5.10) program package.[8] The tables of the coordinates of atoms, bond lengths, bond angles, and anisotropic temperature parameters for compound **1** were deposited with the Cambridge Structure Database.

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