ISSN 1070-3632, Russian Journal of General Chemistry, 2015, Vol. 85, No. 9, pp. 1995–2023. © Pleiades Publishing, Ltd., 2015.
Original Russian Text © Yu.G. Gololobov, I.Yu. Krasnova, 2015, published in Zhurnal Obshchei Khimii, 2015, Vol. 85, No. 9, pp. 1411–1439.

Transformations of Trisubstituted CH-Acids

Yu. G. Gololobov[†] and I. Yu. Krasnova

Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences,
ul. Vavilova 28, Moscow, 119334 Russia
e-mail: irina7krasnova@yandex.ru

Received May 25, 2015

Abstract—The review considers a new approach based on the intramolecular rearrangements of trisubstituted CH-acids in reactions of the corresponding carbanions with strong electrophiles (isocyanates and polynitrofluorobenzenes), leading to the formation of new types of carbamates and bisamides, pyrazolines, nitroindoles nitroindolines, P-barbitrates, P-heptatrienes, and P-azaoctatetraenes.

Keywords: trisubstituted CH-acids, carbanions, C→N migrations, σ complex, isocyanates, polynitrofluorobenzenes, pyrazolines, carbamates, P-zwitter ions, phosphorylated heterocyclic compounds

DOI: 10.1134/S1070363215090017

Bond cleavage and formation processes are known to form the basis of synthetic organic chemistry. Of particular interest are the processes that occur in mild conditions (at room temperatures and normal pressure, in the absence of catalysts and activators) and give interesting and potentially practically useful target products in high yields. Such products normally take place, if the reagents have a sufficiently high reactivity. The present review considers reactions of, on the one hand, fairly active carbanions formed by deprotonation of tertiary CH-acids or stable carbanions (zwitter ions) and, on the other hand, active electrophiles, primarily, isocyanates and fluoronitrobenzenes.

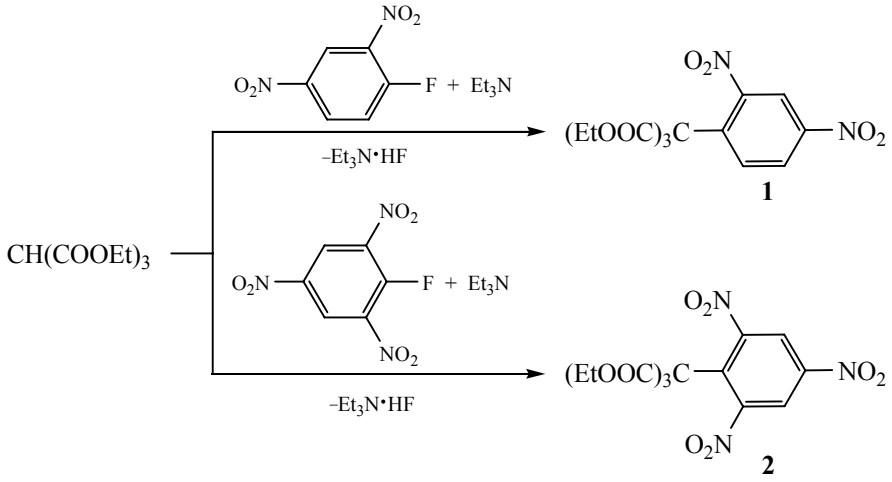
CH-Acids and their derived carbanions are widely used in organic and organoelement synthesis [1–5]. All organic compounds containing a CH bond can formally be classed with CH-acids, and, in this context, the scale of CH acidity of organic compounds extends from methane (pK_a = 56) to tricyanomethane. Of transformations of monosubstituted CH-acids we would like to mention reactions of acetonitrile (pK_a = 31.3) with carboxylic esters [6]; reactions of disubstituted CH-acids (commonly called methylene-active compounds) are the most widely presented in the literature [7–9]; trisubstituted CH-acids (methines [10]) containing three acceptor groups on the central carbon atom have scarcely been studied.

1. Application fields, driving forces, and mechanism of the reactions of carbanions of organic tertiary CH-acids with isocyanates to form carbamates and bisamides via intramolecular C→N migrations of functional groups. Reactions of CH-acids with isocyanates in the presence of bases attract researchers' attention, because they are interesting from the chemical viewpoint and allow synthesis of diverse functionally substituted amides (as stable ammonium salts inclusive) and diverse nitrogenous heterocycles which are of great interest for medicinal chemistry. Therefore, further research into new reactions of CH-acids with isocyanates holds promise both in terms of basic science and in terms of the possibility to obtain new practically useful compounds.

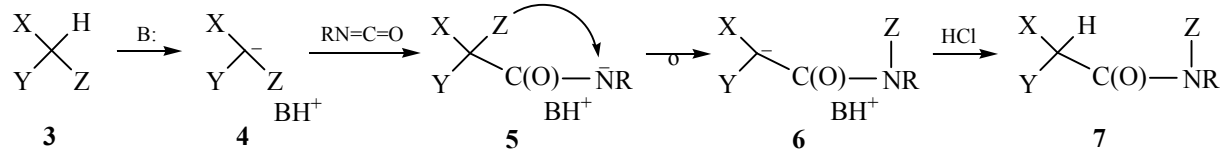
Trisubstituted CH-acids with three electron-acceptor groups on the central atom can exhibit specific properties not typical for disubstituted CH-acids. Reactions of trisubstituted CH-acids suggest introduction of the fourth substituent to the central atom, which may result in a sterically hindered structure. This factor, as well as the presence of weakened C–C bonds may induce one or another molecular transformation to form a more stable structure. For example, nucleophilic aromatic substitution of fluorine in 2,4-di- and 2,4,6-trinitrofluorobenzenes in their reactions with tris(ethoxycarbonyl)methane in the presence of triethylamine gives rise to stable products **1** and **2** (Scheme 1).

[†] Deceased.

Scheme 1.



Scheme 2.



However, in structures **1** and **2** there are no prerequisites for transformations associated with migration of ester groups. Such prerequisites include, among others, the presence of an anionic charge (see Sections 4–7).

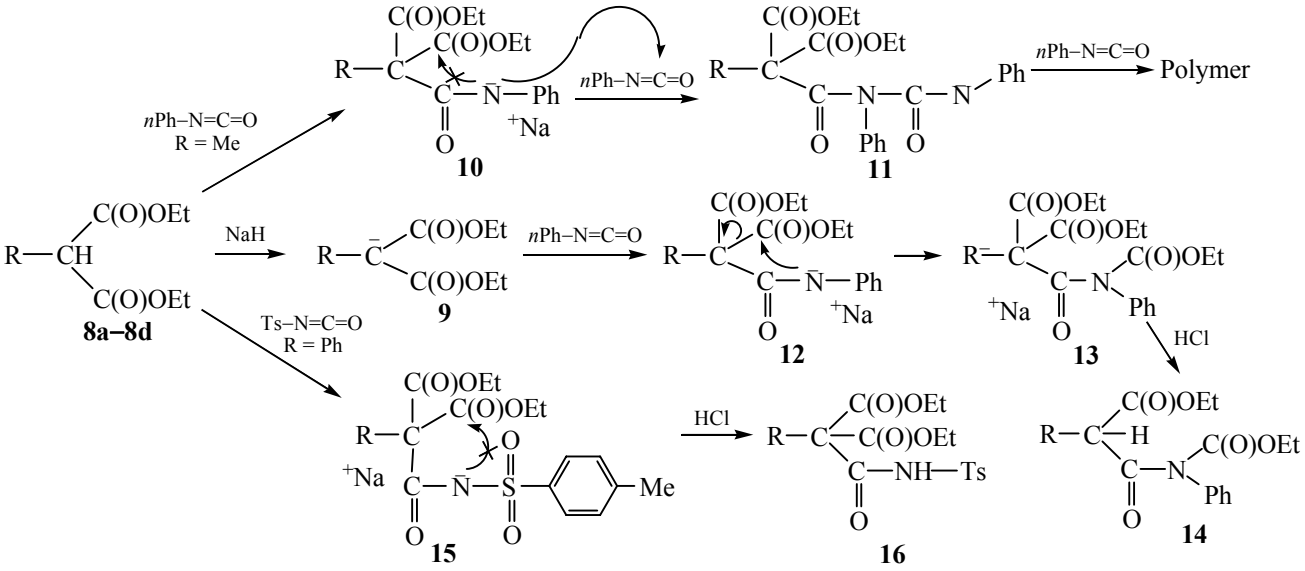
1.1. Reactions of carbanions derived from aryl malonates with isocyanates, involving C→N migration of alkoxycarbonyl groups. Necessary conditions for structural transformations arise in reactions of trisubstituted CH-acids with isocyanates. Under the action of a base CH-acid **3** forms N-anion **4** which, following the general isocyanate reaction pathways, transforms into N-anion **5**, whose formation induces migration of group Z to nitrogen to give the final structure **7** (Scheme 2).

A lot of examples of the realization of this strategy are available; they will be discussed in the present review.

The C→N migrations of electrophilic groups Z by the above scheme have never been described in the literature before our works. Acheson [11] reported migrations of C–C and C–O migrations of alkoxycarbonyl groups. We supposed that the first stage of the reaction with isocyanate of carbanion 4 formed from CH-acid **3** would probably lead to N-anion **5** whose rearrangement would give carbamate **6**. The driving force of the C→N migration of substituent Z would presumably be the energy gain associated with the transformation of N-anion **5** to its isomeric, more delocalized carbanion **6**.

The above reasoning leads us to conclude that C→N migrations of group Z can find wide application. However, it is necessary to find out what structural features of the reactants favor or unfavor this rearrangement. Based on general considerations we can suggest that the first reaction stage should be driven by donor substituents at the carbanion and acceptor substituents at the NCO group, whereas at the second stage the situation should be reverse. However, how the interplay of these substituent properties may affect the final result of the reaction can now be only found out experimentally. Aimed at establishing the regularities and factors that control the reactions under discussion, we studied a series of reactions of ethyl methyl- and arylmalonates with c aryl and tosyl isocyanates [12]. It can be proposed that acceptor substituents at the carbanion center will decrease the nucleophilicity of the carbanion and thus slow down the first reaction stage. Substitution of the highly electrophilic tosyl isocyanate for phenyl isocyanate will undeniably drive the first stage and much slow down the second stage, because the nucleophilicity of the N-anion in the intermediate will be sharply decreased.

Scheme 3.



R = Me (**8a**), Ph (**8b**), 4-$NO_2C_6H_4$ (**8c**), 2,4-$NO_2C_6H_3$ (**8d**).

We performed reactions of phenyl isocyanate with carbanions derived from methyl-, phenyl-, 4-nitrophenyl-, and 2,4-dinitrophenylmalonates. The resulting data were compared with the results of the reaction of tosyl isocyanate with phenylmalonate **8** carbanions (Scheme 3).

It was found the formation of carbamates **14** via 1,3-C→N migration of the C(O)OAlk groups can only at an optimal combination of the nucleophilicity of the carbanion and the electrophilicity of isocyanate. Thus, carbanion **9a** in THF reacts with phenyl isocyanate with heat release and results in anionic polymerization of the latter. Apparently, here N-anion **10** formed at the first stage cannot efficiently attack the carboxyl carbon causing cleavage of the C–C bond, because the methyl substituent decreases the electrophilicity of the ester carbon. At the same time, the reaction of diethyl phenylmalonate carbanion **9b** with phenyl isocyanate in THF at room temperature involves C→N migration of the ethoxycarbonyl group to form carbamate **14.** The IR spectrum of CH-acid **14** shows absorptions bands of the C(O)OEt groups at carbon (1748 cm^{-1}) and nitrogen (1728 cm^{-1}). Due to the presence of a chiral center in compound **14**, the C(O)OEt methylene proton signals in its ^1H NMR spectrum appear as multiplets. The spatial arrangement of the functional groups in carbamate **14** was determined by X-ray method [12].

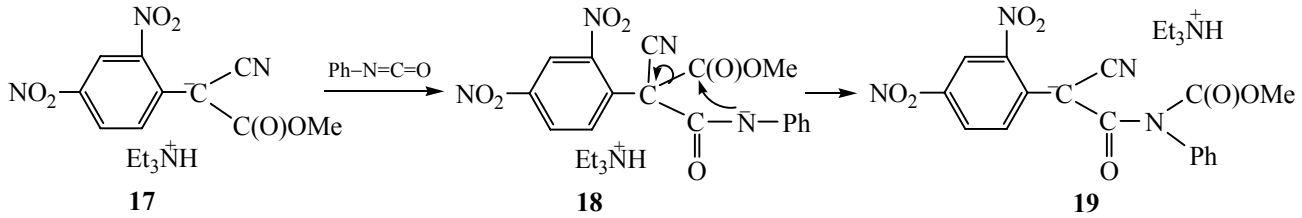
To clarify the role of the nucleophilicity of the carbanion we synthesized the *para*-nitrophenyl analog of **9b**—carbanion **9c**—which, too, fairly readily reacted with phenyl isocyanate to form carbamate **14c**. However, in was found that in the competitive reaction between phenyl- and *para*-nitrophenyl-substituted carbanions **9b** and **9c** *para*-nitrophenyl-substituted product **14c** accumulated 2.5 times slower compared to unsubstituted carbamate **14b**. Furthermore, the formation of carbamate **14d** from (2,4-dinitrophenyl)malonate was associated with severe difficulties, and it could only be detected by spectroscopy.

The latter reaction with (2,4-dinitrophenyl)malonate can be compared with the reaction of carbanion **17** derived from triethylammonium cyano(dinitrophenyl)acetate with phenyl isocyanate, which occurs in rigid conditions to give carbamate **19** (Scheme 4).

Thus, we can conclude that decreasing nucleophilicity of the carbanion unfavors carbamate formation by, probably, slowing down the first reaction stage.

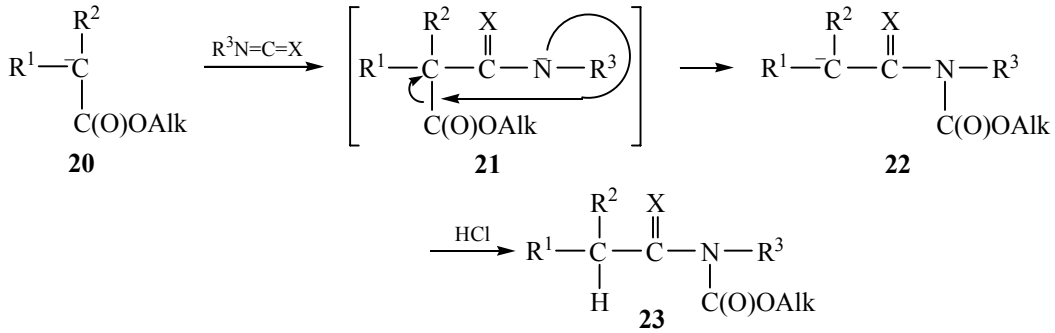
The formation of carbamates should also be hindered if the N-anion has a low nucleophilicity, as this will adversely affect the second reaction stage. We failed to estimate the kinetic contribution of the second stage. However, an illustrative example is provided by the reaction of phenylmalonate carbanion with tosyl

Scheme 4.



17 **18** **19**

Scheme 5.



20 **21** **22** **23**

R^1 = CN, R^2 = Ph; R^1 = COOEt, R^2 = Py^+; R^1 = CN, R^2 = $R^3_3P^+CH_2$, where R^3 = *n*-Pr, *i*-Pr, *n*-Bu, Et_2N; X = O, S; Alk = Me, Et, allyl, propargyl, R^3 = Me, cyclo-C_6H_{11}, Ar.

isocyanate, which stops at the stage of formation of N-anion **17**. Subsequent acidification of the reaction mixture gives amide **19**. This interesting result can be explained by the fact that the low nucleophilicity of N-anion **18** makes impossible an efficient carboxyl attack at room temperature.

Thus, our study of the carbanions of substituted malonic esters with isocyanates allowed us to show for the first time that successful reaction is only possible at an optimal combination of the nucleophilicity of the carbanion and the electrophilicity of the isocyanate. Carbamate formation is prevented by a too low nucleophilicity of the carbanion and a too high electrophilicity of the isocyanate. In such cases either the first or second stage of the process are hindered. The resulting experimental data make it possible to evaluate the scope of the reactions of carbanions with isocyanates, that form carbamates via C→N migrations of the ester group [10, 13, 14].

To find a quantitative measure of an optimal nucleophilic reactivity of carbanions, we made an attempt to evaluate the nucleophilicity of carbanions **20** by means of the MO theory. As the working hypothesis we developed the concept that the second stage of the reaction in question is only possible if the C–C bond neighboring with the functional group in intermediate **21** is much weakened, and this is directly related to the nature of substituents at the carbanionic center. Consequently, it was necessary to quantitatively express the dependence of the nucleophilicity of carbanions **20** on substituents and correlate the resulting data with the features of the reaction of carbanions with isocyanates (Scheme 5).

Taking into account that the nucleophilicity of carbanions is proportional to the HOMO energy, we calculated the HOMO energies for carbanions R^1,R^2C–COOEt **20b** and correlated these data with the results of their reactions with phenyl isocyanate (Table 1).

As seen from the data in Table 1, a positive HOMO energy corresponds to a fairly highly nucleophilic carbanion and, consequently, it successfully reacts with phenyl isocyanate. However, the intramolecular contact of the N-anion formed at the first stage with the ester carbonyl carbon is inefficient. Probably, alkyl substituents hinder both N^-→C(O)OEt attack and C–C bond cleavage.

The HOMO energies ranging from –26 to –14 kcal/mol are optimal, because are characteristic of the carbanions which ensure that both the first and second reaction stages will occur. Carbanions with much more

negative HOMO energies have such a low nucleophilicity that they do not react with phenyl isocyanate.

The described findings give us grounds to suggest that quantum-chemical calculations allow predictions as to whether carbamates can be synthesized by the above scheme, depending on the nature of substituents both in the starting carbanions and in the isocyanates [12].

1.2. Reactions of acetyl carbanions with isocyanates, involving C→N migration of acetyl groups. Proceeding with research into reactions involving intramolecular C→N migration of functional groups, we turned to reactions of isocyanates with carbanions bearing an acetyl group at the carbanion center [15]. As the object for study we chose ketone **24** (content of the enol form 56.4%) which was converted to anion **25** by treatment with sodium hydride in THF. Anion **25** readily reacted with phenyl isocyanate and gave (after acidification of the reaction mixture) amide **28** in which the acetyl group resides at the nitrogen atom of the phenyl isocyanate group inserted into the C–C bond (Scheme 6).

The first stage of the reaction of carbanion **25** with phenyl isocyanate is likely to form N-anion **26**, whose intramolecular interaction with the C=O carbon leads to dissociation of the C–C bond and C→N migration of the acetyl group. Apparently, like with alkoxycarbonyl groups, the driving force of the C→N migrations of the acyl group is the energy gain associated with the isomerization of N-anion **26** into a more delocalized carbanion **27**. Evidence for the formation of C→N migration product **28** is provided by the observation of a singlet signal at 6.06 ppm in the ^{1}H NMR spectrum. Analogous C→N rearrangement takes place in the reaction of carbanion **25** with benzene-1,4-diyl diisocyanate (Scheme 7).

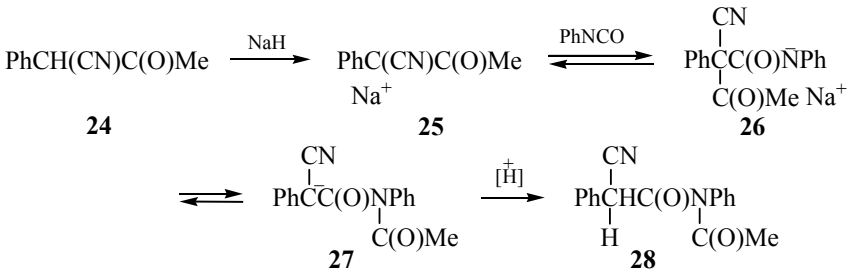
Table 1. HOMO energies in carbanions **22b** in the reaction with phenyl isocyanate

R^1	R^2	*E*(HOMO), kcal/mol
CH_3[a]	CH_3	+27.45
CH_3[a]	Ph	+6.57
CH_3[a]	CN	+0.10
CH_3[b]	EtOC(O)	–4.04
EtOC(O)[b]	EtOC(O)	–26.16
NO_2[b]	Ph	–24.41
CN[b]	Ph	–14.40
Ph[b]	EtOC(O)	–14.73
2,4-NO_2Ph[c]	EtOC(O)	–45.27

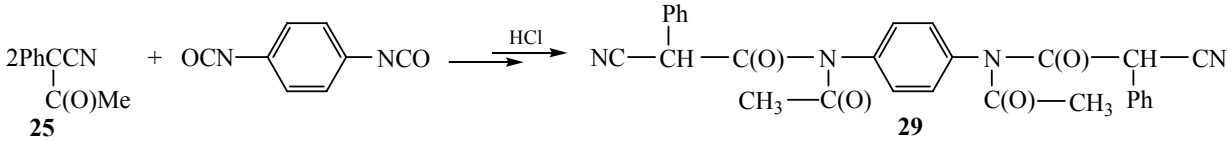
[a] The reaction stops after the first stage, active polymerization of phenyl isocyanate takes place.
[b] Reaction forms carbamates.
[c] Carbanion does not react with phenyl isocyanate.

1.3. Comparative migration ability of the acetyl and ethoxycarbonyl groups. To compare the C→N-migration abilities of the acetyl and ethoxycarbonyl groups, we reacted phenyl isocyanate with the carbanion derived from CH-acid **30** which contains both these groups at the same carbon atom [15]. It was found that the reaction gave ketone **31** rather than its isomeric ester **32** (Scheme 8).

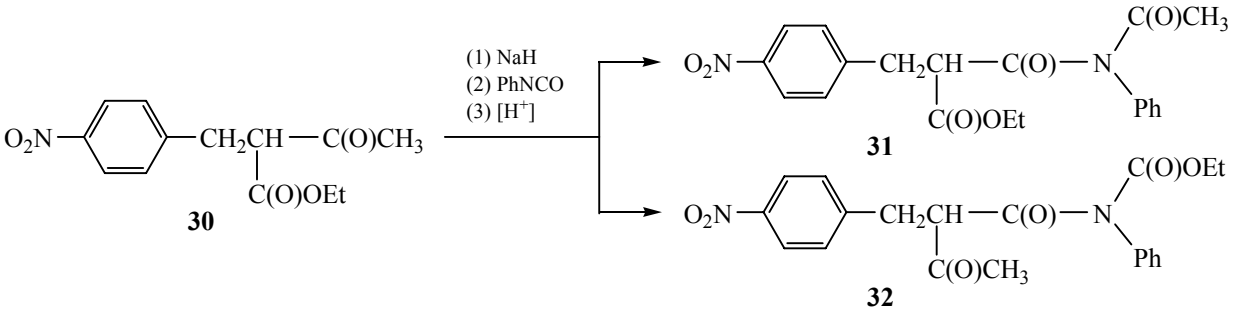
Scheme 6.



Scheme 7.

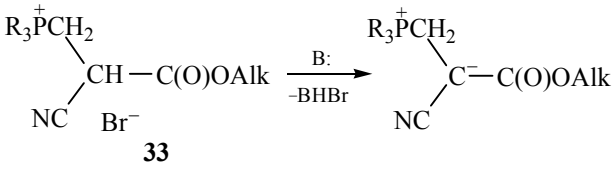


Scheme 8.



Consequently, the acetyl group easier migrates from carbon to nitrogen compared ethoxycarbonyl.

2. Reactions of P-zwitter ions with isocyanates, involving C→N migrations of alkoxycarbonyl or keto groups and leading to carbamates or bisamides with the P-zwitterionic structure. *2.1. Reactions of P-zwitter ions with isocyanates, involving C→N migrations of alkoxycarbonyl groups.* Trisubstituted phosphonium salt CH-acids are of considerable interest. We performed the title reaction with phosphonium salts **33**.

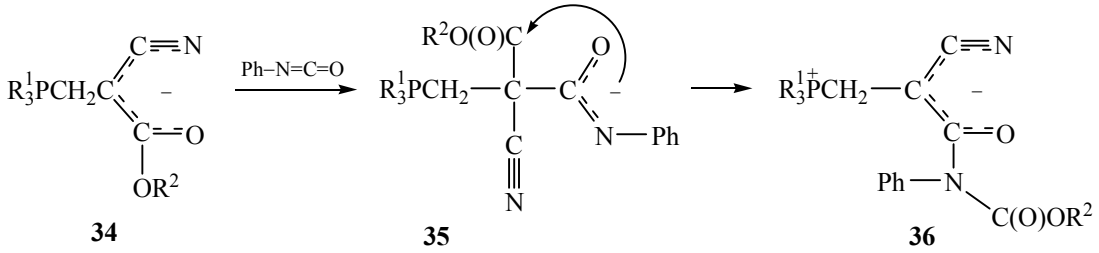


We [16, 17] were the first to show that organophosphorus zwitter ions **34** react with phenyl isocyanate to form carbamate **35** with zwitterionic structure **36** (Scheme 9).

Such transformations are of a fairly general character. At the same time, their result is strongly on the steric and electronic characteristics of both the P-zwitter ions and isocyanates. Of considerable interest are the results obtained in our study of the steric effects of *ortho* substituents in the ring of the isocyanate molecule on carbamate formation by the considered scheme [18, 19] (Scheme 10).

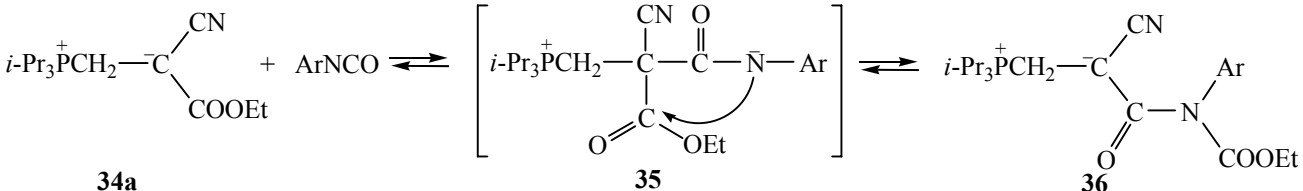
ortho-Alkyl substituents in aryl isocyanates are known to decrease the reactivity of the latter, which is likely associated both with the electronic effects and

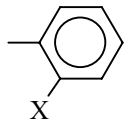
Scheme 9.



R^1 = *i*-Pr, R^2 = Et (**a**); R^1 = Pr, R^2 = Me (**b**); R^1 = Bu, R^2 = Et (**c**); R^1 = Et_2N, R^2 = Et (**d**).

Scheme 10.



Ar =  (**a**), 2,6-$Me_2C_6H_3$ (**b**), 3,5-$Me_2C_6H_3$ (**c**).

with the steric shielding of the reaction centers in the reactants. The second stage involves nucleophilic attack of the nitrogen atom of N-anion **35** on the carbonyl carbon of the alkoxycarbonyl group. The rate of the second reaction stage can, too, be sensitive to the steric effects of *ortho* substituents in the aromatic ring. Evidence showing that steric effects play an important role in the considered transformations is provided by a comparison of the reactivities of 2,6-dimethyl- and 3,5-dimethylphenyl isocyanates toward zwitter ion **34a** (Scheme 10).

The yield of carbamate **36b** in the reaction of the isocyanate with an *ortho* arrangement of the methyl groups is as low as 4.7% (^{31}P NMR), whereas the yield of carbamate **36c** in the reaction with the isocyanate in which the methyl substituents are arranged *meta* to the isocyanate function is up to 95%. The structure of carbamate **36c** was determined by X-ray diffraction (XRD) analysis [19].

Further evidence for the essential role of *ortho* substituents on the formation of carbamates **36** by the above scheme was provided by comparative experiments with *ortho*-methyl-, *ortho*-ethyl, and *ortho*-isopropyl isocyanates. Table 2 lists the results of these experiments. As seen from the table, consecutive replacement of hydrogen by alkyl groups (from methyl to isopropyl) adversely affects the carbamate formation process, which requires a longer reaction time to achieve reasonable yields of carbamates.

It should be noted that the formation of carbamates **36** is quite a selective process, as evidenced by the fact that the ^{31}P NMR spectrum of the reaction mixture displays no other signals than signals of P-zwitter ions: starting **34a** and final **36**. The reaction mixture also contains minor amounts of triisopropylphosphines and its oxide formed on the partial dissociation of the P-zwitter ion into triisopropylphosphine and ethyl 2-cyanoacrylate, caused by heating. Electronic factors, too, contribute something, but the contributions of both factors are still impossible to assess separately.

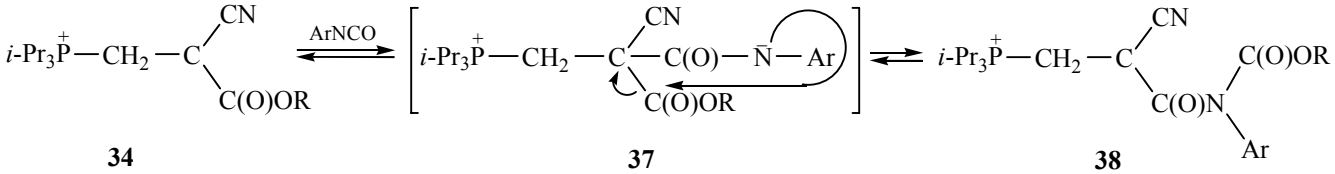
Table 2. Effect of the *ortho* substituent on the formation of carbamate **36**

Substituent X	Reaction time, h	Yield, %	Charton's steric parameter of substituent X
H	48	95	0
Me	700	90	0.52
Et	1000	80	0.56
i-Pr	2000	60	0.76

Zwitter ions **34b** and **34c** derived from allyl and propargyl cyanoacrylates, too, smoothly react with excess aryl isocyanates by a general scheme involving isocyanate insertion into the C–C bond of the starting zwitter ion [20] (Scheme 11).

Carbamates **38b** and **38c** formed by alkoxycarbonyl migration from carbon to nitrogen have spectral characteristics typical of this class of compounds. However, it should be noted that the signals of isopropyl methyl protons and protons of the CH_2 group on phosphorus in the ^{1}H NMR spectrum of carbamate **38b** are broadened, while other proton signals, as expected, appear as multiplets. As the temperature is raised to 55°C all proton signals become well-resolved. This fact can be explained in terms of frozen rotation of the 1-naphthyl substituent about the C–N bond of the carbamate fragment in compound **38b**. Such freezing, already at room temperature, creates enantiomeric asymmetry, as a result of which protons of the isopropyl and methylene groups at the phosphorus atoms, having different surroundings, become diastereotopic. At 55°C, the l-naphthyl group at the nitrogen atom starts to rotate freely, the molecule is no longer asymmetric, and this is reflected in the ^{1}H NMR spectrum. Such atropoisomerism was considered in detail in [21, 22].

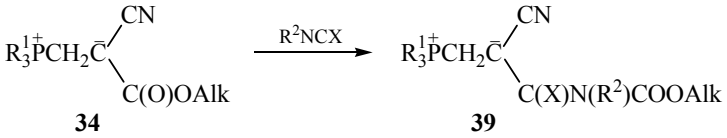
Scheme 11.



34 **37** **38**

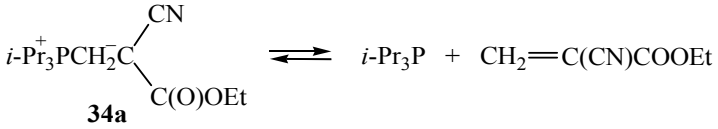
R = $CH_2CH{=}CH_2$, Ar = 1-$C_{10}H_7$ (**a**); R = $CH_2C{\equiv}CH$, Ar = Ph (**b**).

Scheme 12.



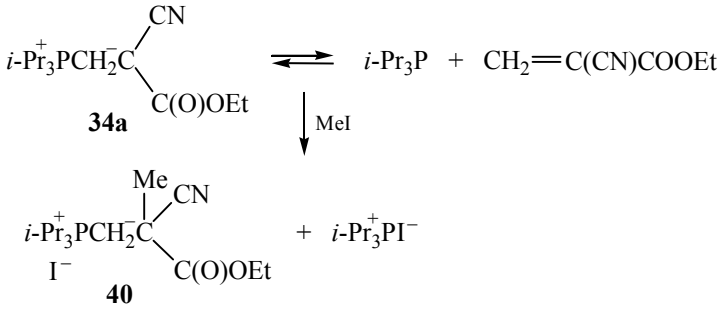
34 **39**

Scheme 13.



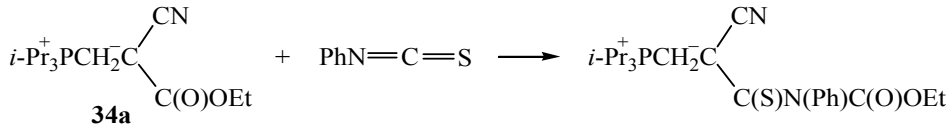
34a

Scheme 14.



34a **40**

Scheme 15.



34a

In [22] we determined the barrier to rotation about the C–N bond for the analog of compound **38b** with R = Et ($\Delta G_c^{\neq}$ = 63.0±0.1 kJ/mol) and its coalescence temperature (T_c = 32±4°C). Apparently, the l-naphthyl radical in compound **38b** has a close barrier to rotation about the C–N bond.

The rate and direction of the reactions of P-zwitter ions **34** with iso(thio)cyanates are strongly dependent on the electronic and steric characteristics of the reactants. Such zwitter ions fairly readily react with phenyl-, *meta*-, or *para*-substituted isocyanates RNCX to form carbamates **39** [23] (Scheme 12).

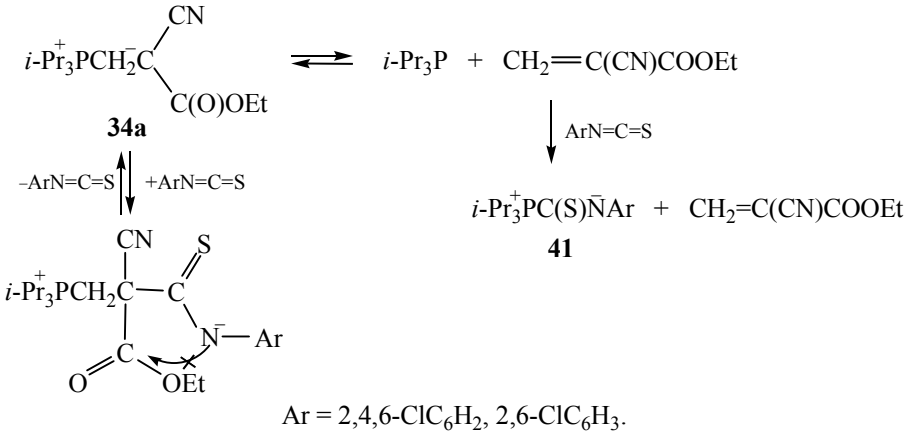
At the same time, the reactions of bis-*ortho*-substituted aryl isocyanates and isothiocyanates with zwitter ion **34** are a special case. Thus, for example, 2,2,4-trimethylphenyl isocyanate in similar conditions does not at all react with P-zwitter ion **34a**. The ^{31}P NMR spectrum (in CH_2Cl_2 or $CDCl_3$) of an individual crystalline zwitter ion **34a** shows, along with the base signal (38.7 ppm), minor signals from triisopropylphosphine (20.6 ppm). Consequently, we deal here with equilibrium shifted well to the left (Scheme 13).

This equilibrium explains the results of reactions of zwitter ion **34a** with methyl iodide, bis(*ortho*-chlorophenyl) isocyanates, and mercury dichloride. The reaction of zwitter ion **34a** with methyl iodide (especially with a considerable excess of the latter) gives not only phosphonium salt **40**, but also triisopropyl(methyl)phosphonium iodide (Scheme 14).

The reaction of zwitter ion **34a** with phenyl isothiocyanate involves C→N migration of the ethoxycarbonyl group (Scheme 15).

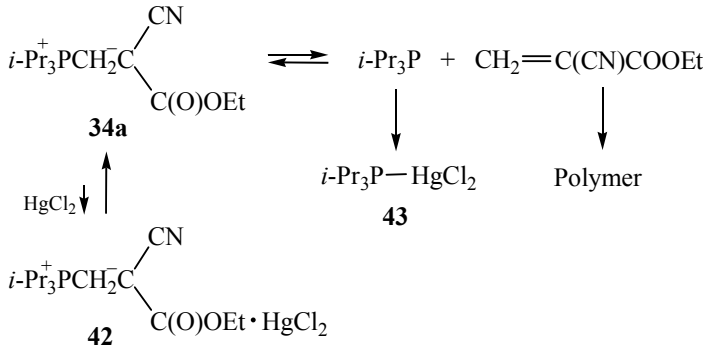
However, the reactions with 2,2-di- and 2,2,4-trichlorophenyl isocyanates results in almost exclusive formation of zwitter ions **41** as a result of reaction of triisopropylphosphine with di- and trichlorophenyl isocyanates (Scheme 16).

Scheme 16.

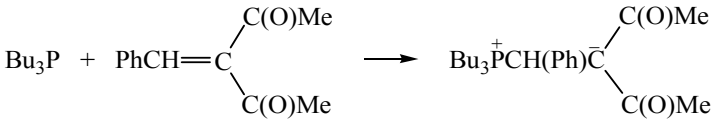


Ar = 2,4,6-ClC_6H_2, 2,6-ClC_6H_3.

Scheme 17.



Scheme 18.



44

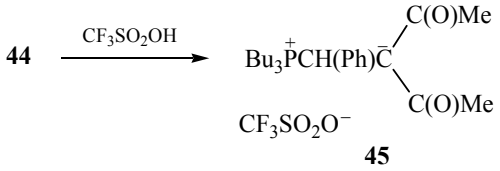
Such an unusual result is probably explained by the steric hindrance created by the *ortho*-chlorine substituents in aryl isocyanates at the second stage of the reaction which involves nucleophilic attack of the N-anion on the ethoxycarbonyl carbon. The first stage is reversible, which is favored by the facile polymerization of ethyl cyanoacrylate under the reaction conditions.

The fact that the reaction takes an unusual route appears to be mainly explained by steric factors associated with the presence of fairly bulky chlorine substituents in the *ortho* positions of the phenyl ring. However, reactions of zwitter ion **34a** with sterically uncongested highly electrophilic reagents lead to the same results. Thus, the reaction of zwitter ion **34a** with mercury dichloride in methylene chloride lasts as little as a few minutes and gives complex **43**. It can be suggested that the initially formed unstable complex **42** which transforms to a stable crystalline complex **43** (Scheme 17).

2.2. Reactions P-zwitter ions with isocyanates, involving C→N migrations of keto groups. To study migration of the keto group in P-zwitter ions, we synthesized zwitter ion **44** [18] by reacting tributylphosphine with 3-benzylidenepentane-2,4-dione (Scheme 18).

The protonation of zwitter ion **44** forms a crystalline phosphonium salt **45**, whose structure was assessed by NMR spectroscopy [18] (Scheme 19).

Scheme 19.



45

The anionic charge in zwitter ion **44** is strongly delocalized in the O–C–C–C–O pentad. Thus, if the carbonyl absorption band in the IR spectrum of salt **45** is observed at 1750 cm^{-1}, then the respective band for zwitter ion **44** shifts to 1480 cm^{-1}. In the reactions with phenyl, cyclohexyl, or 3,4-dichlorophenyl isocyanates, zwitter ion **44** transforms, following the general scheme of isocyanate insertion into the C–C bond, into zwitter ions **46** which has one keto group at the carbanion center and the other, at the nitrogen atom (Scheme 20).

2.3. Reaction kinetics. In [24, 25] we performed a spectrophotometric kinetic study of the described processes under pseudo-first-order conditions in aryl isocyanate [acetonitrile, high excess of salt (0.01–0.05 M), λ = 370 nm, 20°C] and showed that the reaction is first-order in each reagent and second-order overall.

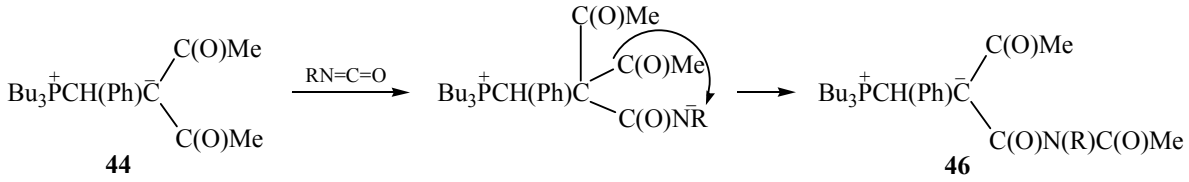
The kinetic and activation parameters of these reaction (k_{II} = 33.48 L mol^{-1} min^{-1}, $\Delta H^{\neq}$ = 7.63 kcal/mol, $\Delta S^{\neq}$ = –33.63 eu) are quite close to those of the reactions with the phosphorus-containing analog [k_{II} = 31.08 L mol^{-1} min^{-1}, $\Delta H^{\neq}$ = 2.66 kcal/mol, $\Delta S^{\neq}$ = –50.74 eu]. It is noteworthy that the aryl-substituted carbanion is even slightly more reactive, which is undeniably explained by the much lower acceptor power of the phenyl substituent compared to the *i*-$Pr_3P^+CH_2$ ion and, consequently, higher nucleophilicity of carbanion **47,** in complete agreement with the previously proposed mechanism for the reaction of P-zwitter ion **48** with isocyanate via a concerted cyclic transition state with a strongly delocalized anionic charge [25] (Scheme 21).

Further evidence for this explanation is provided by the fact that the rate of the reaction with carbaniona **48** is only slightly affected by the polarity of the solvent: The k_{II} (L mol^{-1} min^{-1}) in acetonitrile, dioxane, and THF are 33.4, 23.8, and 48.8, respectively. Such a low sensitivity of the reaction rate to the polarity of the medium is characteristic of concerted processes and well agrees with the results for the phosphorus analog.

Further experiments showed that not only ester but also other electrophilic groups, like acetyl, can migrate to the nitrogen center. This finding prompted us to study the kinetic regularities and mechanism of this reaction using P-zwitter ion **49** as the carbanion.

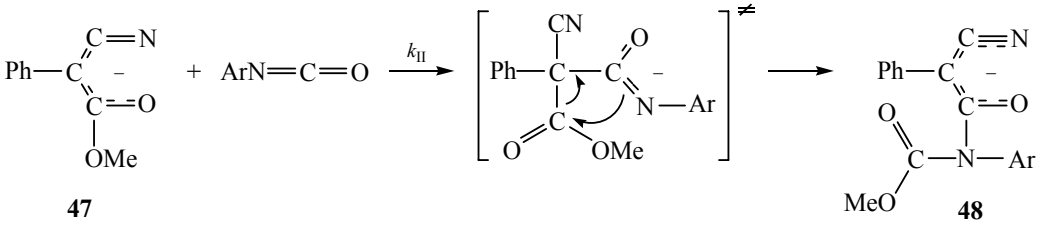
The kinetic study was performed by spectrophotometry in an acetonitrile solution under pseudo-first-order conditions with respect to aryl isocyanate and with a high excess of phosphonium carbanion **49** (*c* = 0.01–0.05 M). It was found that the reaction is

Scheme 20.



R = Ph, *cyclo*-C_6H_{11}, 3,4-$Cl_2C_6H_3$.

Scheme 21.



first-order in each reagent and second-order overall. The resulting kinetic and activation parameters of the reactions of zwitter ion **49** with a series of aryl isocyanate are listed in Table 3. In general, they are in a good agreement with the reaction mechanism, but, at the same time, highlight some essential additional details. Thus, it is the first time that we reliably established a negative temperature coefficient for the reaction of zwitter ion **49** with *o*-nitrophenyl isocyanate. This is in itself quite a rare phenomenon implying that the reaction occurs via formation of a strongly exothermic prereaction complex. It should be noted that previously in the same reaction of zwitter ion **49** just with this isocyanateом we observed a positive, while quite low, activation enthalpy (2.66 kcal/mol), which, too, is likely to be associated with the formation of the corresponding prereaction complex. At present this fact is reliably established on the basis of ample experimental evidence, and this makes us to look in a new way at the mechanism of this unique reaction, even though not revising it radically (Scheme 22).

According to the proposed mechanism, the reaction begins with the formation of a cyclic four-membered prereaction complex **50** (due to Coulomb and dipole interactions quite natural in this system), which predetermines a highly ordered structure of the forming transition state **51**; this reasoning is in a good agreemnt with the observed large negative activation entropies.

Table 3. Kinetic parameters of the reactions of zwitter ions **49** with aryl isocyanates (acetonitrile, 30°C)

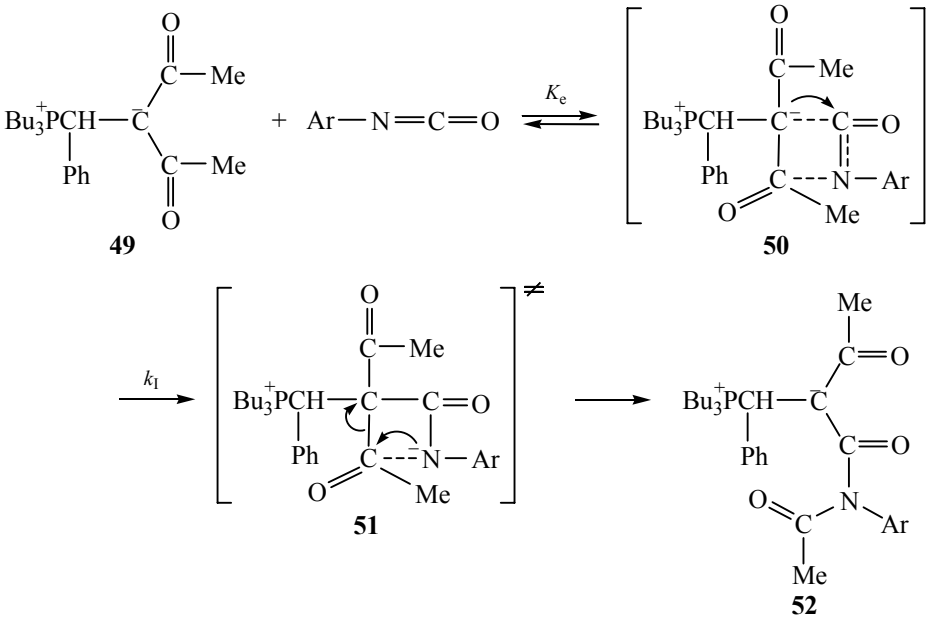
Ar	λ, nm	k_{II}·, L mol^{-1} min^{-1}	$\Delta H^{\neq}$, kcal/mol	$-\Delta S^{\neq}$, eu
o-$O_2NC_6H_4$	370	42.46	–6.4	80.4
3,4-$Cl_2C_6H_3$	320	0.270	7.7	43.8
o-MeC_6H_4	330	0.076	9.2	41.3

The intracomplex attack of the carbanion on the isocyanate carbon (the most electrophilic carbon atom in this system) is the rate-limiting stage. The subsequent attack of the nitrogen atom on the acetyl carbonyl carbon in transition state **51,** accompanied by C–C bond cleavage in the acetyl group and formation the final product, zwitter ion **52,** which, in essence, is the product of insertion of aryl isocyanate into the acetyl C–C bond, is a fast process.

The overall reaction rate in this case will be described by the kinetic following equation: $w = K_e k_I$[ArNCO][carbanion], where K_e is the equilibrium constant of formation of the prereaction complex; k_I, rate constant of the rate-limiting intracomplex reaction stage; and [ArNCO] and [carbanion], concentrations of aryl isocyanate and carbanion, respectively.

According to the above equation, the apparent rate constant of the second-order reaction is equal to the

Scheme 22.



product of two elementary constants: $k_{II} = K_e k_I$, i.e. it in itself is not an elementary constant. Therefore, one should be careful in interpreting kinetic data and, in particular, activation parameters which are determined from the temperature dependence of the apparent rate constant k_{II} and, consequently, too, are nothing more that apparent values. At the same time, with such kinetic schemes these "drawbacks" are minimized, because equilibrium constants are much less sensitive to temperature than rate constants.

The proposed reaction mechanism is well consistent with kinetic results (obtained both previously and in the present work) and, in particular, very well explains the essential variations in reactivity over the aryl isocyanate series, observed in the kinetic experiment (Table 1). The isocyanate with the acceptor nitro group in the aromatic ring is more than two orders of magnitude more reactive compared to aryl isocyanates with less acceptor (3,4-dichlorophenyl) and donor (*o*-tolyl) substituents. This, in agreement with the proposed mechanism, is associated with two interrelated reasons: stability of prereaction complex **50** (i.e. higher equilibrium constant of its formation K_e) and facility of the subsequent electron density transfer from the carbanion onto the isocyanate carbon atom (the limiting reaction stage characterized by the rate constant k_I). In our specific case, as the electrophilicity of the isocyanate carbon varies (with donor or acceptor substitution in the aromatic ring of aryl isocyanates), both constants vary in parallel with each other, which explains such a considerable net effect.

Thus, the kinetic study of new reactions involving C→N migrations of the ethoxycarbonyl or acetyl groups both in phosphorus-containing and organyl carbanions showed that these reactions have a common mechanism featuring formation of prereaction complex **50** and subsequent concerted substitution reactions leading to previously unknown highly conjugated betains with an unusual structure.

However, our attempts to detect intermediate **50** in the course of our spectral study on the reactions of P-zwitter ions with aryl isocyanates have not met with success. In the ^{31}P NMR spectra of the reaction mixtures with unsubstituted and *ortho*-substituted aryl isocyanates, no signals assignable to this intermediate were found. The reactions are highly selective, and the spectra of the reaction mixtures showed two signals with synchronously chaging intensities: the signal of the starting zwitter ion **49** and the signal of the forming carbamate **52**.

We expected that the steric shielding of the reaction centers by *ortho* substituents, which slows down the overall process but has no effect of the rate of the first stage, would allow us to detect intermediate **50**. However, it could be detected neither in this case nor with the low-reactive phenyl isothiocyanate.

3. Synthesis and mechanism of carbamate formation in the reactions of pyridinium ylides with isocyanates, involving C→N migrations of alkoxycarbonyl groups. To find out the scope of carbamate formation in reactions of carbanions with isocyanates, as well as taking into account that certain pyridine and carbamate derivatives are known as valuable medicines, we studied reactions of pyridinium ylides with isocyanates [26]. Ylide **53c** was especially interesting to introduce in these reactions, because it contains a fragment of the widely used cordiamine drug.

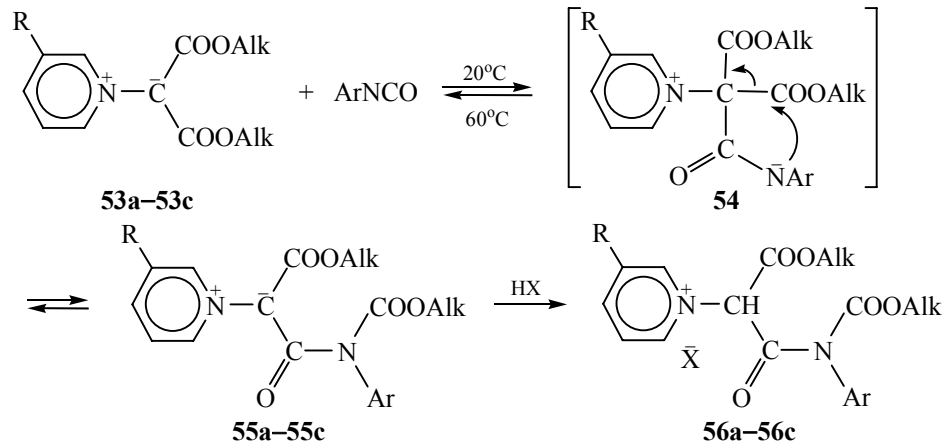
The reactions of ylides **53** with isocyanates in CH_2Cl_2 at room temperature gave carbamates **55**, thereby providing evidence for the general nature of the rearrangement involving C→N migration of alkoxycarbonyl groups [27] (Scheme 23).

According to IR data, the anionic charge in the starting ylides **53** is delocalized over both COOAlk groups (the bands of conjugated COOAlk grooups are observed at 1600–1660 cm^{-1}), but in the rearrangement products—carbamates **55—**only one COOAlk group is conjugated with the anionic charge (1580–1590 cm^{-1}), and, at the same time, a band assocciated with unconjugated COOAlk groups appears near 1720 cm^{-1}.

The progress of the conversion of ylides **53** into carbamates is readily traced by ^1H NMR spectroscopy.

The reactions of isocyanates with ylides **53** are reversible, and, therewith, the degree of conversion of the latter into carbamates **55** is strongly dependent on the steric and electronic characteristics of substituents in the isocyanate group. For example, cyclohexyl isocyanate even in a 5-fold excess very slowly reacts with кратном избытке реагирует с ylide **53b** and, by the ^1H NMR data, the equlibrium muxture of ylide **53b** (64%) and the corresponding carbamate (36%) at room temperature is formed within 30 days. *Ortho* substituents in the starrting aryl isocyanates, too, slow down the process substantially. At the same time, *para*-nitrophenyl isocyanate (excess 70%) reacts with ylide **53b** completely within 1 day to form carbamate **55a**. According to the data, the resulting crystalline carbamates dissolved in $CDCl_3$ decompose to give the starting ylides within a few weeks. Attempted

Scheme 23.



Alk = Me, R = H (**53a**); Alk = Et, R = H (**53b**); Alk = Et, R = C(O)NEt$_2$ (**53c**); Alk = Et, R = H, Ar = 4-NO$_2$C$_6$H$_4$ (**55a**); Alk = Et, R = H, Ar = 4-EtOOCC$_6$H$_4$ (**55b**); Alk = Et, R = CONEt$_2$, Ar = Ph (**55c**); Alk = Me, R = H, Ar = Ph, X = ClO$_4$ (**56a**); Alk = Et, R = H, Ar = = 4-NO$_2$C$_6$H$_4$, X = MeSO$_3$ (**56b**); Alk = Et, R = CONEt$_2$, Ar = Ph, X = I (**56c**).

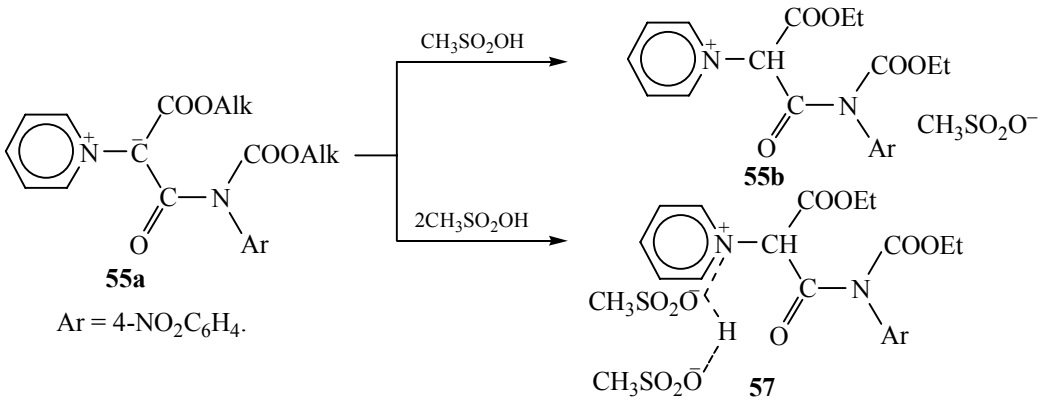
recrystallization of carbamates **55** (isolated by low-temperature crystallization) from boiling acetone resulted in their complete decomposition to the starting pyridinium ylides. Addition of strong acids to colored methylene chloride solutions of ylides **53** led to complete decoloration of the solutions as a result of formation of colorless salts **56**. The latter are stable on heating and storage.

It is interesting to note that carbamate **55a** forms monosalt **56b** with an equimolar amount of methanesulfonic acid and a crystalline double salt **57** with excess methanesulfonic acid. The structure of salt **57** is discussed in [26] (Scheme 24).

Of considerable interest is the mechanism of rearrangement of adducts **54** into carbamates **55**. The second stage of the reactions of pyridinium ylides with isocyanates is a nucleophilic substitution reaction, where N-anion attacks the ester carbon. As known, reactions of nitrogenous bases with carboxylic esters normally proceed via expulsion of the alkoxy group and lead to the corresponding amides. If such reactions occur intermolecularly, their final products are cyclic amides. Thus, the reaction with isocyanates of lithium salts containing one ester group [28] forms 4-membered cycles due to intramolecular interaction of the amide group with ester fragment. Therewith, the leaving group is EtO, which allows synthesis of diverse cyclic amides in 40–90% yields (Scheme 25).

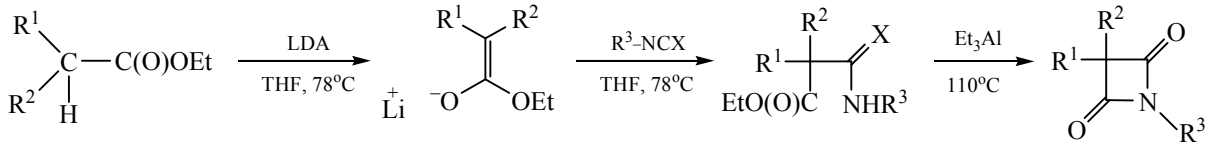
In the transformations we considered here, the leaving group is an ester group and the bond to be cleaved is C–C rather than C–O, which is a rare example in organic chemistry. The reason for the

Scheme 24.



Ar = 4-NO$_2$C$_6$H$_4$.

Scheme 25.



$R^1 = R^2 = Me$, X = O; $R^1 = R^2 = Me$, X = S; $R^1 = H$, $R^2 = Et$, X = S; $R^1 = Me$, $R^2 = Et$, X = S; $R^1 = H$, $R^2 = C(O)OMe$, X = S; $R^1 = C(O)Me$, $R^2 = Et$, X = S; $R^1 = (HC{=}CMe_2)$, X = S; $R^1 = (HC{=}CMe_2)$, X = O; $R^3 = 4\text{-}MeOC_6H_4$.

preferred cleavage of the C–C bond in the present case relates to the electron-acceptor effect of the alkoxycarbonyl group and the positive charge of the pyridinium ring, which weaken the C–C bond. At the same time, the C−C bond cleavage gives rise to carbanion **55**, where the anionic charge is stronger delocalized than in the parent carbanion **53**, as evidenced by the IR data. For example, the band of the conjugated ethoxycarbonyl group in the IR spectrum of the rearrangement product **55a** is observed at 1591 cm^{-1}, whereas the respective band in the spectrum of the parent ylide **53b** appears at 1658 cm^{-1}.

What is the mechanism of the transformation of intermediates **59** into the rearrangement products **62**? Whether a 4-membered intermediate like **60** or **62** forms or a new C–N bond forms synchronously with an old C–C bond cleavage? In our study on analogous transformations in reactions isocyanates with phosphorus-containing zwitter ions we failed to detect intermediate products by ^{31}P NMR spectroscopy. Therefore, a mechanism involving direct nucleophilic substitution at the sp^2-carbon atom, similar to the mechanism of nucleophilic substitution at the olefinic carbon in certain types of unsaturated compounds, was proposed.

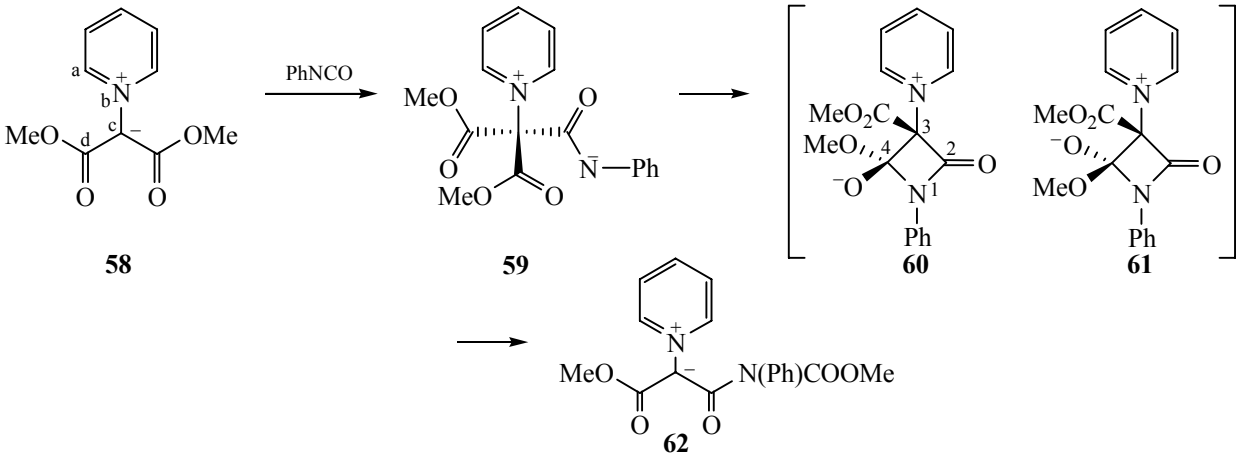
To find out the mechanism of the studied rearrangement considered here and, in particular, to determine the structure of the adduct formed at the first reaction stage, we performed semiempirical quantum-chemical calculations by the AM1 and PM3 methods and DFT (B3LYP/6-31G*) calculations of pyridinium ylide **58**, adduct **59**, and carbamate **62**, as well as possible intermediate azetidinones **60** and **61** [27] (Scheme 26).

The structure of ylide **58** has never been reported in the literature. According to our calculations, the system is nonplanar. The abcd torsion angle is 18.6° (PM3), 31.5° (AM1), and 50.5° (DFT), respectively. The rotational barriers are, too, not very high: $\Delta\Delta H_f$ = 4.6 (PM3) and 4.8 kcal/mol (AM1). The reaction of ylide **58** with phenyl isocyanate, leading to adduct **59**, is endothermic (ΔE = 5.1 kcal/mol, DFT).

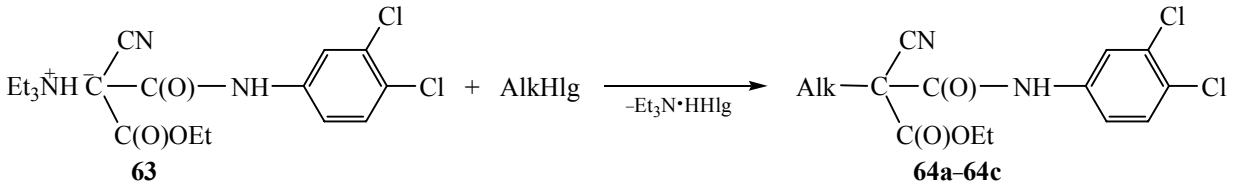
The mechanism of the subsequent rearrangement of adduct **59** into carbamate **62** is unknown. We could suggest the intermediate formation of azetidinones **60** or **61** followed by ring opening to form the final carbamate **62**.

However, even though the potential energy surfaces of azetidinones were thoroughly examined at the

Scheme 26.



Scheme 27.



63 **64a–64c**

AlkHlg = CH_3I, CH_2=$CHCH_2Br$, $C_6H_5CH_2Cl$; Alk = CH_3 (**a**), CH_2CH=CH_2 (**b**), $CH_2C_6H_5$ (**c**).

semiempirical level of theory (AM1, PM3), no local minima corresponding to structures **60** and **61** were found.

According to the DFT (B3LYP/6-31G*) calculations, the rearrangement of adduct **60** into carbamate **62** is an exothermic process (ΔE = 17.9 kcal/mol). The energy of the transition state is low (the potential barrier for the direct and reverse reactions are 7.5 and 25.4 kcal/mol, respectively).

Thus, our quantum-chemical calculations gave evidence showing that the reaction of ylide **58** with phenyl isocyanate involves initial formation of adduct **60** which directly, with a low potential barrier and without forming cyclic intermediate products, rearranges into carbamate **62**.

3.1. Certain chemical properties of amides derived from tertiary CH-acids. The above-described functionally substituted amides belong to a fairly poorly studied class of derivatives of methanetricarboxylic acids. The accumulation of strong electron acceptors at one carbon atom much weakens the bond between these functional groups with the central carbon atom. Therefore, such compounds should be functionalized in mild conditions. Below we present four types of their transformations: alkylation, arylation, halogenation, and dimethylaminomethylation.

A few examples of alkylation of trisubstituted CH-acids, which are at all not very numerous, are described by Tsunoda et al. [29]. The nucleophilicity of triethylammonium salt **63a** having three strong electron acceptors at the central carbon atom is fairly low. Nevertheless, active alkyl halides react with salt **63a** under slight heating in acetonitrile or benzene to form the substitution products **64** with reasonable yields [30] (Scheme 27).

Noteworthy is the difference in spectral characteristics between the starting salt **63a** and alkylation products **64**. The CN, C(O)OEt, and C(O)NHAr groups in salt **63a** are conjugated with the carbanionic center, and the corresponding absorption bands appear at 2185 (CN), 1634 [C(O)OEt], and 1601 cm^{-1} [C(O)NHAr]. The respective absorption bands in the IR spectra of compounds **64** are shifted to higher frequencies: 2215–2251 (CN), 1734–1761 (COOEt), and 1649–1696 cm^{-1} [C(O)NHAr].

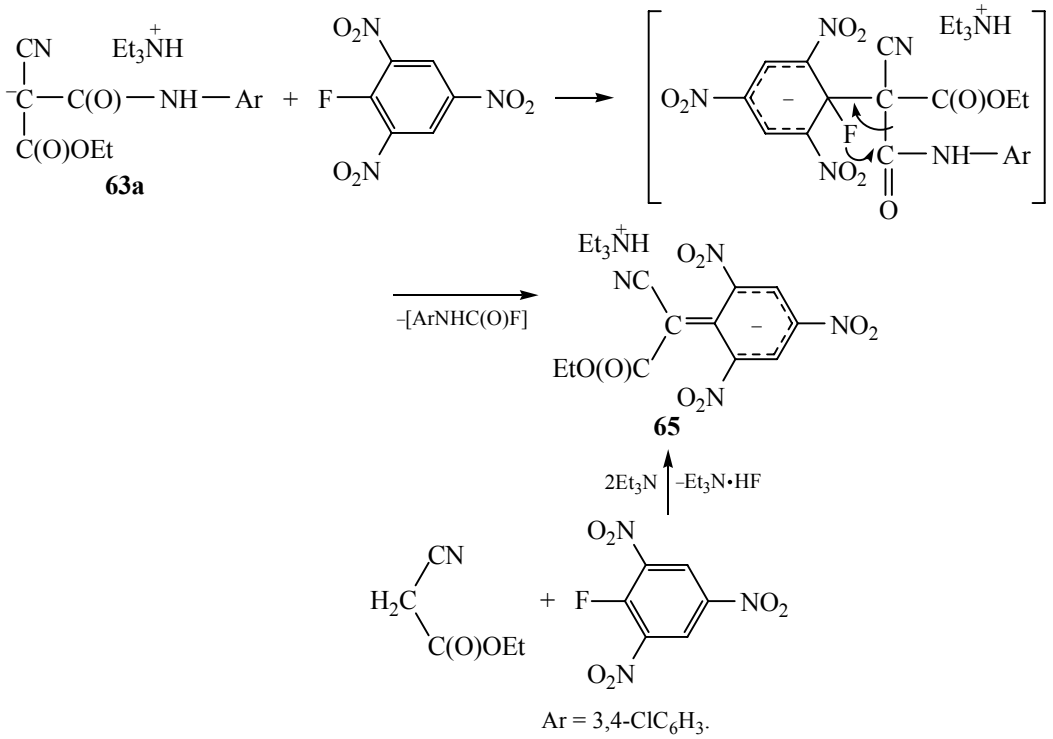
If the alkylation of triethylammonium salt **63a** occurs by the classical scheme, their arylation is a more complicated process. The low nucleophilicity of the carbanion of salt **63a** is manifested in that it cannot be arylated with 2,4-dinitrofluoro(chloro)benzene. 2,4,6-Trinitrofluorobenzene is the only to react with salt **63a** in in the absence of catalysts in a DMFA solution to form a C–C bond. However, the reaction, along with arylation, involves elimination of the amido group to give heptatriene **65**. Apparently, one more reaction product is (3,4-dichlorophenyl)carbamoyl fluoride. Evidence for this suggestion is provided by the presence in the ^{19}F NMR spectrum of the reaction mixture of a signal at δ_F = –5.9 ppm. The driving force of this quite an unusual transformation is likely to be the formation of the highly conjugated heptatriene structure **65** (Scheme 28).

The structure of heptatriene **65** was confirmed by independent synthesis. To this end, ethyl cyanoacetate was reacted with 2,4,6-trinitrofluorobenzene in the presence of triethylamine.

Methylation of amides derived from methanetricarboxylic acids under phase-transfer conditions in the presence of K_2CO_3 has never been reported in the literature. The methylation of CH-acids **66** with methyl iodide in the presence of freshly calcined K_2CO_3 in acetonitrile or benzene proceeds very smoothly and gives compound **67** in 50–60% yield (Scheme 29).

There are also no published examples of the halogenation of secondary amides derived from methanetricarboxylic acids. Therefore, it is quite interesting to

Scheme 28.



Ar = 3,4-ClC_6H_3.

note that it is quite interesting to note that amides **66** undergo facile phase-transfer bromination or iodination in methylene chloride in the presence of calcined K_2CO_3 to form the corresponding halogenation products **68** in reasonable yields (Scheme 30).

The bromine and iodine atoms in methanetricarboxylic acid derivatives **68** are highly depleted in electron density, and, therefore, we still failed to substitute them by other functional groups.

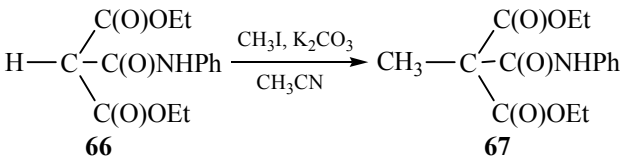
Mannich aminomethylation is widely used to convert active CH-acids into the corresponding substituted amines [31, 32]. Most carboxylic acid esters are fairly weak CH-acids, and, therefore, only those of them can enter the aminomethylation reaction that have a sufficiently acidic α-hydrogen atom. Substituted esters of malonic acid are known to fairly easily aminomethylated under Mannich reaction conditions [33].

It was reported [34] the aminomethylation of tertiary CH-acids with (alkylthiomethyl)dialkylamines. The reactions of 2-methylpropanedithioates with (alkylthiomethyl)dialkylamines proceed via C-aminomethylation to form *S*- and *O*-alkyl 3-(dialkylamino)-2,2-dimethylpropanedithioates (Scheme 31).

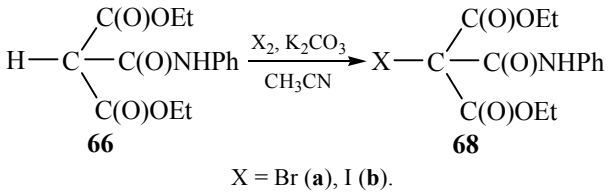
At the same time, less CH-acidic esters of 2-methylptopanedithioic acid react with tetramethylenediamine to form the corresponding amides (Scheme 32).

We made an attempt to dimethylaminomethylate acid **66** with tetramethylenediamine. The reaction proved to occur smoothly and gave the target amine **69** (Scheme 33).

Scheme 29.

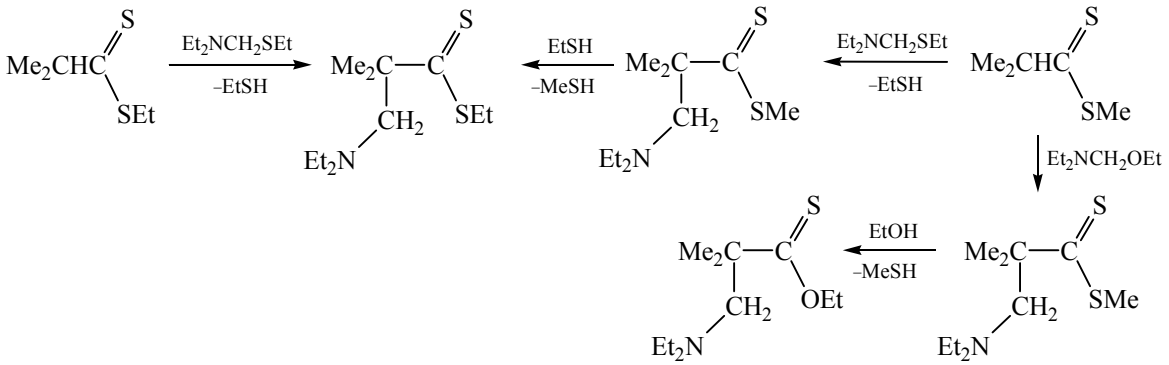


Scheme 30.

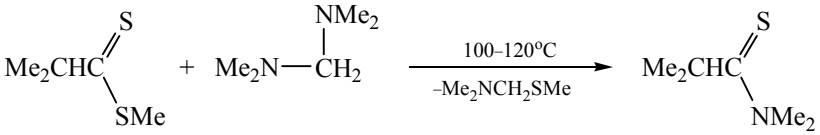


X = Br (**a**), I (**b**).

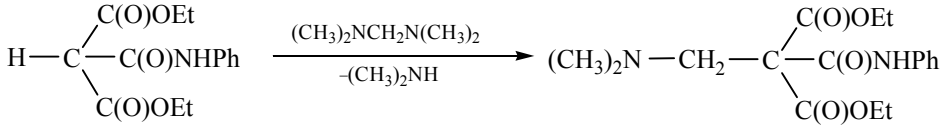
Scheme 31.



Scheme 32.



Scheme 33.



66 **69**

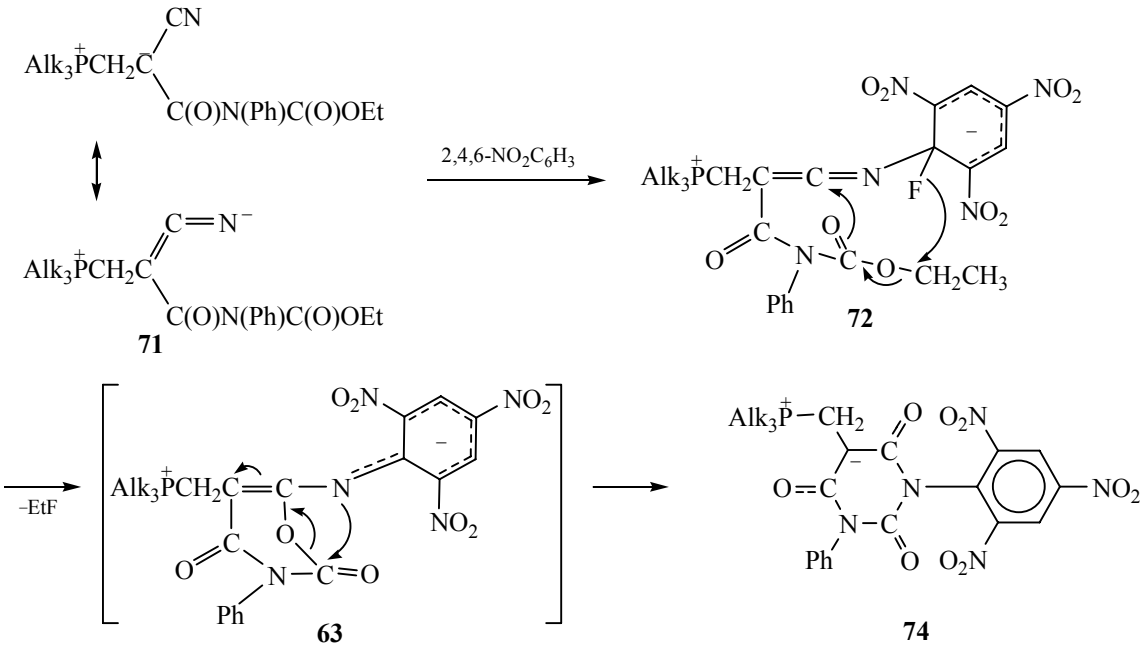
Fast reaction was observed when CH-acids **66** were added to a THF solution of tetramethylenediamine; therewith, dimethylamine was evolved.

4. Reactions of carbanions with nitrohalobenzenes. Unusual decomposition of F-σ-complexes. Synthesis of P-barbiturates, P-heptatrienes, and P-azaoctatetraenes. *4.1. Synthesis of phosphorus-containing barbiturates***.** Barbiturates belong to one of the most important classes of drugs. At the same time, only few representatives of this class of compounds containing phosphorus-containing functional groups have been described, and barbiturates with nitro groups in N-aromatic rings have been unknown. However, zwitter-ionic barbiturates with nitroaromatic substituents are of interest to synthesize in terms of search for medicines with new properties.

Proceeding with research on the reactivity of phosphorus-containing zwitter ions with respect to polynitrohalobenzenes, we reacted cyano-substituted carbanions **71** resulting from the reactions between P-zwitter ions and isocyanates with 1-fluoro-2,4,6-trinitrobenzene [35]. As judged from the changes in the composition of the reaction mixture with time (^{19}F and ^{31}P NMR monitoring), this reaction involves a few stages, including probably an intramolecular concerted dissociation of intermediate **72**, resulting in the evolution of ethyl fluoride and formation of oxazinedione **73** which isomerizes into barbiturate **74** (Scheme 34).

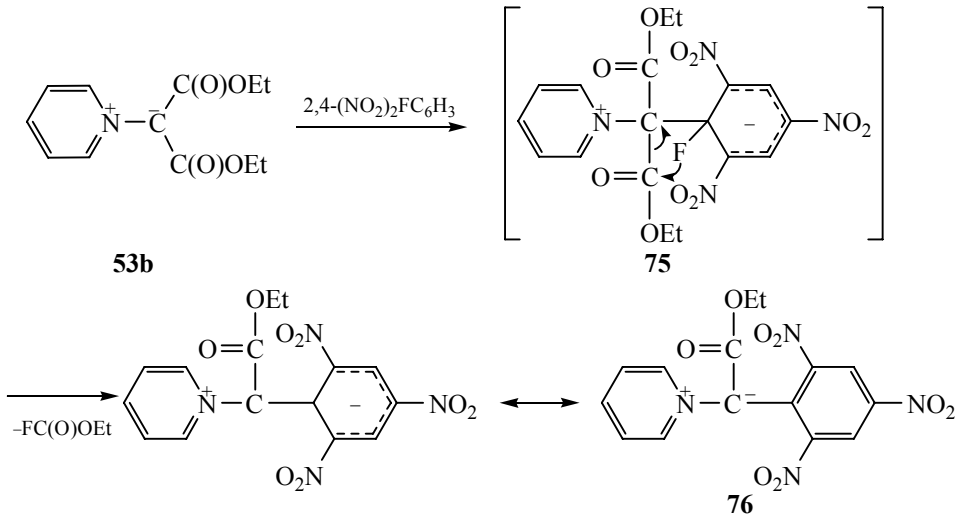
It is interesting to note that the analogous reaction [36] with a zwitter ion like **71** but with an *ortho*-ethylphenyl substituent at the carbamate nitrogen atom stops at the stage of formation of an oxazinedione like **73** due probably to the steric and electronic effects of the *ortho*-ethyl group. The reaction occurs in a methylene chloride solution at room temperature and is complete, according to the ^{31}P NMR data, in 10 days. The ^{19}F NMR spectrum detects formation of a fluorine-containing compound at δ_P = –211 ppm, which is assignable to ethyl fluoride. After the reaction mixture has stood for some time in an open vessel this signal disappears, obviously, due to evaporation of the low-boiling ethyl fluoride. The solvent was then removed, and the residue was crystallized from ethyl acetate to

Scheme 34.



Alk = *i*-Pr (**a**); *n*-Bu (**b**).

Scheme 35.



isolate crystalline compounds in yields of 50–60%; the composition and structure of the products was established by elemental and XRD analysis, as well as IR and ^{1}H, ^{13}C, ^{19}F, and ^{31}P NMR spectroscopy. It should be noted that all the mentioned arylations of ordinary salts of cyanocarbanions leads to no other products but C-derivatives. N-Arylation occurs exclusively in cyano-substituted zwitter ions **71**.

Apparently, the N-arylation of zwitter ions **71** takes place because the nitrogen atom in them is not blocked by a counterion and accessible for electrophilic attack, whereas in ordinary cyanocarbanion salts the counterion is coordinated to nitrogen.

4.2. Synthesis of heptatriene compounds with the N- and P-zwitterionic structure. 4.2.1. Reaction with 2,4,6-trinitrofluorobenzene of pyridinium ylide derived from malonic ester. As mentioned above, the reaction with isocyanates of pyridinium ylide derived from malonic ester produces carbamates via cleavage of a weakened C–C bond at the second stage of the process.

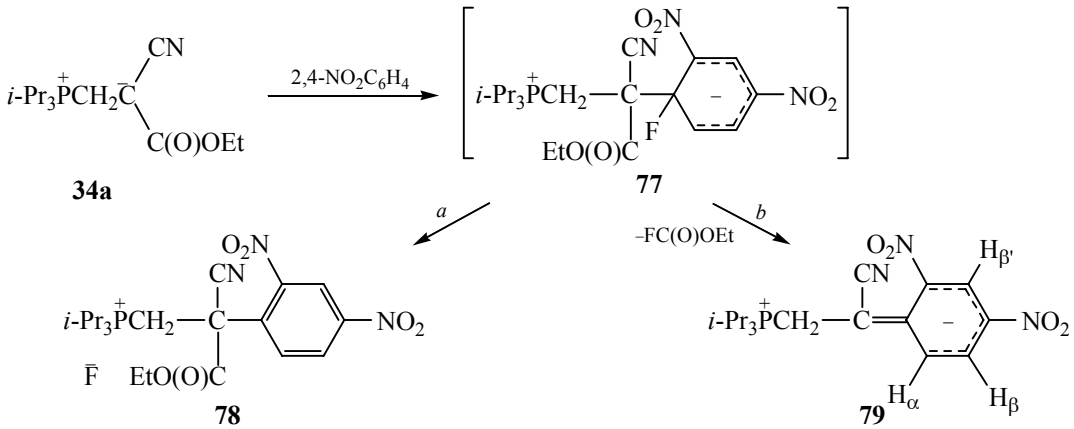
We set ourselves the task to discover new 2-step transformations of pyridinium ylide **53b**, too, involving cleavage of the weak C–C bond. To this end, we had to find a reagent which would generate a fairly strong nucleophilic center at the second reaction stage. Our attention has focused on reactions with polynitrofluorobenzenes, because nucleophilic aromatic substitution reactions generally proceed via formation of a σ-complex like **75** having an easily leaving negatively charged halide ion which would induce the carbon–carbon bond cleavage in C–C(O)OEt (Scheme 35).

Actually, the reaction of ylide **53b** with 2,4,6-trinitrofluorobenzene was found to result in quantitative formation of heptatriene **76** [37]. There-with, according to the IR and NMR data, the reaction also formed ethyl fluoroformate. There are strong reasons to suggest that ethyl fluoroformate and heptatriene **76** are formed **at** the stage of dissociation of σ-complex **75**. Consequently, we observed a new type of transformations of σ-complexes, when fluorine does not leave as the fluoride ion but is incorporated into the ester group. As this takes place, a C=C bond is formed, thereby involving the carboxyl group in the conjugation chain and stabilizing the heptatriene system. Evidence for the involvement of the carboxyl and *para*-nitro groups in conjugation comes from the IR and UV spectra. The UV spectra (acetone) contain maxima at λ_{max} = 419 (ε = 18300 L mol^{-1} cm^{-1}) and 535 nm (ε = 24300 L mol^{-1} cm^{-1}). The IR spectra show strong bands of conjugated ester groups near 1643 cm^{-1}, which implies a high degree of delocalization of the negative charge. The IR spectra also contain strong NO_2 absorption bands at 1264 (*para*-NO_2) and 1322 cm^{-1} (*ortho*-NO_2). In the ^{1}H NMR spectrum, the ring proton signals of the negatively charged heptatriene fragment in compound **76** are strongly shifted upfield with respect to the aromatic proton signals of 2,4,6-trinitrofluorobenzene (8.67 and 9.18 ppm, respectively).

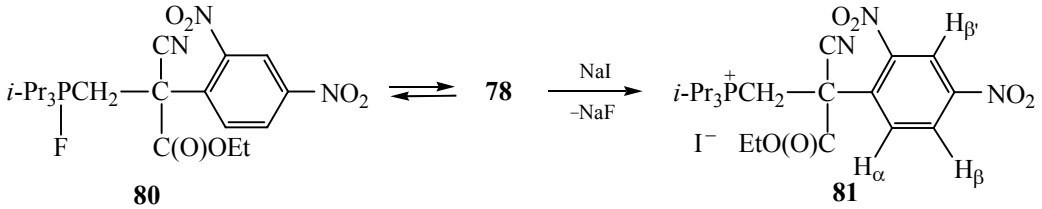
A very important question arises: Whether the above reaction provides a unique example of a principally new route of aromatic nucleophilic substitution or there are other reactions, where the fluorine atom leaves not as the fluoride ion but as a fluorine-containing organic derivative. To answer this question, we had to formulate requirements to structural features that make compounds capable of reacting with polynitrofluorobenzenes.

4.2.2. Reaction with 2,4-dinitrofluorobenzene of phosphorus-containing 1,3-zwitter ion **34a** derived from cyanoacetic acid. We supposed that the reaction considered in the previous section can have a fairly broad scope. To enter such reactions, the carbanionic center in the starting zwitter ion should bear an ester group, as well as an electron-acceptor radical to weaken the neighboring C–C bond. Phosphorus-containing zwitter ion **34a** meets these requirements. But, unlike pyridinium ylide, P-zwitter ion **34a** possesses a more diverse reactivity, and, therefore, its reactions with nitrohalobenzenes can take a more complicated route. Actually, P-zwitter ion **34a** readily reacts with 2,4-dinitrofluorobenzene in methylene chloride, but the result of this reaction strongly depends with its conditions [38]. The reaction in mild conditions (–20°C, dilute solution) normally occur as a normal arylation (route *a*), that at 20°C in a concentrated solution forms ethyl fluoroformate and a new zwitter ion **79** (route *b*) (Scheme 36).

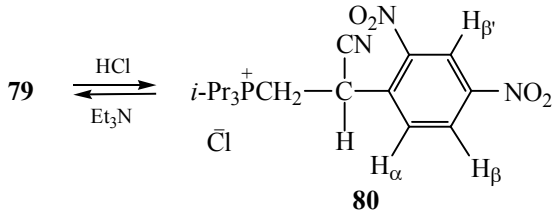
Scheme 36.



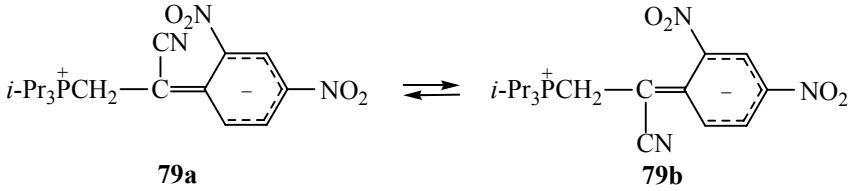
Scheme 37.



Scheme 38.



Scheme 39.



It is important to note that phosphonium salt **78** does not transform into heptatriene **79** under the reaction conditions. This fact implies that, actually, the zwitter ion reacts with 2,4-dinitrofluorobenzene along two independent routes. In solution phosphonium salt **78** exists in tautomeric equilibrium of fluorophosphorane **80**. If fluorine is replaced by iodine, the final reaction product is iodide **81** as crystals (Scheme 37).

The structure of heptatriene **79** was confirmed by XRD analysis, according to which the anionic charge in the zwitter ion is delocalized over the [N–C–C–C–C–C–C–N–O]$^-$ system from the cyano to *para*-nitro group. The formation of such a highly conjugated system is likely to be one of the driving forces for the zwitter ion formation.

On treatment with acid heptatriene **79** immediately transforms into an aromatic derivative **80** (Scheme 38).

According to the IR and ^{1}H and ^{31}P NMR data, in solution zwitter ion **79** exists as a *cis/trans* mixture (Scheme 39).

The structural assessment of the prevailing stereoisomer was based on the nuclear Overhauser effect (NOE). In the ^{1}H NMR spectrum (Table 4), there is a correlation between the signals of methylene protons (3.72 ppm) and ring *ortho*-proton (7.14 ppm), which suggests a cysoid structure of zwitter ion **79a**. This fact suggests that compound **79a** prefers the same stereoform both in the crystal state and in solution.

Thus, the conclusion can be drawn that we, too, discovered a new, fairly general nucleophilic substitution reaction which yields not an aromatic derivative but a highly conjugated negatively charged polyene. The formation of the latter is accompanied by a release of ethyl fluoroformate rather than the fluoride ion.

4.2.3. Formation of azaoctatetraene in the reaction of P-zwitter ion **34a** with 2,4,6-trinitrofluorobenzene. P-Zwitter ion **34a** contains a carbanionic and a phosphonium centers and acidic hydrogen atoms in the methylene group, and alkoxycarbonyl and cyano groups. Obviously, each of the mentioned functional groups can act as the reaction center, depending on the nature of the transformation. Alkyl halides mainly attack the negatively charged carbon atom. The result of two-stage reactions naturally depends on the

Table 4. Comparison of the spectral characteristics of compounds **79a** and **79b**

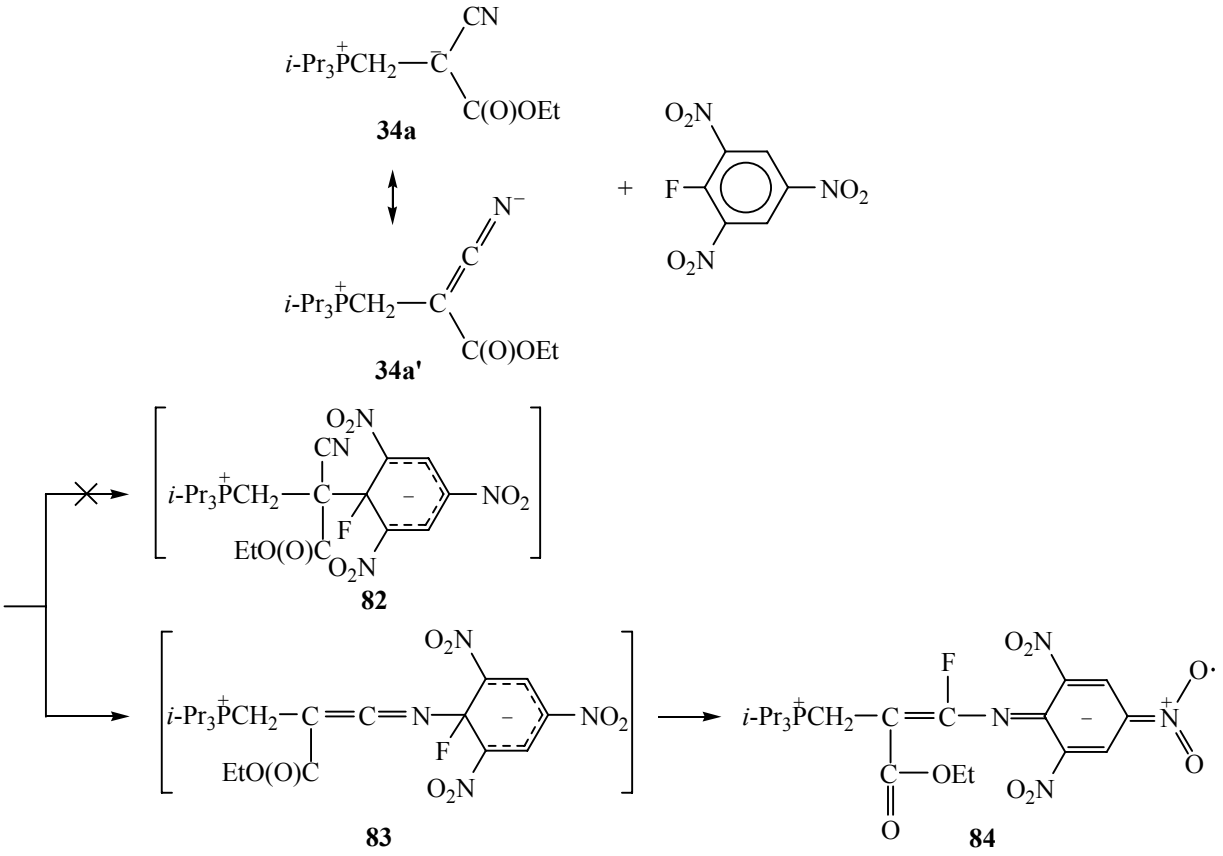
Compound	**79a**	**79b**
Fraction in the DMSO-d_6 solution	83.5	16.5
δ_P, ppm	44.52	44.68
$\delta(i\mathrm{Pr_3P{+}C\underline{H}_2})$, ppm	3.74 d ($^2J_{HP}$ 12.2 Hz)	3.20 d ($^2J_{HP}$ 12.8 Hz)
$\delta(CH_\alpha)$, ppm	7.12 d ($^3J_{HH}$ 7.5 Hz)	7.72 d ($^3J_{HH}$ 6.9 Hz)
$\delta(CH_\beta)$, ppm	7.54 d.d ($^3J_{HH}$ 7.5, $^4J_{HH}$ 2.1 Hz)	7.97 d.d ($^3J_{HH}$ 6.9, $^4J_{HH}$ 1.8 Hz)
$\delta(CH_{\beta'})$, ppm	8.32 d ($^4J_{HH}$ 2.1 Hz)	8.59 d ($^4J_{HH}$ 1.8 Hz)

transformations of reaction intermediate. Our long-term experience with nucleophilic in aromatic halides shows that the halogen atom in such reactions is always released as the halide anion or, like in the above discussed examples, as fluoroformate.

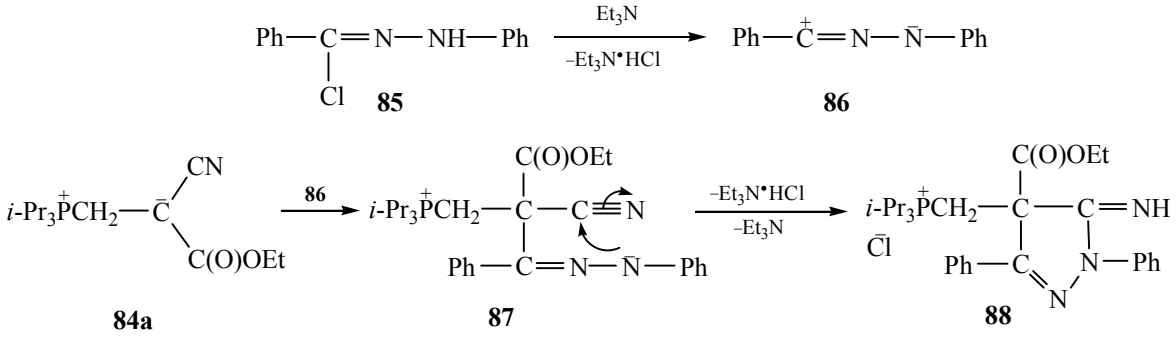
To gain a deeper insight into defluoroformylation reactions of σ-complexes, we reacted zwitter ion **34a** with 2,4,6-trinitrofluorobenzene [38] (Scheme 40).

The result of the reaction proved quite unexpected. According to the IR, UV, and NMR data, the reaction resulted in quantitative formation of σ-complex **82**. However, a more detailed study of the structure of the reaction product by XRD analysis [39] made us to suggest intermediate formation of an N-σ-complex **83**. Probably, the second *ortho*-nitro group, by steric reasons, prompts zwitter ion **34a** to react in its N-mesomeric form **34a'**. We assume that σ-complex **83** is stabilized intramolecularly via 1,3-migration of the fluoride ionto the electrophilic ketenimine carbon atom to form a superconjugated system. The energy gain associated the formation of the latter system is

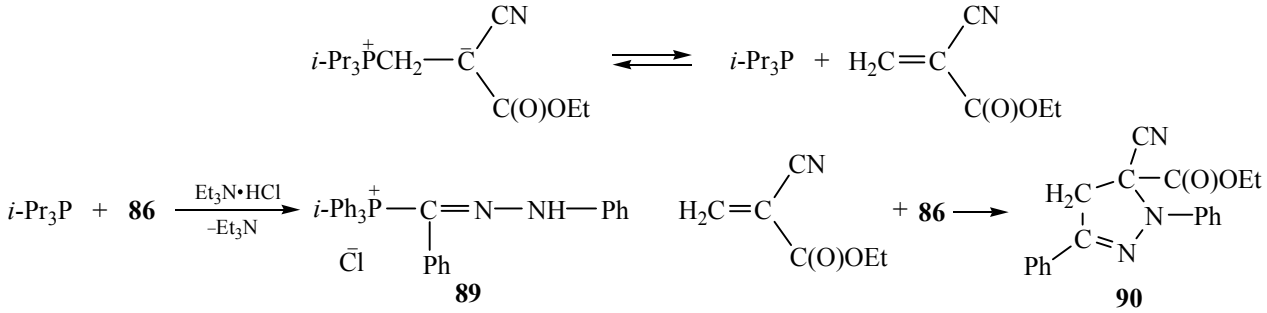
Scheme 40.



Scheme 41.



Scheme 42.



undoubtedly the driving force of the rearrangement. The conjugation system includes 11 atoms, from the carboxyl to *para*-nitro group. We did not find in the literature any mentioning of reactions of cyanoacetic acid esters with electophiles, which involve both the C- and N-nucleophilic centers. Up to now only reactions involving the C-carbanionic center have been described. Thus, we are the first to discover a dual reactivity of the C^{-}–CN–C=C=N^{-} system.

5. Synthesis of phosphorus-containing pyrazolines in the reaction of C,N-diphenylnitrilimine with the zwitter ion obtained from triisopropylphosphine and ethyl 2-cyanoacrylate. In the present section we will mostly focus on the reactions involving addition of C,N-substituted nitrilimines generated by dehydrochlorination of the corresponding chlorides with organic bases. It should be noted that for the reagents with an active double bond we primarily used vinyl ketones, ethyl vinylmalonates, 1,2-(diethoxycarbonyl)ethylenes, cyclooctatetraenes, and alkyl methacrylates.

We supposed that the reactions of zwitter ion **34a** with 1,3-dipolar ions (for example, diphenylnitrilimine) would lead to a stable cyclic system but could hardly predict what would by the target of N-anion attack (COOAlk, CN, or CH_2P^{+} carbon) at the second reaction stage.

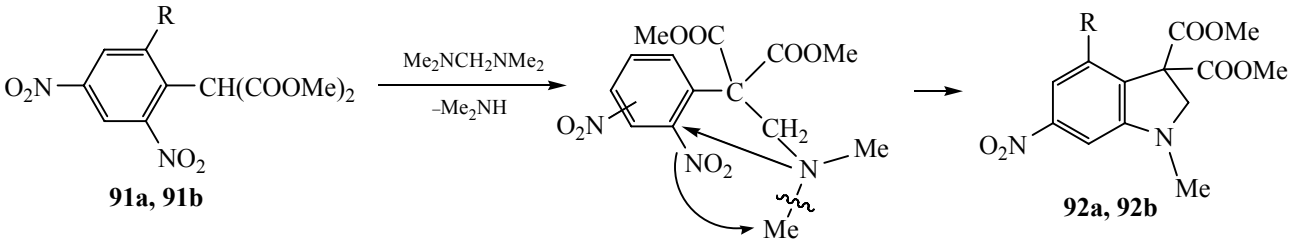
To realize the considered approach, we reacted zwitter ion **34a** with diphenylnitrilimine **84** generated in the reaction medium from the corresponding acid chloride and triethylamine. As would be expected, one of the reaction products was phosphorus-containing substituted pyrazoline **88** which was obviously formed by intramolecular attack with N-anion **87** of the cyano carbon. The composition and structure of heterocycle **88** were confirmed by elemental analysis, IR and ^{1}H, ^{13}C, and ^{31}P NMR spectroscopy, as well as XRD analysis [40] (Scheme 41).

Molecule **88** contains a chiral center, which complicates its NMR spectra.

It should be noted that the yield of phosphorus-containing pyrazoline **88** (^{31}P NMR data) is less than 10%. The main route of the reaction in question leads to previously unknown phosphonium salt **89** and 5-cyano-5-(ethoxycarbonyl)-1,2-diphenylpyrazoline **90** (Scheme 42).

The structure of compounds **89** and **90** was proved both by spectral methods and by XRD analysis. A characteristic feature of the ^{1}H NMR spectrum of

Scheme 43.



R = H (**a**), NO_2 (**b**).

pyrazoline **90** is that the ring methylene protons appear as an AB system with ^2J = 17.2 Hz.

The formation of pyrazoline **90** can be explained by the fact that zwitter ion **34a** sometimes acts as triisopropylphosphine due to the presence of equilibrium between the zwitter ion, triisopropylphosphine, ethyl 2-cyanoacrylate.

Triisopropylphosphine reacts with imine **86** and converts into phosphonium salt **89**, while pyrazoline **90** is formed by the reaction of imine **86** with the released ethyl 2-cyanoacrylate. We have to admit that ethyl 2-cyanoacrylate not only polymerizes under the action of trimethylamine, but also enters in part in the cycloaddition reaction with imine **86**. It worth noting that we did not find published examples of addition of C,N-substituted nitrilimines to esters of 2-cyanoacrylic acid. The formation of the pyrazoline ring by a direct intramolecular attack of N-anion **87** on the carbon atom of the CH_2P group is hardly possible, because in this case one would expect formation of the isomeric 4-cyano-4-(ethoxycarbonyl)-1,3-diphenylpyrazoline, but this product was not detected in the reaction mixture.

Thus, zwitter-ion **34a** acts here not only as triisopropylphosphine, but also as ethyl 2-cyanoacrylate and thus can be used to synthesize diverse heterocyclic compounds. The synthesis of pyrazolines by the addition of nitrilimines to esters of 1-aryl-2-cyanoacrylic acid, described by Hassaneen et al. [41], is likely to be of little promise in the case of pyrazoline **90**, because adding triethylmine to a mixture containing 2-cyanoacrylates leads to immediate polymerization of the latter.

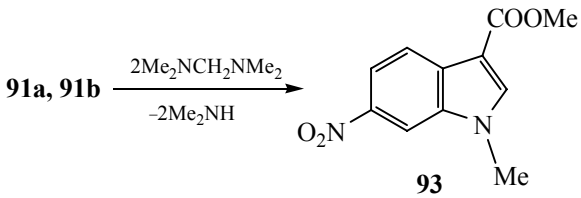
6. Tertiary CH-acids and tetramethylmethylenediamine in the synthesis of nitroindolines and indoles. There are only a few reported examples of indolines and indoles containing nitro substituents in the phenyl ring [42, 43]. In our research on reactions of nitrophenylmalonates with tetramethylmethylenediamine we discovered new unexpected transformations leading to nitro-substituted indolines and indoles.

Tetramethylmethylenediamine is an active reagent for Mannich aminomethylation. However, Mannich reactions with trisubstituted CH-acids have never been reported in the literature. We reacted tetramethylmethylenediamine with 2,4-di- and 2,4,6-trinitrophenylmalonates. In these reactions we observed three specific features. If the classical Mannich aminomethylation occurs fairly easily and in mild conditions, CH-acids **91a** and **91b** react with tetramethylmethylenediamine only under heating in benzene at 80°C. Apparently, steric factors prevent effective protonation of tetramethylmethylenediamine. However, elevated temperature activates the aminomethylation product and it cyclizes to form indoline **92** via an unusual intramolecular attack of the *ortho*-nitro group in the phenyl ring [44] (Scheme 43).

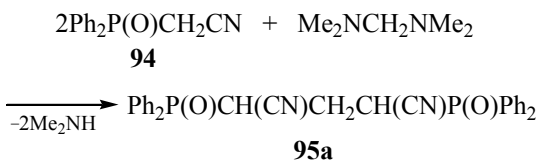
The reaction with 2 mol of tetramethylmethylenediamine and in more rigid conditions (120°C, 3–5 h) gives indoles in yields of up to 30% [44] (Scheme 44).

The process does not require catalysts and an inert atmosphere to occur. The structure of the reaction products, both indolines **92** and indoles **93** was proved by up-to-date physicochemical methods, including XRD analysis.

Scheme 44.



Scheme 45.



The discovery that nitroindolines **92** and nitroindoles **93** can form by the above schemes is of fundamental importance. A great number of catalytic syntheses of indolines and indoles, which make use of cyclizations involving the NH function are known [45].

7. Synthesis of 1,3-bisphosphorylated glutaronitriles. We suggested that 1,3-bisphosphorylated glutaronitriles could be synthesized by coupling methylene-active compounds with bisdiaminomethanes. Actually, due to the fairly highly CH acidity of compound **94** its reaction with tetramethylmethylenediamine proceeds fairly smoothly (benzene, 80°C, 3–4 h) and gives 1,3-bis(diphenylphosphinoyl)-glutaronitrile **95c** in 70–75% yield [46]. The structure of the reaction product as a racemic bis(phosphine oxide) was confirmed by elemental analysis and IR and ^{1}H, ^{31}P, and ^{13}C NMR spectroscopy, as well as XRD analysis (Scheme 45).

It was found that compound **95a** is a racemate: the chiral atoms C^{1} and C^{3} have the same configuration. The cyano groups in this compound are located on the opposite sides of the P–C–C–C–P chain and do not contact with the phosphoryl phosphorus atom. The latter fact casts doubts on the explanation of Krajewski and Mayer [47] of the observation of two equivalent signals in the ^{31}P NMR spectrum of compound **95** by intramolecular donor-acceptor interaction between the cyano group and the phosphorus atom in position 4 with respect to this group. In fact, the ^{31}P NMR spectrum of racemate **95** contains a single signal (δ_P = 27.5 ppm). The methylene protons are equivalent (as would be expected in a racemate) and appear in the ^{1}H NMR spectrum as two triplet signals with $^{2}J_{HP}$ = 15.28 Hz and $^{3}J_{HH}$ = 7.48 Hz.

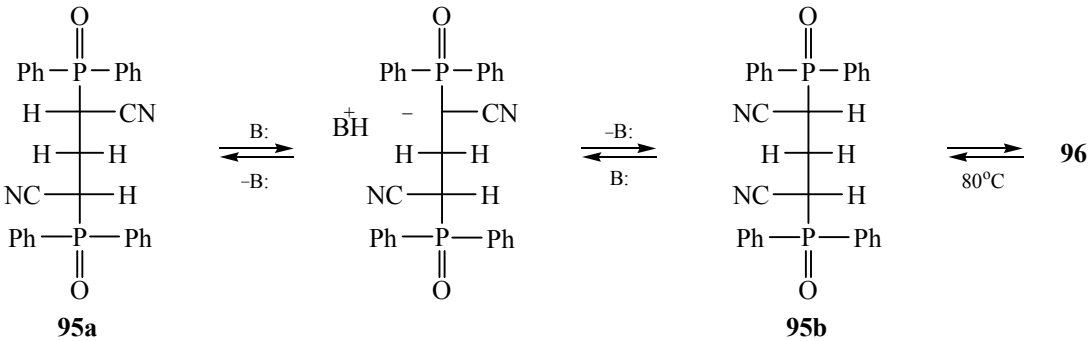
Racemate **95a** is stable both in solid and in neutral solutions but in the presence of acids and bases it isomerizes by half to a *meso* form **95b.** The latter forms with racemate **95a** an equimolar adduct **95a**,**b** which is sufficiently stable at room temperature. The methylene protons in *meso* form **95b** are nonequivalent and appear as quite a complicated multiplet near 2.5 ppm. Obviously, in solution we deal with equilibrium in the system racemate **95**–base B–*meso* form **95b**–adduct **96**, in which the latter is the most thermodynamically stable structure (Scheme 46).

Chromatography on chiral columns leads to dissociation of adduct **96**. Racemate **95a** gives two equivalent peaks, each assignable to the D or L enantiomer, whereas *meso* form **95b** gives a single signal. The area of the signal of the *meso* form and the total area of the D- and L-enantiomer signals are equal to each other.

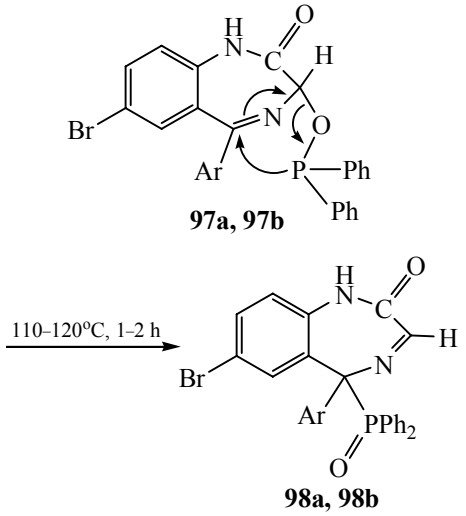
The revealed specific properties of the diastereomers **95a** and **95b** explain why the reaction with excess tetramethylmethylenediamine takes the above-described route to form adduct **96** which is stable in a basic medium.

8. **1,3-Azaallyl rearrangement in the synthesis of tertiary 1,4-banzodiazepine CH-acids.** 3-Substituted 1,4-benzodiazepines show broad-spectrum pharmacological activity. 3-Phosphorylated 1,4-benzodiazepines are trisubstituted CH-acids, and, therefore, they can serve as the starting materials for diverse syntheses, pat of which was discussed in the previous sections. It was found that the reaction route leading to the

Scheme 46.

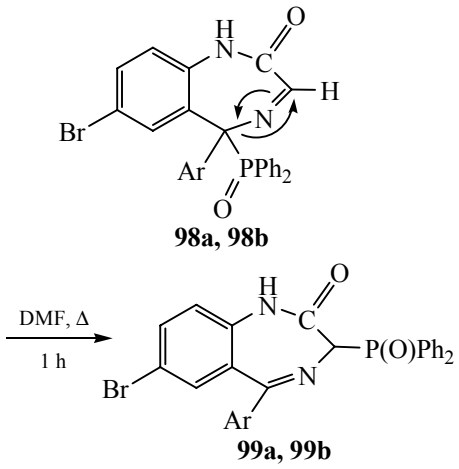


Scheme 47.



Ph (**a**), *o*-ClC_6H_4 (**b**).

Scheme 48.



Ph (**a**), *o*-ClC_6H_4 (**b**).

considered structures, includes at its kinetic stage the azaallyl rearrangement, where phosphinite **97** transforms into phosphine oxide **98** [48]. Such isomerizations of trivalent to pentavalent phosphorus compounds with a P–C bond have never been reported in the literature (Scheme 47).

This process represents a new type of 1,3-phosphorotropic migrations. However, the 5-C carbon atom in 1,4-benzodiazepine is overloaded with substituents and, therefore, boiling in DMF results in complete isomerization of compound **98** into trisubstituted CH-acid **99** (Scheme 48) (cf. [49]).

9. Pseudohalide properties of the azido group in C-azido-substituted tertiary 1,4-benzodiazepine CH-acids. To synthesize phosphorylated compounds with an N–C bond in the 3 position of 1,4-benzodiazepine, we made use of the Staudinger reaction [50] of organic azides with various trivalent phosphorus compounds, leading to phosphorus imides [51, 52], which are valuable reagents for the synthesis of functionally substituted amines, nitrogenous heterocycles, and other nitrogen-containing compounds (Scheme 49).

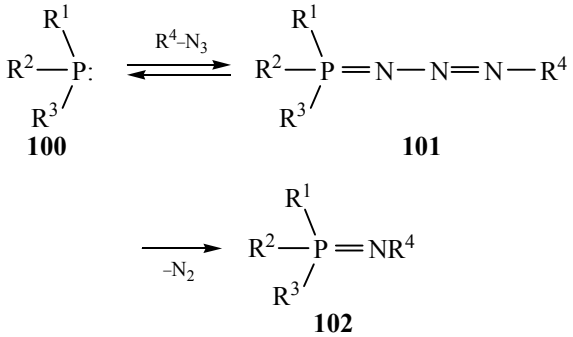
The first stage of the Staudinger reaction involves reversible formation of triazene **101**, whose stability is controlled by both electronic and steric factors. Bulky substituents at the phosphorus and nitrogen atoms stabilize triazenes. When substituents are small in volume, triazenes decompose, evolving nitrogen and forming imides. However, triazenes **101** are released in the free state. Sometimes triazenes decompose back in view of the reversibility of the first reaction stage.

In the present section we consider the results of studies on the reactions of triethyl- and tricyclehexylphosphine with 1,4-benzodiazepine **103** containing a 3-azido substituent. The choice of these phosphines was motivated by the expectation that they would allow to trace the effect of steric factors on the reaction result.

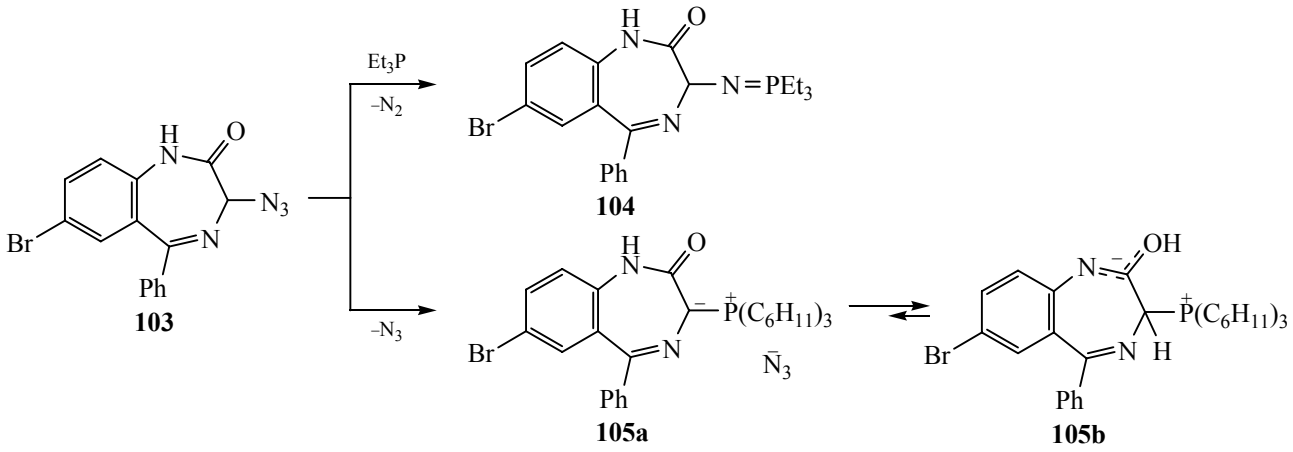
It was found that triethylphosphine reacted with azide **103** to form imide **104**. At the same time, the reaction of tricyclohexylphosphine with the azide proved to be quite surprising [53] (Scheme 50).

After mixing toluene solutions of tricyclohexylphosphine and azide **103** we observed bright coloration of the reaction mixture and gradual formation of a crystalline precipitate which, by the IR and UV data,

Scheme 49.

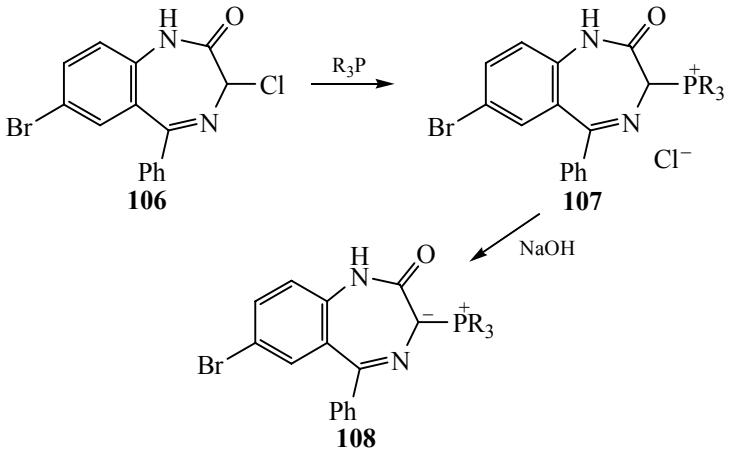


Scheme 50.



X = $P(C_6H_{13})_3$.

Scheme 51.



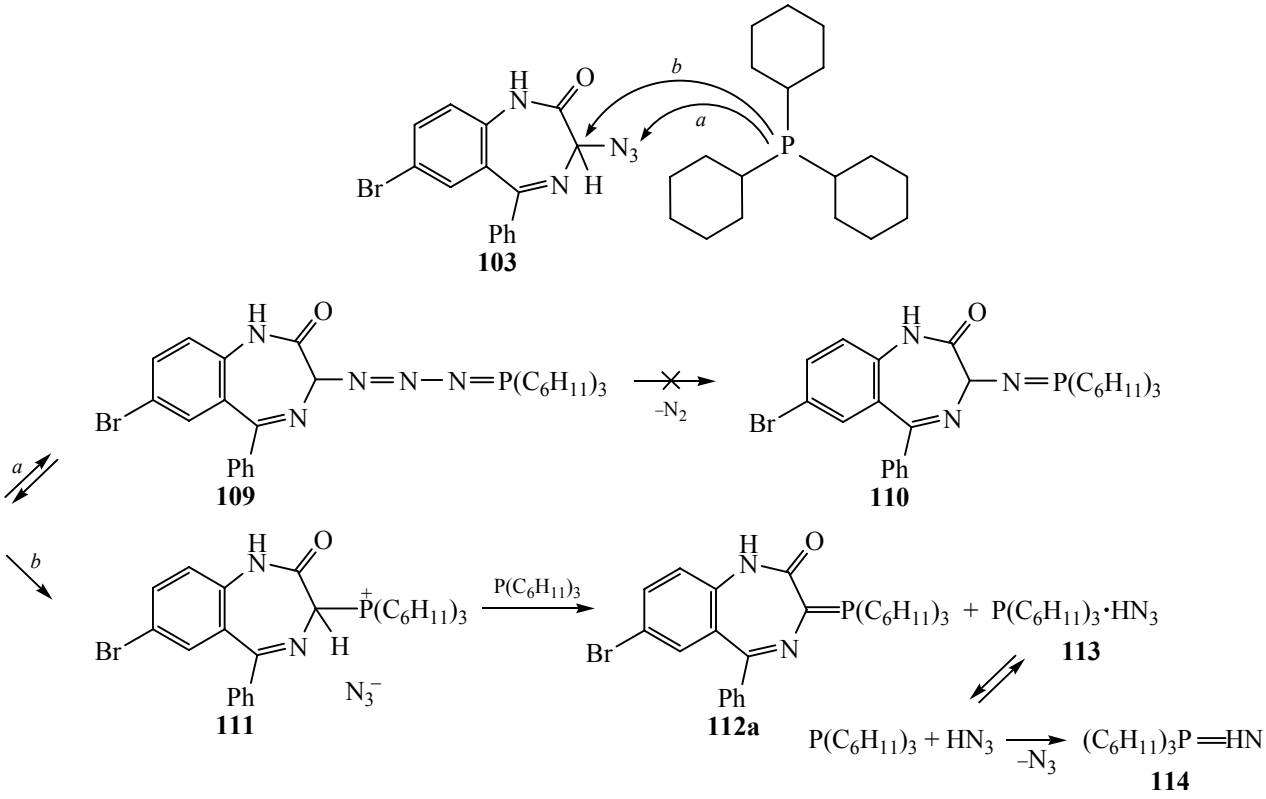
R = Et, *cyclo*-C_6H_{11}.

was identified as ylide **105a**, but is a $CDCl_3$ solution its structure, according to the NMR data, corresponded to zwitter ion **105b**. Ylides **108** prepared from triethyl- and tricyclohexylphosphines and chloride **106** (Scheme 51).

The formation of ylide **112a** in the reaction of azide **103** with tricyclohexylphosphine can be explained, assuming that the azido group in the heterocycle in the α position to the imino nitrogen possesses an enhanced mobility and is eliminated as the azide anion under the action of the fairly strongly nucleophilic tricyclohexylphosphine. Under this assumption, route *b* becomes the main reaction pathway, because route *a* cannot occur, because triazene **109** is impossible to be transformed into imide **110** for steric reasons. Under the action of the second mole of tricyclohexylphosphine salt **111** transforms into ylide **112a**. Actually, the reaction with a double excess of tricyclohexylphosphine much increases the yield of ylide **112a**. The NH_3 salt of tricyclohexylphosphine **113** exists in equilibrium with its components, and therefore, it transforms into imide **114** (δ_P = 45.7 ppm) by the Staudinger reaction (Scheme 52).

Thus, we discovered a new reaction in which the azido group exhibits preudohalide properties in the reaction of 3-azido-7-bromo-5-phenyl-1,2-dihydro-3*H*-1,4-benzodiazepin-2-one **103** with tricyclohexylphosphine. Obviously, the azido group exhibited such

Scheme 52.



properties because, one the one hand, it has enhanced mobility in heterocycle **103** under the influence of the α-imino nitrogen and, on the other hand, due to the presence of bulky groups at the phosphorus atom, which prevented the transformation of triazene **109** with nitrogen evolution.

REFERENCES

1. Ayres, D.C., *Carbanions in Synthesis*, London: Oldbourne, 1966.
2. Cram, D.J., *Fundamentals of Carbanion Chemistry*, New York: Academic, 1965.
3. Ozaki S., *Chem. Rev*., 1972, vol. 72, no. 5, p. 457. DOI: 10.1021/cr60279a002.
4. Ulrich, H., *Chemistry and Technology of Isocyanates*, New York: Wiley, 1996, p. 98.
5. Reutov, O.A., Beletskaya, I.P., and Butin, K.P., *CH-Kisloty* (CH-Acids), Moscow: Nauka, 1980.
6. Uchida, A., Douama, A., and Matsuda, S., *Bull. Chem. Soc. Jpn*., 1970, vol. 43, p. 963.
7. Yadav, J.S., Reddy, B.S.S., Basak, A.K.B., Visali, B., Narsaiah, A.V., and Nagaiah, K., *Eur. J. Org. Chem*., 2004, vol. 2004, no. 3, p. 546. DOI: 10.1002/ejoc.200300513.
8. Marcia de Figueiredo, R., Mazziotta, A., Pereira de Sant'Ana, D., Palumbo, C., and Gasperi, T., *Curr. Org. Chem*., 2012, vol. 16, no. 19, p. 2231. DOI: 10.2174/138527212803520290.
9. Yuan Shizhen, Li Zhen, Xu Ling, *Res. Chem. Intermed*., 2012, vol. 38, no. 2, p. 393. DOI: 10.1007/s11164-011-0355-2.
10. Gololobov, Yu.G., *Chin. J. Chem*., 2005, vol. 23, p. 1103. DOI: 10.1002/cjoc.200591103.
11. Acheson, R.M., *Acc. Chem. Res*., 1971, vol. 4, p. 177.
12. Gololobov, Yu.G., Borisov, J.A., Slepchenkov, N.V., Petrovsky, P.V., and Neljubina, J.V., *Heteroatom Chem*., 2010, vol. 21, no. 3, p. 119. DOI: 10.1002/hc.20585.
13. Gololobov, Yu.G., Kardanov, N.A., Khrustalyov, V.N., and Petrovskii, P.V., *Tetrahedron Lett*., 1997, vol. 38, p. 7437. DOI: 10.1016/S0040-4039(97)01750-4.
14. Gololobov, Yu.G., Linchenko, O.A., Petrovskii, P.V., Starikova, Z.A., and Garbuzova, I.A., *Heteroatom Chem*., 2007, vol. 18, p. 108. DOI: 10.1002/hc.20267.
15. Gololobov, Yu.G., Galkinap M.A., Dovgan', O.V., Krasnova, I.Yu., Petrovskii, P.V., Schmutzler, R., Karacar, A., Freytag, M., and Jones, P.G., *Russ. J. Org. Chem*., 2001, vol. 37, p. 1061. DOI: 10.1023/A:1013158208411.

16. Gololobov, Yu.G., Kolomnikova, G.D., and Krylova, T.O., *Izv. Akad. Nauk Ser. Khim*., 1995, no. 1, p. 186.

17. Krylova, T.O., Shishkin, O.V., Struchkov, Yu.T., Kolomnikova, G.D., and Gololobov, Yu.G., *Zh. Obshch. Khim*., 1995, vol. 65, no. 8, p. 1393.

18. Gololobov, Yu.G., Galkina, M.A., Dovgan', O.V., Krasnova, I.Yu., Petrovskii, P.V., Antipin, M.Yu., Lyssenko, K.A., and Schmutzler, R., *Russ. Chem. Bull*., 2001, vol. 50, p. 279. DOI: 10.1023/A:1009538620098.

19. Gololobov, Yu.G., Petrovskii, P.V., Ivanova, E.M., Linchenko, O.A., Schmutzler, R., Ernst, L., Jones, P.G., Karacar, A., Freytag, M., and Okucu, S., *Russ. Chem. Bull*., 2003, vol. 52, no. 2, p. 427. DOI: 10.1002/chin.200338148.

20. Gololobov, Yu.G., Senchenya, N.G., Linchenko, O.A., Petrovskii, P.V., and Garbuzova, I.A., *Russ. J. Gen. Chem*., 2006, vol. 76, p. 1106. DOI: 10.1134/S1070363206070176.

21. Gololobov, Yu.G., Petrovskii, P.V., Dovgan, O.V., Krasnova, I.Yu., Schmutzler, R., Ernst, L., Jones, P.G., Karaçar, A., Freytag, M., and Okucu, S., *Phosphorus, Sulfur, Silicon, Relat. Elem*., 2002, vol. 177, p. 1677. DOI: 10.1080/ 10426500212242.

22. Gololobov, Yu.G., Galkin, V.I., Petrovskii, P.V., Linchenko, O.A., Zueva, E.M., Mubarakova, L.G., Cherkasov, R.A., Schmutzler, R., Ernst, L., Jones, P.G., and Freytag, M., *Russ. Chem. Bull*., 2003, vol. 52, p. 1920. DOI: 10.1023/B:RUCB.0000009633.66133.e9.

23. Gololobov, Yu.G., Galkina, M.A., Dovgan', O.V., Guseva, T.I., Kuz'mintseva, I.Yu., Senchenya, N.G., and Petrovskii, P.V., *Russ. Chem. Bull*., 1999, vol. 48, no. 9, p. 1622. DOI: 10.1007/BF02494803.

24. Galkin, V.I., Bakhtiyarova, Yu.V., Mal'tsev, D.B., Galkina, I.V., Gololobov, Yu.G., and Linchenko, O.A., *Russ. Chem. Bull*., 2006, vol. 55, no. 5, p. 879. DOI: 10.1007/s11172-006-0346-4.

25. Galkin, V.I., Bakhtiyarova, Yu.V., Gololobov, Yu.G., Polezhaeva, N.A., and Cherkasov, R.A., *Heteroatom. Chem*., 1998, vol. 9, p. 665. DOI: 10.1002/(SICI)1098-1071(1998)9:7<665::AID-HC11>3.0.CO;2-I.

26. Gololobov, Yu.G., Dovgan, O.V., Golding, I.R., Petrovskii, P.V., and Garbuzova, I.A., *Heteroatom Chem*., 2002, vol. 13, p. 36. DOI: 10.1002/hc.1104.

27. Gololobov, Yu.G., Kashina, N.V., Linchenko, O.A., Petrovskii, P.V., Gambaryan, N.P., and Friedrichsen, W., *Russ. Chem. Bull*., 2003, vol. 52, no. 10, p. 2261. DOI: 10.1023/B:RUCB.0000011888.26449.21.

28. Garnelli, G., Giacomini, D., Panunzio, M., Martelli, G., and Spunta, G., *Tetrahedron Lett*., 1987, vol. 28, no. 31, p. 3593. DOI: 10.1016/S0040-4039(00)95544-8.

29. Tsunoda, T., Nagino, C., Oguri, M., and Ito, S., *Tetrahedron Lett*., 1996, vol. 37, no. 14, p. 2459. DOI: 10.1016/0040-4039(96)00318-8.

30. Gololobov, Yu.G., Linchenko, O.A., Gol'ding, I.R., Galkina, M.A., Krasnova, I.Yu., Garbuzova, I.A., Petrovskii, P.V., and Lyssenko, K.A., *Russ. Chem. Bull*., 2005, vol. 54, no. 10, p. 2398. DOI: 10.1007/s11172-006-0129-y.

31. Risch, N., Arend, M., and Westermann, B., *Angew. Chem. Int. Ed*., 1998, vol. 37, p. 1044. DOI: 10.1002/(SICI)1521-3773(19980504)37:8<1044::AID-ANIE1044>3.0.CO;2-E.

32. Uneme, V., Mitsudera, V., Kamikado, T., Kono, Y., Manabe, Y., and Numata, M., *Biosci. Biotechnol. Biochem*., 1992, vol. 56, p. 2023. DOI: 10.1271/bbb.56.2023.

33. Bohme, H., Mundlos, V., and Keitzer, G., *Chem. Ber*., 1958, vol. 91, p. 656. DOI: 10.1002/cber.19580910329.

34. Danchenko, M.N. and Gololobov, Yu.G., *Zh. Org. Khim*., 1983, vol. 19, p. 4.

35. Gololobov, Yu.G., Khrustalev, V.N., Slepchenkov, N.V., Peregudov, A.S., and Antipin, M.Yu., *Mendeleev Commun*., 2010, p. 39. DOI: 10.1016/j.mencom.2010.01.015.

36. Gololobov, Yu.G., Slepchenkov, N.V., Peregudov, A.S., and Starikova, S.A., *Mendeleev Commun*., 2010, p. 277. DOI: 10.1016/j.mencom.2010.09.013.

37. Gololobov, Yu.G., Linchenko, O.A., Petrovskii, P.V., Khrustalev, V.N., and Garbuzova, I.A., *Heteroatom Chem*., 2007, vol. 18, p. 421. DOI: 10.1002/hc.20315.

38. Gololobov, Yu.G., Linchenko, O.A., Petrovskii, P.V., Khrustalev, V.N., and Garbuzova, I.A., *Mendeleev Commun*., 2007, p. 232. DOI: 10.1016/j.mencom.2007.06.017.

39. Gololobov, Yu.G., Linchenko, O.A., Starikova, Z.A., Garbuzova, I.A., and Petrovskii, P.V., *Russ. Chem. Bull*., 2005, vol. 54, no. 10, p. 2471. DOI: 10.1007/s11172-006-0142-1.

40. Gololobov, Yu.G., Linchenko, O.A., Trishin, Yu.G., Petrovskii, P.V., and Starikova, Z.A., *Russ. Chem. Bull*., 2004, vol. 53, no. 4, p. 889. DOI: 10.1023/B:RUCB.0000037859.83219.10.

41. Hassaneen, H.M., Mousa, H.A., Ezmirly, S.T., and Shawali, A.S., *Can. J. Chem*., 1998, vol. 66, p. 1386.

42. Kawase, M., Miyake, Yu., and Kikugawa, Ya., *J. Chem. Soc. Perkin Trans. 1*, 1984, p. 1401. DOI: 10.1039/P19840001401.

43. Vorob'eva, S., Buyanov, V., and Suvopov, N., *Chem. Heterocycl. Compd*., 1991, vol. 27, no. 5, p. 506. DOI: 10.1007/BF00473994.

44. Gololobov, Yu.G., Peregudov, A.S., Barabanov, S.V., Petrovskii, P.V., and Khrustalev, V.N., *Tetrahedron Lett*., 2011, vol. 52, p. 6713. DOI: 10.1016/j.tetlet.2011.09.14.

45. Dianyu Liu, Guowei Zhao, and Lan Xiang, *Eur. J. Org.*

Chem., 2010, vol. 2010, p. 3975. DOI: 10.1002/ejoc.201000323.

46. Gololobov, Yu.G., Barabanov, S.V., Peregudov, A.S., Petrovskii, P.V., and Khrustalev, V.N., *Russ. Chem. Bull*., 2012, vol. 61, p. 1250. DOI: 10.1007/s11172-012-0169-4.
47. Krajewski, J.J. and Mayer, J.W., *Can. J. Chem*., 1974, vol. 52, p. 3626.
48. Gololobov, Yu.G., Krasnova, I.Yu., Barabanov, S.V., Khrustalev, V.N., Andronati, S.A., and Pavlovsky, V.I., *Tetrahedron Lett*., 2014, vol. 55, p. 4879. DOI: 10.1016/j.tetlet.2014.07.010.
49. Onys'ko, P.P., Kim, T.V., Kiseleva, E.I., and Sinitsa, A.D., *Tetrahedron Lett*., 1992, vol. 33, p. 691. DOI: 10.1016/S0040-4039(00)92344-X.
50. Schtaudinger, H. and Meyer, J., *Helv. Chim. Acta*, 1919, vol. 2, p. 635.
51. Gololobov, Yu.G., Zhmurova, I.N., and Kasukhin, I.N., *Tetrahedron,* 1981, vol. 37, p. 437. DOI: 10.1016/S0040-4020(01)92417-2.
52. Gololobov, Yu.G. and Kasukhin, I.N., *Tetrahedron,* 1992, vol. 42, p. 1353. DOI: 10.1016/S0040-4020(01)92229-X.
53. Gololobov, Yu.G., Krasnova, I.Yu., Barabanov, S.V., Andronati, S.A., and Pavlovskiy, V.I., *Izv. Akad. Nauk, Ser. Khim*., 2015, no. 1, p. 233.