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C→N Migration of methoxycarbonyl and acetyl groups in reactions of functionally substituted carbanions with aryl isocyanates. Kinetics and mechanism of the reactions

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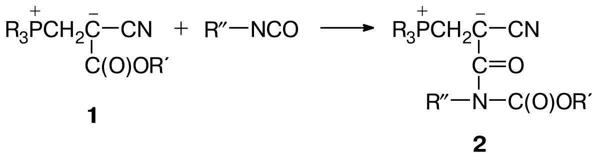
The kinetics and mechanism of C→N migrations of methoxycarbonyl and acetyl groups in the reactions of the sodium derivative of methyl (2-cyano-2-phenyl)acetate and 1,1-diacetyl-2-phenyl-2-tributylphosphonioethanide with aryl isocyanates were studied by spectrophotometry. The reactions afford a prereaction complex *via* a concerted mechanism, according to which the nucleophilic attack of the carbanionic center to the carbon atom of the isocyanate group and the subsequent nucleophilic attack of the nitrogen atom to the carbonyl carbon atom, resulting in the C—C bond cleavage, occur almost simultaneously in the framework of the same transition state.

Key words: kinetics, reaction mechanism, migrations of methoxycarbonyl and acetyl groups, phosphorus-containing zwitterions, aryl isocyanates.

The reactions of alkyl and aryl isocyanates with phosphabetaines **1**, which were synthesized from 2-cyanoacrylates and tertiary phosphines, have previously been shown[1—5] to proceed not *via* the usual scheme of interaction of zwitterions with electrophiles but afford the products of insertion of the latter into the anionic moiety of a zwitterion molecule with the C—C bond cleavage (Scheme 1).

Scheme 1



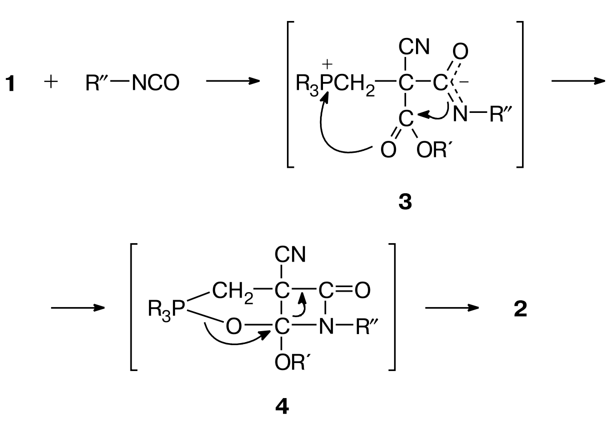
$$R_3\overset{+}{P}CH_2\overset{-}{C}(CN)\,C(O)OR' + R''{-}NCO \longrightarrow R_3\overset{+}{P}CH_2\overset{-}{C}(CN){-}C(=O){-}N(R''){-}C(O)OR'$$

1 **2**

R, R′ = Alk; R″ = Alk, Ar

The structures of betaines **2** were determined by X-ray diffraction analysis. The most probable reaction mechanism was proposed[2] (Scheme 2).

Scheme 2



A distinctive feature of this scheme is the intermediate formation of unstable phosphorane **4** from intermediate **3**. However, based on the results of studying the kinetics and mechanism of this reaction, which is unusual for substituted aryl isocyanates, we proposed[6,7] the mechanism that does not involve the formation of intermediate **4**.

According to this mechanism, the nucleophilic attack of the anionic center of phosphabetaine **1a** on the carbon atom of the isocyanate group and the subsequent nucleophilic attack of the nitrogen atom to the ethoxycarbonyl group, resulting in the C—C bond cleavage, occur almost

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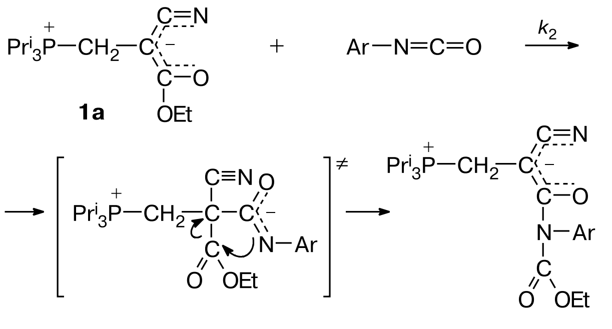
simultaneously *via* the concerted mechanism within the same transition state (Scheme 3).

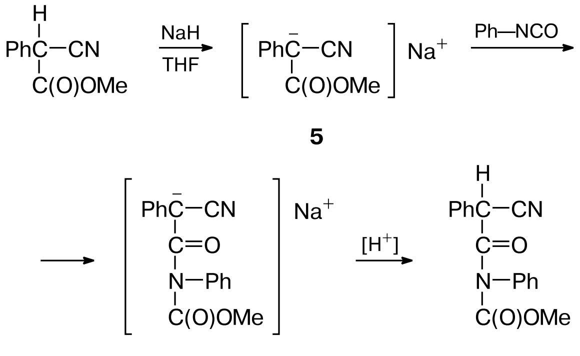
Scheme 3



2a

The driving force of migration of the ethoxycarbonyl group to the nitrogen atom was assumed to be excessive steric hindrance of the activated complex and an energy gain from a more efficient delocalization of the anionic charge in product **2a** that formed. The conclusion that the phosphorus atom is not involved directly in this reaction (so-called "electrophilic assistance" [2]) was experimentally checked. For this purpose, we studied[8] the reactions of aryl isocyanates with carbanion **5** (Scheme 4), which gave the same synthetic result, namely, migration of the ester group to the nitrogen atom, and thus confirmed completely the above conclusions.

Scheme 4



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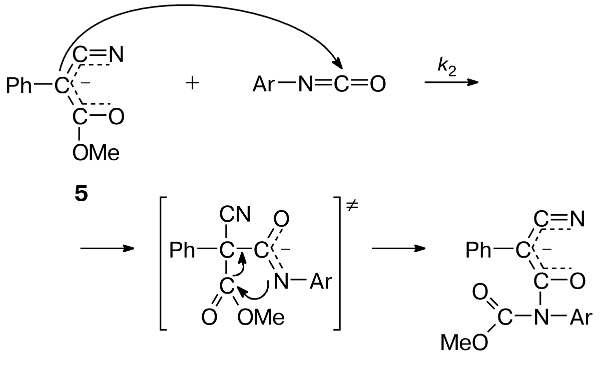
In the present work, we studied the kinetics and mechanism of this reaction using as an example the sodium derivative of methyl (2-cyano-2-phenyl)acetate **5** with *o*-nitrophenyl isocyanate, which possesses, according to the earlier obtained data,[6] the highest reactivity in the series of aryl isocyanates used. The spectrophotometric study of the reaction kinetics under the conditions of the pseudo-first-order with respect to aryl isocyanate (acetonitrile, high excess of salt **5** (0.01—0.05 mol L^{-1}), λ = 370 nm, 20 °C) made it possible to establish that the reaction proceeds *via* the general second order and the first order with respect to each reactant.

Results and Discussion

The kinetic and activation parameters of this reaction (k_2 = 33.48 L mol^{-1} min^{-1}, $\Delta H^{\neq}$ = 7.6 kcal mol^{-1}, $\Delta S^{\neq}$ = –33.6 eu) are very close to those for the reactions of phosphorus-containing analogue **1a** (k_2 = 31.08 L mol^{-1} min^{-1}, $\Delta H^{\neq}$ = 2.7 kcal mol^{-1}, $\Delta S^{\neq}$ = –50.7 eu).[6,7] Note that aryl-substituted carbanion **5** is somewhat more highly reactive than compound **1a** because of a considerably lower withdrawing ability of the phenyl substituent compared to the $Pr^i_3P^+CH_2$ fragment and, as a consequence, higher nucleophilicity of this carbanion. At the same time, the higher reactivity of the latter compared to that of the phosphorus analogue casts doubt on the earlier[6,7] assumption about the role of steric factors as the driving force of migration of the ester group. However, our results indicate anyway that there is no electrophilic assistance from the phosphonium phosphorus atom and, hence, it is not necessary to include the step of formation of phosphorane of the type **4** into the reaction mechanism.

Thus, the reaction under study (Scheme 5) proceeds in complete accord with the mechanism proposed previously[6] for the reaction of phosphorus-containing zwitterion **1a** with isocyanate (see Scheme 3) through the concerted cyclic transition state with a high degree of localization of the anionic charge.

Scheme 5



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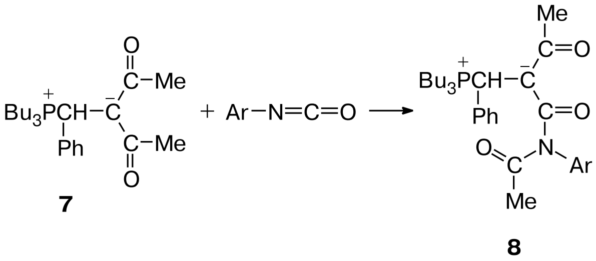
Ar = 2-$NO_2C_6H_4$

This conclusion can additionally be argued by the rather weak influence of the solvent polarity on the rate of the reaction discussed: the k_2 value is 33.4, 23.8, and 48.8 L mol^{-1} min^{-1} in MeCN, dioxane, and THF, respectively. Such an insignificant sensitivity of the reaction rate to a change in the medium polarity is characteristic of concerted processes and well agree with the results obtained for the phosphorus-containing analogue.[6,7]

The further experimental studies showed that both the ester group and other electrophilic groups[9] (in particular, acetyl) can migrate to the nitrogen center. This finding stimulated us to study the kinetic regularities and mechanism of this transformation (Scheme 6).

Scheme 6



Ar = 2-$NO_2C_6H_4$, 3,4-$Cl_2C_6H_3$, 2-MeC_6H_4

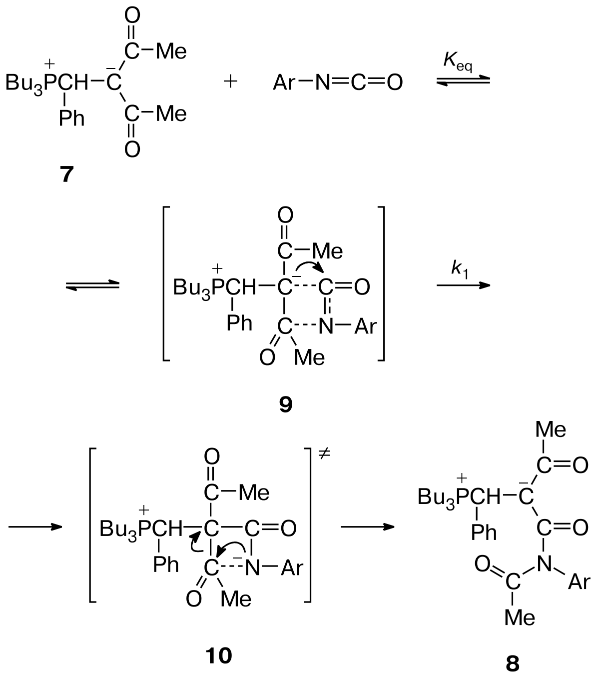
As in the previous investigations, the kinetics was studied by spectrophotometry in a MeCN solution under the conditions of the pseudo-first-order with respect to aryl isocyanates at high excess of phosphonium carbanion **7**, which was varied from 0.01 to 0.05 mol L^{-1}. The reaction was found to proceed *via* the general second order and the first order with respect to each reactant. The resulting kinetic and activation parameters of the reactions of betaine **7** with a series of aryl isocyanates (MeCN, 30 °C) (see Scheme 6) and the wavelengths of kinetic monitoring are presented below.

Ar	λ /nm	k_2 /L mol^{-1} min^{-1}	$\Delta H^{\neq}$ /kcal mol^{-1}	$-\Delta S^{\neq}$ /eu
2-$NO_2C_6H_4$	370	42.46	–6.4	80.4
3,4-$Cl_2C_6H_3$	320	0.270	7.7	43.8
2-MeC_6H_4	330	0.076	9.2	41.3

As a whole, the results obtained agree well with the mechanism earlier proposed by us, although these data introduce a whole series of substantial supplements. For instance, we reliably established for the first time the negative temperature coefficient for the reaction of betaine **7** with *o*-nitrophenyl isocyanate, which is a very rare phenomenon indicating the formation of a strongly exothermic prereaction complex. It was just this isocyanate that in the reaction with phosphabetaine **1a** demonstrated earlier[6,7] although the positive but very low activation energy (2.7 kcal mol^{-1}), which probably can be caused by the formation of the corresponding prereaction complex. Now this fact has been reliably and repeatedly confirmed experimentally, providing a new insight into the mechanism of this unique reaction (without changing, however, its main features).

Thus, the obtained kinetic data make it possible to modify the previously proposed[6] reaction mechanism, supplementing it by the formation of prereaction complex **9** according to Scheme 7, which is common, most likely, for all similar transformations.[10]

Scheme 7



According to this mechanism, the reaction begins from the formation of cyclic four-membered prereaction complex **9** (due to the Coulomb and dipole-dipole interactions) that predetermines the highly ordered structure of the subsequent transition state **10**, which is well consistent with the observed high negative activation entropy.

The inner-complex attack of the carbanion on the most electrophilic (in this system) carbon atom of the isocyanate group is the rate-determining step of the process. After this, the fast attack of the nitrogen atom on the carbonyl carbon atom of the acetyl group occurs *via* the concerted mechanism in the activated complex **10** and is accompanied by the cleavage of the C—C bond of this group with the initial framework of the molecule followed by the formation of the final product. The latter is zwitterion **8**, being, in essence, the product of insertion of aryl isocyanate into the mentioned C—C bond.

According to this scheme, the general reaction rate is described by the kinetic equation

$$W = K_{eq}k_1[\mathrm{ArNCO}][\mathrm{CA}], \qquad (1)$$

where K_{eq} is the equilibrium constant of formation of the prereaction complex; k_1 is the rate constant of the inner-complex rate-determining step of the reaction; [ArNCO] and [CA] are the concentrations of the aryl isocyanate and carbanion, respectively.

According to Eq. (1), the apparent rate constant of the second-order reaction is equal to the product of two elementary constants

$$k_2 = K_{eq}k_1,$$

i.e., this constant itself is not elementary. This fact needs careful treatment of kinetic data, in particular, of the activation parameters, which are determined from the temperature plot of the k_2 rate constant and, hence, are "apparent" values. At the same time, for similar kinetic schemes, these specific features are reduced to minimum, because equilibrium constants are considerably less temperature-sensitive than rate constants.

The proposed mechanism agrees completely with the kinetic results obtained both previously[6,7] and in this work. In particular, this mechanism explains satisfactorily the experimentally observed substantial differences in the reactivity of aryl isocyanates under study (see above). The isocyanate with the strongly withdrawing nitro group in the aromatic ring exceeds in reactivity aryl isocyanates with less withdrawing (3,4-dichlorophenyl) and releasing (*o*-tolyl) substituents by more than two orders of magnitude. According to the mechanism proposed, this is caused by two mutually related factors: strength of prereaction complex **9** (*i.e.*, higher K_{eq} constant) and easiness of the subsequent electron density transfer from the carbanion to the carbon atom of the isocyanate group (rate of the rate-determining step characterized by the k_1 constant). In this case, the both constants change in parallel with a change in the electrophilicity of the carbon atom of the isocyanate group (which is caused, in turn, by the introduction of releasing or withdrawing substituents into the aromatic ring of aryl isocyanates), which predetermines such a considerable overall effect.

Thus, the kinetic study of the reactions accompanied by the C→N migration of the ethoxycarbonyl or acetyl groups in both the phosphorus- and organyl-containing carbanions made it possible to establish the general character of this migration, whose distinctive features are the formation of a prereaction complex followed by the concerted substitution reactions, resulting in new highly conjugated betaines with unusual structures.

Experimental

Methods of syntheses and characteristics of the reagents and reaction products have been described earlier.[1—4,8] Solvents were prepared according to known procedures,[11] and their purity was checked in blank experiments by the absence of changes in the electronic absorption spectra of solutions of aryl isocyanates in purified solvents for 1 day.

Kinetic studies were carried out by the spectrophotometric method on a Perkin—Elmer Lambda-35 spectrophotometer in a temperature-controlled cell in an interval of 20—50 °C (±0.1 °C) under the conditions of the pseudo-first order with respect to aryl isocyanates at high excess of the carbanionic reactants, which was varied from 0.01 to 0.05 mol L^{-1}. The wavelengths in the UV spectra of aryl isocyanates used for kinetic measurements are given in the text. The error in determination of the rate constant was at most ±5%, that for the activation enthalpy did not exceed ±0.5 kcal mol^{-1}, and the determination error for the activation entropy was at most ±1 eu.

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