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On the nature of intermediates in the reactions of carbanions of diethyl arylmalonates with isocyanates

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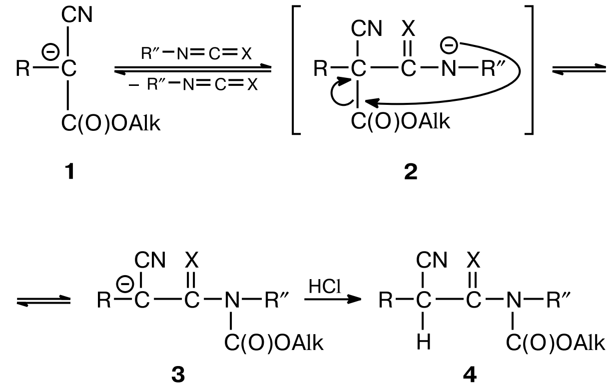
A reaction of ethyl phenyl- and 4-nitrophenylmalonate carbanions with *para*-tolylsulfonyl isocyanate leads to stable addition products, the corresponding substituted *para*-tolylsulfonylacylamides.

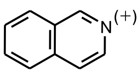
Key words: ethyl phenyl- and 4-nitrophenylmalonate carbanions, *para*-tolylsulfonyl isocyanate, *para*-tolylsulfonylacylamides.

During consideration of mechanism for the formation of carbamates by the reaction of isocyanates with carbanions **1** based on phosphorus-containing zwitterions,[1,2] phenylcyanacetic esters,[3] and pyridinium ylides[4], it was suggested that *N*-anion **2** is formed as an intermediate (Scheme 1). The formation of the intermediate **2** was confirmed by the data of quantum chemical calculations for the reaction of pyridinium ylide, malonic ester derivative, with phenyl isocyanate.[4] At the same time, experiments using ^{1}H NMR spectroscopy and kinetic data[2] did not show formation of intermediate **2** as kinetically stable species on the reaction coordinate.

To answer the question whether the intermediate *N*-anion **2** is formed in the transformations under study, we considered a model reaction of carbanions **5a,b** with tosyl isocyanate (Scheme 2). We presumed that if the reactions with aryl isocyanates proceed according to Scheme 1 through the formation of *N*-anions **2**, then the analogous reaction with tosyl isocyanate according to Scheme 2 will lead in the first step to the stable intermediate **6**, the nucleophilicity of which should be extremely low due to the strong electron-withdrawing power of the tosyl group.

Scheme 1

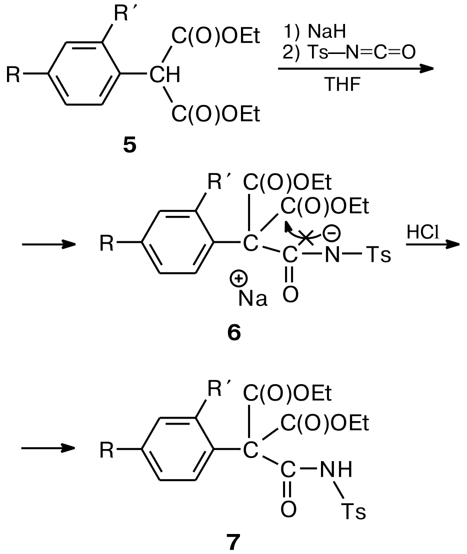


R = Ph; Py$^{(+)}$;  ; R′$_3$P$^{(+)}$CH$_2$,

R′ = Pr^n, Pr^i, Bu^n, Et$_2$N;

X = O, S; Alk = Me, Et, allyl, CH≡CCH$_2$; R″ = Me, *cyclo*-C$_6$H$_{11}$, Ar.

Scheme 2



R = R′ = H (**a**); R = NO$_2$, R′ = H (**b**). Ts = SO$_2$C$_6$H$_4$Me-*p*

In fact, the reaction of tosyl isocyanate with carbanions obtained in the solution of THF from CH acid **5a,b** and NaH proceeds at room temperature and, after acidifi-

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cation of the reaction mixture with dilute hydrochloric acid, leads to the isolation of stable amides **7a,b** in high yields. The carrying out the reaction under consideration at 65 °C does not lead to the formation of the corresponding carbamates of the type **3**, which, no doubt, is due to the low nucleophilicity of the *N*-anion in the intermediate **6**. The composition and structures of amides **7a,b** were inferred from the data of elemental analysis, IR and NMR spectra. In contrast to carbamates obtained from malonic ester derivatives and aryl isocyanates,[3] which contain the signals of two different ethoxy groups in the ^{1}H NMR spectrum, the ^{1}H NMR spectra of amides **7a,b** exhibit signals for the protons of the ethoxycarbonyl groups as a single group. To study specificities in the spatial arrangement of substituents in the molecule of amide **7a**, we performed its X-ray diffraction analysis (Fig. 1). The main geometric parameters of amide **7a** are close to the expected values. Insignificant flattening (the sum of the bond angles is 358(1)°) of the nitrogen atom, apparently, is due to its conjugation with the C=O group. Statistical analysis of the Cambridge Structural Database showed that the arrangement of arylsulfone and amide groups observed in **7a** is quite rare. Direct analogs of compound **7a** containing the fragment $N(H)—C(O)—C(R)_2C(O)OAlk$ have not been earlier studied, and the only known analogs are compounds, in which the nitrogen atom is in a heterocycle.[5,6] Conformational analysis of the molecule showed that the aromatic rings have a transoid arrangement with respect to the central sulfonamide chain, whereas the ester group O(6)C(10)O(7) is placed directly over the plane of the tolyl substituent. Such an arrangement of substituents is due to both the steric reasons and the presence of the intramolecular interactions. In the crystal, the hydrogen atom of the NH group and O(4) atom of the carboxylate fragment form an H bond (N...O 2.655(2) Å, NHO 140(1)°), which, apparently, results in insignificant elongation of the C—O(4) bond (1.2142(18) Å) as compared to the C—O(3) and C—O(6) bonds (1.2072(19) and 1.1937(19) Å). The six-membered H-bound cycle has the chair conformation. In addition to the H bond specified, in the crystal of **7a** there also exist a number of shortened contacts formed by the O(1), O(3), and O(7) atoms with the distances 2.979(2) and 3.026(2) Å, which is frequent enough phenomenon for the specific O···O interactions in crystals.[7]

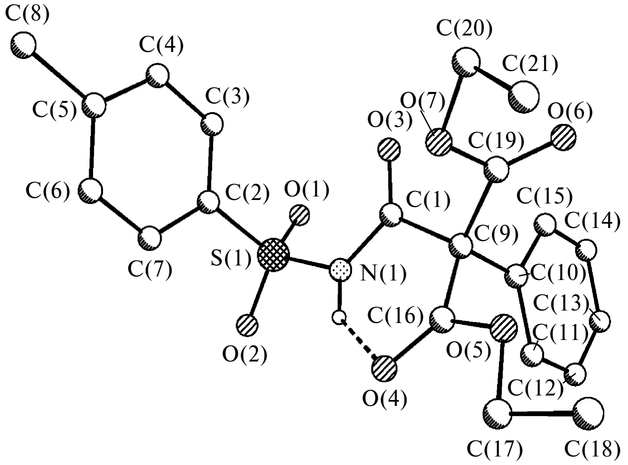

Fig. 1. General view of compound **7a**. Hydrogen atoms, excluding the atoms of the NH group, are not shown.

In conclusion, it was experimentally shown that the reaction of carbanions, arylmalonic ester derivatives, with isocyanates (using the reaction with tosyl isocyanate as an example) indeed leads in the first step of the reaction to the formation of *N*-anions as the intermediates. It is quite obvious that the reaction of carbanions with aryl isocyanates according to Scheme 1 initially also leads to *N*-anions **2**, but due to their high nucleophilic activity, an intramolecular attack $N^{(-)}\rightarrow C(O)OEt$ takes place, which is accompanied by a concerted cleavage of the C—C bond and transfer of the ester group from the carbon atom to the nitrogen atom.

Experimental

^{1}H NMR spectra were recorded on a Bruker AMX-400 spectrometer in the solvent $CDCl_3$. IR spectra were recorded on a Nicolet Magna-IR-750 Fourier-spectrometer (KBr).

***N-p*-Tolylsulfonyl[bis(ethoxycarbonyl)phenyl]acetamide (7a).** Diethyl phenylmalonate (1 g, 4.23 mmol) was added dropwise to a suspension of NaH (0.15 g, 4.23 mmol) in THF (10 mL) followed by stirring for 10 min. *para*-Tolylsulfonyl isocyanate (1.70 g, 8.5 mmol) was added dropwise to the clear solution. After 4 h, the reaction mixture was mixed with diethyl ether (30 mL), The salt formed was filtered off, washed with diethyl ether, and treated with dilute (1 : 10) hydrochloric acid in the presence of benzene (50 mL). The organic layer was dried with Na_2SO_4 for 12 h. Benzene was evaporated *in vacuo* and the residue was twice crystallized from a mixture of light petroleum—diethyl ether (1 : 1) to obtain colorless crystals (1.45 g, 79.2%), m.p. 93—94 °C. Found (%): C, 58.10; H, 5.25; N, 3.20; S, 7.34. $C_{21}H_{23}NSO_7$. Calculated (%): C, 58.19; H, 5.31; N, 3.23; S, 7.39. ^{1}H NMR, δ: 1.21 (t, 6 H, $C\underline{H}_3CH_2O$, $J_{H,H} = 10.5$ Hz); 2.41 (s, 3 H, CH_3—Ph); 4.27 (q, 2 H, $CH_3C\underline{H}H'O$, $J_{H,H} = 10.5$ Hz); 4.25 (q, 2 H, $CH_3CH\underline{H}'O$, $J_{H,H} = 10.5$ Hz); 7.10 (d, 2 H, H_{arom}, $J_{H,H} = 11.5$ Hz); 7.84 (d, 2 H, H_{arom}, $J_{H,H} = 11.5$ Hz); 7.22—7.3 (m, 6 H, H_{Ph}); 10.64 (s, 1 H, NH). IR (ν/cm^{-1}): 1706 (C(O)N), 1760, 1734 (COOEt), 3183 (NH).

***N-p*-Tolylsulfonyl[bis(ethoxycarbonyl)-4-nitrophenyl]acetamide (7b).** Colorless crystals (0.9 g, 53%) were obtained under conditions of preceding experiment from diethyl 4-nitrophenylmalonate (1 g, 3.55 mmol), NaH (0.13 g, 3.55 mmol), and *para*-tolylsulfonyl isocyanate (1.40 g, 7.10 mmol). M.p. 124—125 °C. Found (%): C, 52.68; H, 4.63; N, 5.82; S, 6.64. $C_{20}H_{22}N_2SO_9$. Calculated (%): C, 52.71; H, 4.62; N, 5.82; S, 6.65. ^{1}H NMR, δ: 1.24 (t, 6 H, $C\underline{H}_3CH_2O$, $J_{H,H} = 7.20$ Hz); 2.44 (s, 3 H, CH_3—Ph); 4.31 (q, 2 H, $CH_3C\underline{H}H'O$, $J_{H,H} = 7.20$ Hz); 4.33 (q, 2 H, $CH_3CH\underline{H}'O$, $J_{H,H} = 7.20$ Hz); 7.29 (d, 2 H, H_{arom}, $J_{H,H} = 8.0$ Hz); 7.37 (d, 2 H, H_{arom}, $J_{H,H} = 9.0$ Hz); 7.87 (d, 2 H, H_{arom}, $J_{H,H} = 8.02$ Hz);

8.10 (d, 2 H, H_{arom}, $J_{H,H}$ = 9.0 Hz); 10.71 (s, 1 H, NH). IR (ν/cm^{-1}): 1526, 1361 (NO_2), 1703 (C(O)N), 1761, 1722 (COOEt), 3256 (NH).

X-ray diffraction data. Crystals **7a** ($C_{21}H_{23}NO_7S$, M = 433.46) are monoclinic, space group is $P2_1/n$ at 100 K, a = 9.7338(6), b = 8.7805(6), c = 25.2144(16) Å, β = 92.021(5)°, V = 2153.7(2) Å^3, Z = 4 (Z' = 1), d_{calc} = 1.337 g cm^{-3}, μ(Mo-Kα) = 1.92 cm^{-1}, F(000) = 912. Intensities of 23020 reflections were measured on a Bruker SMART 1000 CCD diffractometer (λ(Mo-Kα) = 0.71072 Å, ω-scanning, 2θ < 58°) and 5711 independent reflections (R_{int} = 0.0424) were used in further refining. The structure was solved by the direct method and refined using the full-matrix least squares method on F^2 in anisotropic-isotropic approximation. The hydrogen atom of the NH group was localized from the differential Fourier syntheses, whereas positions of the C(H) protons were calculated geometrically. The final value of nonconfident factors for **7a**: wR_2 = 0.1092 and GOOF = 1.002 for all the independent reflections (R_1 = 0.0458 were calculated on F for 3224 observed reflections with $I > 2\sigma(I)$). All the calculations were performed using the SHELXTL PLUS 5.0 program package.

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