

Intramolecular Electrophilic Rearrangements in Saturated Acyclic Systems. C→N Migrations of Acetyl Group*

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Received December 30, 1999

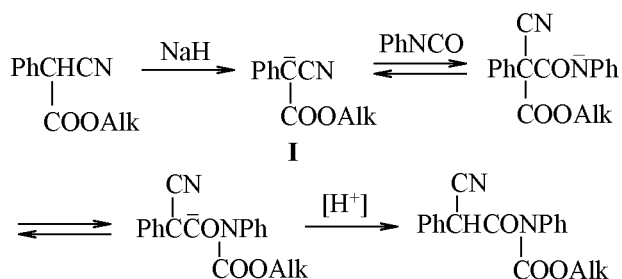
Abstract—Reactions between isocyanates and carbanions with an acetyl group at the carbanion center occur via rearrangement of the intermediate N-anions into isomeric C-anions by C→N-migration of the MeC(O) group. The acetyl group undergoes migration easier than the ethoxycarbonyl group. The P-zwitterionic rearrangement products were subjected to X-ray diffraction analysis.

In the preceding communications of this series [1–10] reactions were described of iso(thio)cyanates with carbanions **I** and **II**, derivatives of CH-acids with a single labile hydrogen at the carbanion center. The reactions occurred in an unusual way with migration of COOAlk group from carbon atom to the negatively charged nitrogen. Thus the reaction results in an insertion of iso(thio)cyanates into a C–C bond: this process was not known before with iso(thio)cyanates (Schemes 1 and 2).

In extension of the studies on intramolecular C→N migration of electron-deficient groups we investigated the isocyanates reactions with carbanions **V** and **XII** containing an acetyl group at the carbanion center.

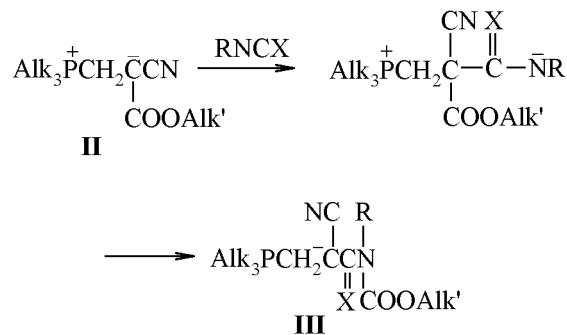
Ketone **IV** (56.4% of enol form) being transformed into the corresponding anion **V** by treatment

Scheme 1.



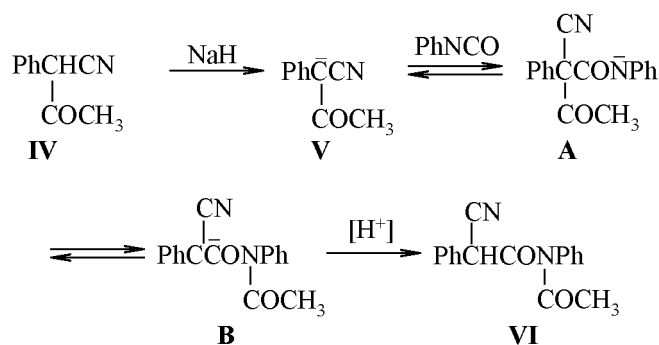
with sodium hydride in anhydrous THF readily reacts with phenyl isocyanate; the acidification of the reaction mixture yields amide **VI** containing the acetyl group not at the carbon but at the nitrogen of the phenylisocyanate group inserted in the C–C bond (Scheme 3).

Scheme 2.



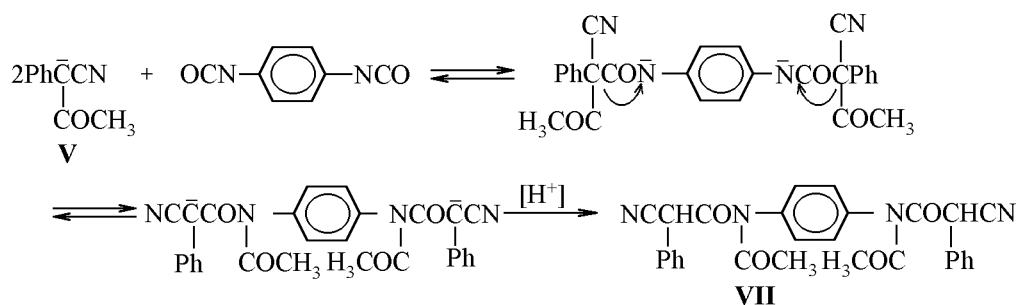
X = O, S; R = Alk', Ar.

Scheme 3.

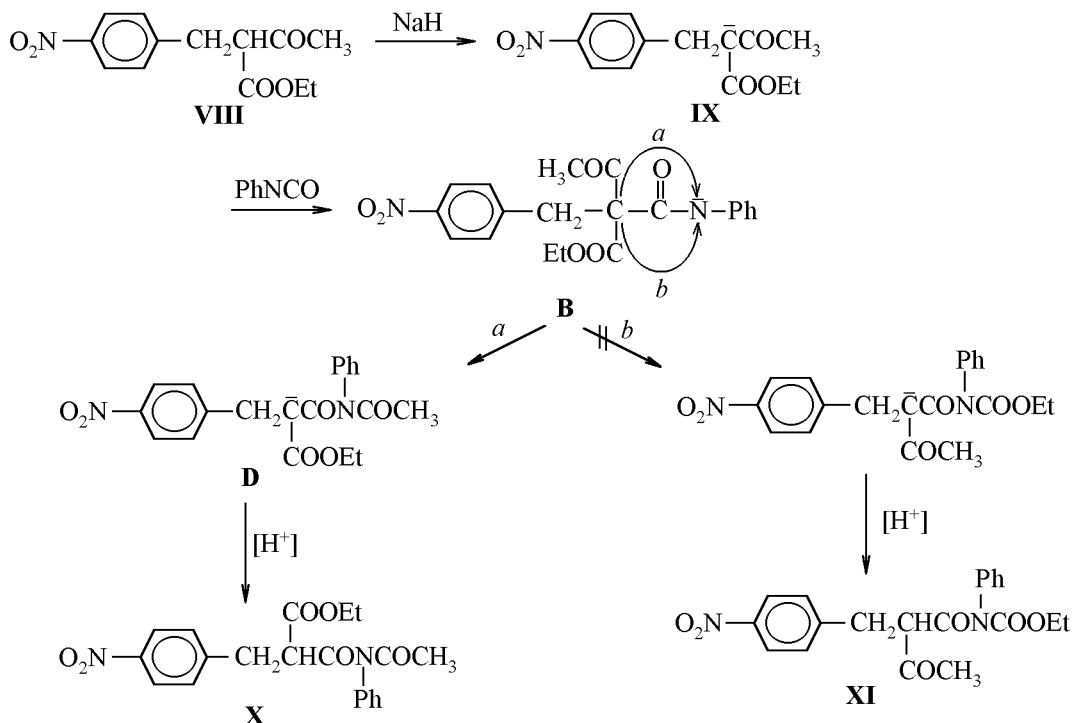


* The study was carried out under financial support of the Russian Foundation for Basic Research (grant no. 98-03-33117a) and DFG (Aktenreichen 436 RUS 17/44/99).

Scheme 4.



Scheme 5.



The first stage of carbanion **V** reaction with phenyl isocyanate apparently affords N-anion (**A**); intramolecular contact of the latter with the keto group carbon induces the cleavage of the C–C bond and a migration of the acetyl group from carbon to nitrogen. It is essentially a nucleophilic substitution at the carbon atom where the carbanion plays the role of a leaving group. Such processes were considered by Hesse when treating the cycle expansion reactions with isocyanates [11]. Obviously like in the case of such migrations of alkoxy-carbonyl group the driving force of the C→N shift of the acyl group is the energy gain at transformation of the N-anion (**A**) into an isomeric C-anion (**B**) [8].

The products of COOEt group C→N migration (Scheme 1) are characterized by an appearance of a singlet in 6 ppm region of the ^1H NMR spectrum

belonging to a methine proton [7]. The methine proton resulting from the C→N migration of the acetyl group should likely appear in the similar region (Scheme 3, compound **VI**). Actually, the ^1H NMR spectrum of compound **VI** contains a singlet at 6.06 ppm. In the ^{13}C NMR spectrum appear the signals of C=O group carbon (167.4 and 172.6 ppm) (Table 1). In the same table are given the results of calculation of the chemical shifts in the ^1H and ^{13}C NMR spectra of compound **VI** performed according to additive scheme.

Likewise occurs the C→N-rearrangement in reaction between carbanion **V** and 1,4-phenylene diisocyanate (Scheme 4).

We carried out a comparison of C→N-migration ability of ethoxycarbonyl and acetyl groups by per-

Table 1. ^1H and ^{13}C NMR spectra of reaction products obtained in keeping with Schemes 4 and 5 and the corresponding spectra calculated along the additive procedure

Compd. no.	^1H NMR spectrum, δ , ppm (J , Hz)	^{13}C NMR spectrum, δ_c , ppm (J_{CH} , Hz)				
		$\text{CHC}(\text{O})\text{N}<$	$>\text{N}\text{C}(\text{O})\text{CH}_3$	$\text{N}\text{COOC}_2\text{H}_5$	COOC_2H_5	COCH_3
VI	2.06 s (3H, CH_3), 6.06 s (1H, CHCN), 7.2–7.43 m (10H, 2Ph)	167.4	172.6	–	–	–
VIa	2.47 s (3H, CH_3), 5.06 s (1H, CHCN), 7.33–7.76 m (10H, 2Ph)	160.60	167.13	–	–	–
X	1.18 t (3H, CH_3CH_2 , J_{HH} 7.2), 2.08 s (3H, CH_3CO), 3.26 d.d (1H, $\text{CH}_\alpha\text{H}_\beta\text{CH}$, $J_{\text{H}\alpha\text{H}\beta}$ 14, $J_{\text{HH}\alpha}$ 6.4), 3.37 d.d (1H, $\text{CH}_\alpha\text{H}_\beta\text{CH}$, $J_{\text{H}\beta\text{H}\alpha}$ 14, $J_{\text{HH}\beta}$ 8.4), 4.12 q (2H, CH_2CH_3 , J_{HH} 7.2), 4.53 d.d (1H, CHCH_2 , $J_{\text{HH}\alpha}$ 6.4, $J_{\text{HH}\beta}$ 8.4), 7.53 d (2H, $\text{C}_6\text{H}_4\text{NO}_2$, J 8.4), 7.13–7.65 m (5H, C_6H_4), 8.17 d (2H, $\text{C}_6\text{H}_4\text{NO}_2$, J 8.4)	168.7 (2J 3.43)	170.72 (2J 6.34)	–	172.56 (2J 4.22)	–
XIa	1.23 t (3H, CH_3CH_2), 2.23 s (3H, CH_3CO), 2.92 q (1H, $\text{CH}_\alpha\text{H}_\beta\text{CH}$), 3.65 q (1H, $\text{CH}_\alpha\text{H}_\beta\text{CH}$), 3.91 q (2H, CH_2CH_3), 3.87 d.d (1H, CHCH_2), 7.33 d (2H, $\text{C}_6\text{H}_4\text{NO}_2$), 6.85–7.34 m (5H, C_6H_5), 8.28 d (2H, $\text{C}_6\text{H}_4\text{NO}_2$)	170.54	–	151.89	–	206.15

^a Spectrum calculated by additive procedure.

forming reaction of phenyl isocyanate with carbanion **IX** containing both these groups at the carbanion center (Scheme 5).

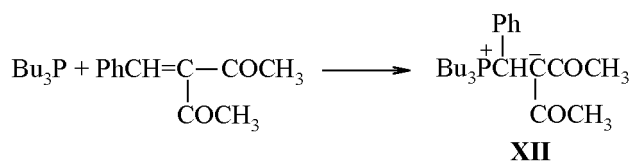
In the ^1H NMR spectrum of the reaction product obtained along Scheme 5 are observed signals characteristic of CH_2CH moiety (Table 1). However this group should be present both in carbamate **XI** and amide **X**, and therefore the ^1H NMR spectrum is not sufficient for assignment of the product structure. Therewith the ^{13}C NMR spectrum indicated with certainty that the reaction afforded exclusively amide **X** and not carbamate **XI** or their mixture. Table 1 contains the data on ^{13}C NMR spectrum of compound **X** and the calculation results performed by additive scheme for isomer **XI**. In the ^{13}C NMR spectrum of compound **X** are present characteristic signals of $\text{C}=\text{O}$ carbons (172.58, 170.72, and 168.83 ppm) belonging apparently to carbonyls of amide [$\text{Me}(\text{CO})\text{N}$ and $\text{CHC}(\text{O})\text{N}$ respectively] and ester groups; no carbon signal from the keto group of isomer **XI** is observed. In the calculated carbamate **XI** spectrum the signal from the keto group carbon is located at 206.15 ppm. Therefore in keeping with Scheme 5 migration from carbon to nitrogen occurs only with acyl group.

The rearrangements under consideration are conveniently followed on reaction between iso-

cyanates and phosphorus-containing carbanion **XII** with the use of ^{31}P NMR spectroscopy. The previously unknown P-zwitterion **XII** was prepared along procedure from [12] where the analogous carbanions were obtained by reaction with trimethyl-, dimethylphenyl-, or diethylphenylphosphine with 3-benzylidenepentane-2,4-dione. We reacted with the latter triisopropylphosphine and tributylphosphine. Note that in contrast to tributylphosphine the triisopropylphosphine even at large excess and in minimum amount of solvent reacts with 3-benzylidene-2,4-dione very slowly and not selectively. We failed to obtain therewith the corresponding P-zwitterion. Apparently in the triisobutylphosphine the phosphorus atom is considerably sterically hindered. At the same time the tributylphosphine relatively fast and selectively reacted with 3-benzylidene-2,4-dione to yield P-zwitterion **XII** (Scheme 6).

P-Zwitterion **XII** formed in dichloromethane on removing the solvent slowly crystallizes at room

Scheme 6.



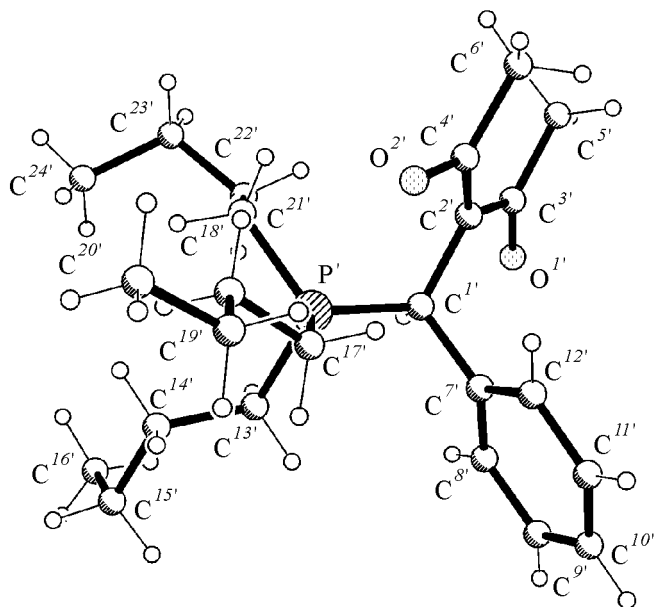


Fig. 1. Structure of compound **XII** in a crystal.

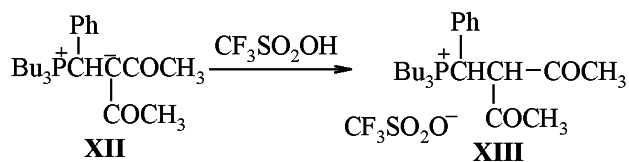
temperature. Note that apparently due to high hydrophobicity zwitterion **XII** is well soluble in ethyl ether and even in pentane. Since such zwitterions are known to rearrange into isomeric ylides through self-protonation due to the presence of a labile α -hydrogen we have established the structure of zwitterion **XII** by X-ray diffraction analysis. In the crystalline state the compound **XII** molecule exists as a zwitterion with a tetrahedral phosphorus atom and a planar carbanion center around which the sum of angles amounts to 360° .

As show IR and X-ray data the anion charge in the zwitterion **XII** is strongly delocalized in the pentade $O^1-C^3-C^2-C^4-O^2$ (Fig. 1). For instance, whereas the absorption band of the carbonyl group in the IR spectrum of compound **XIII** appears in the region 1750 cm^{-1} , in the spectrum of zwitterion **XII** the frequency of the absorption of the carbonyl group conjugated with the anion charge is shifted to 1480 cm^{-1} .

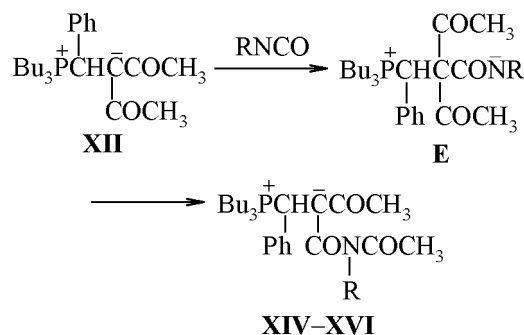
It is known that the bond lengths of $C=O$ (in ketones) and $C-C$ (in paraffins) are 1.23 and 1.54 Å respectively, whereas in compound **XII** obviously because of conjugation the bond lengths $C^3=O^1$, $C^4=O^2$ and C^2-C^3 , C^2-C^4 are equal respectively to 1.2499, 1.2710, and 1.4062, 1.4313 Å.

The protonation of zwitterion **XII** (Scheme 7) gives rise to a crystalline phosphonium salt **XIII**; its structure follows from the NMR data. The most informative are the resonances from $P-CH-CH$

Scheme 7.



Scheme 8.



$R = \text{cyclo-C}_6\text{H}_{11}$ (**XIV**), Ph (**XV**), $3,4\text{-Cl}_2\text{C}_6\text{H}_3$ (**XVI**).

moiety that appear in the ^1H NMR spectrum as typical doublets of doublets.

Zwitterion **XII** readily reacts in dichloromethane solution at room temperature with cyclohexyl, phenyl, or 3,4-dichlorophenyl isocyanates to furnish amides **XIV-XVI** with the acyl attached to the nitrogen of the amide group (Scheme 8).

The structure of reaction products was established from ^1H , ^{13}C , and ^{31}P NMR and IR spectra, and from X-ray diffraction study. It is interesting that compound **XV** crystallized with one water molecule that in the hydrate is linked by a hydrogen bond to the amide group conjugated with the anion charge (Fig. 2). The zwitterionic structure of compound **XV** is determined by the presence of a phosphonium group and of carbanion center located in β -position to the phosphorus atom. The X-ray data show that both carbanion center and amide nitrogen have planar structure. The sum of angles at the carbanion center is 359.9° , at the amide nitrogen 359.8° .

In the reaction products obtained along Scheme 8 the negative charge is significantly delocalized in the pentade $O^1-C^3-C^2-C^5-O^2$ as show IR spectra and X-ray analysis data. In the IR spectra of compounds **XIV** and **XVI** the absorption bands of carbonyl groups are observed in the region 1470–1490 (conjugated keto group), 1528–1574 (conjugated CO from the amide group), and 1623–1667 cm^{-1} (nonconjugated CO from the amide group). The nonconjugated amide $C=O$ groups in compounds **VI** and **VII** have the respective absorption bands in 1693–

1728 cm^{-1} region. The length of the α - β C-C bond in ketones is 1.516 Å [13] whereas in compound **XV** the C²-C³ bond is considerably shorter, 1.411 Å. At the same time the length of the C³-O¹ bond of keto group (1.257 Å) is more than the standard C=O length value in ketones (1.215 Å). Likewise is shortened the C²-C⁵ bond (1.41 Å) and extended the C⁵-O² bond (1.23 Å) in the amide fragment of the molecule as compared with the similar bond in acetamide (1.21 Å).

Analogous trends appear in compounds **XIV** and **XVI** (Figs. 3, 4).

Characteristic bond lengths in compound **XIV** are as follows Å: N-C⁶ 1.3624 (19), N-C⁵ 1.4494(18), O³-C⁶ 1.2278(18), O¹-C³ 1.2602(17), O²-C⁵ 1.2420(16), C²-C⁵ 1.412(2), C²-C³ 1.4204(19). Characteristic angles, deg: C⁶NC⁵ 122.05(12), C⁶NC⁸ 118.23(12), C⁵NC⁸ 118.41(12), O¹C³C² 119.24(13), O¹C³C⁴ 115.62(12), C²C³C⁴ 125.14 (14), O²C⁵C² 124.42(13), O²C⁵N 116.06(13), C²C⁵N 119.52(12).

Characteristic bond lengths in compound **XVI** are as follows Å: N-C⁶ 1.381(2), N-C⁵ 1.5049(18), O¹-C³ 1.2509(18), O²-C⁵ 1.2321(18), O³-C⁶ 1.2210(19), C²-C⁵ 1.406(2), C²-C³ 1.425(2).

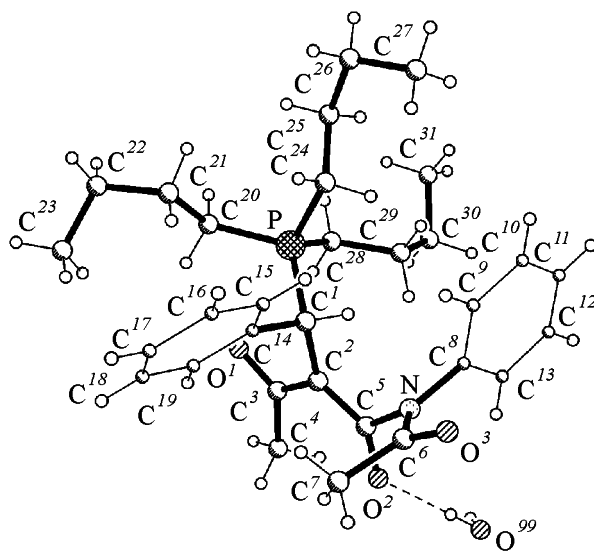


Fig. 2. Structure of compound **XV** in a crystal.

Characteristic angles, deg: C⁶NC⁸ 123.74(13), C⁶NC⁵ 118.91(12), C⁸NC⁵ 116.64(12), O¹C³C² 119.97(14), O¹C³C⁴ 118.15(13), C²C³C⁴ 121.88 (14), O²C⁵C² 129.62(14), O²C⁵N 115.19(13), C²C⁵N 115.18(12).

Thus the migration of electron-deficient group from a carbon to a negatively charged nitrogen in the

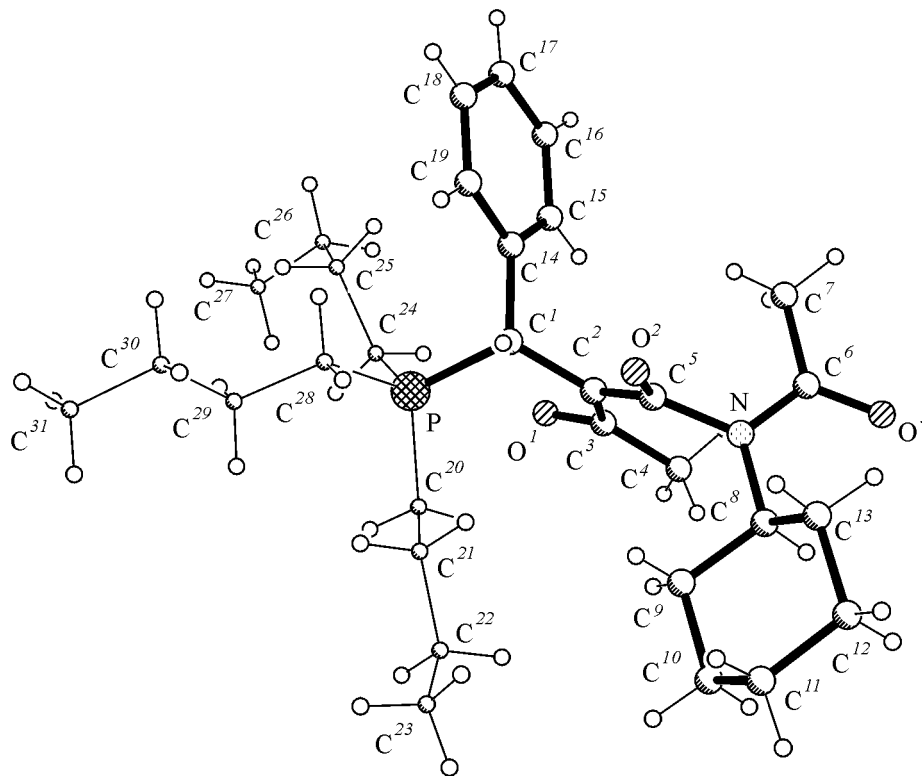


Fig. 3. Structure of compound **XIV** in a crystal.

Table 2. Yields, melting points, and elemental analyses of compounds obtained

Compd. no.	Yield, %	mp, °C	Found, %		Formula	Calculated, %	
			C	H		C	H
VI	37	77–79	72.85	5.08	C ₁₇ H ₁₄ N ₂ O ₂	73.37	5.07
VII	20	102–103	69.64	5.02	C ₂₈ H ₂₂ N ₄ O ₄	70.28	4.63
X	78	–	62.15	5.42	C ₂₀ H ₂₀ N ₂ O ₆	62.54	5.21
XII	67	70	73.22	10.04	C ₂₄ H ₃₉ O ₂ P	73.85	10.00
XIII	71	116–117	55.24	7.49	C ₂₅ H ₄₀ F ₃ O ₅ PS	55.55	7.96
XIV	85	136–137	72.42	9.79	C ₃₁ H ₅₀ O ₃ NP	71.23	10.3
XV	32	99–100	70.29	8.71	C ₃₁ H ₄₄ O ₃ NP	70.58	8.72
XVI	32	119	64.26	7.39	C ₃₁ H ₄₂ Cl ₂ O ₃ NP	64.36	7.26

series of acyclic saturated compounds occurs not only with alkoxy carbonyl but also with acyl groups.

EXPERIMENTAL

NMR spectra were recorded on spectrometer Bruker AMX-400, ¹H (400.26 MHz), ¹³C (100.68 MHz) and ³¹P (162.02 MHz), (δ, ppm relative to TMS, CDCl₃, and 80% H₃PO₄ for ¹H, ¹³C, ³¹P respectively). IR spectra were registered on Specord M-82 instrument. The reactions were carried out under dry nitrogen atmosphere. The solvents used were preliminary thoroughly purified and dried. Sodium hydride contained 90% of the main substance. The elemental analyses, yields, and melting points of compounds are listed in Table 2.

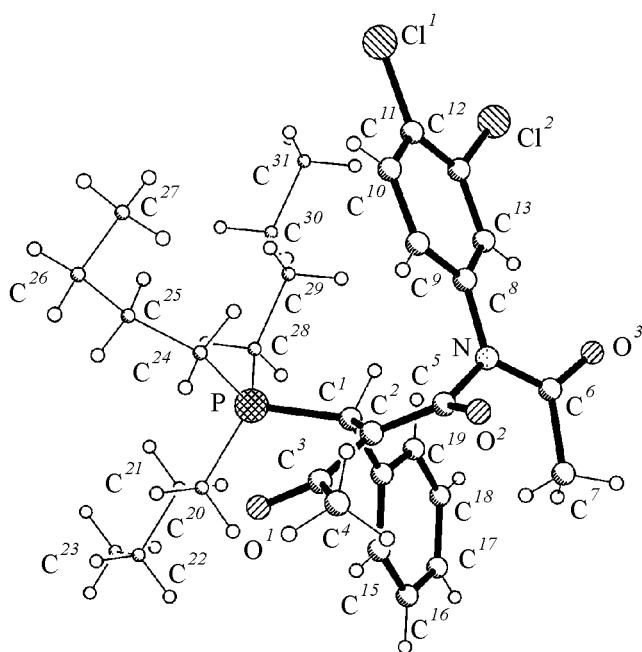


Fig. 4. Structure of compound **XVI** in a crystal.

Phenylcyanoacetic acid (N-acetyl-N-phenyl)-amide (VI). To a solution of 0.8 g (5 mmol) of 1-phenyl-1-cyanopropan-2-one in 80 ml of THF was added at stirring 0.2 g (5.25 mmol) of sodium hydride. In 2 h was added dropwise 0.6 g (5 mmol) of phenyl isocyanate in 20 ml of THF, and the mixture was stirred for 2 h at 20°C. Then to the stirred reaction mixture at 4°C was added a mixture of 5.0 mmol of trifluoroacetic acid and 20 ml of hexane. The precipitated sodium trifluoroacetate was filtered off, the solvent was removed in a vacuum, and to the residue was added ether. The ether solution was evaporated in a vacuum, and the solid residue was recrystallized from hexane. ¹H NMR spectrum (δ, ppm): 2.064 s (3H, CH₃), 6.06 s (1H, CHCN), 7.2–7.43 m (10H, 2Ph). IR spectrum, ν, cm⁻¹: 2976 (H–CCN), 2251 (CN), 1728 [C(O)CH₃], 1700 [C(O)N–].

Bis[N-acetyl-N-(cyanophenylacetyl)]phenylene-1,4-diamine (VII). To a solution of 1 g (6.24 mmol) of 1-phenyl-1-cyanopropan-2-one in 40 ml of THF was added at stirring and cooling to 4°C 0.25 g (6.24 mmol) of sodium hydride. In 1 h was added dropwise a solution of 0.5 g (3.12 mmol) of 1,4-phenylene diisocyanate in 20 ml of THF, and the mixture was stirred for 3 h at 4°C. The reaction mixture was left standing overnight. Then to the stirred reaction mixture at 4°C was added a mixture of 0.71 g (6.24 mmol) of trifluoroacetic acid and 20 ml of anhydrous hexane. The sodium trifluoroacetate was filtered off, the solvent was removed in a vacuum, and to the residue was added ethyl ether. At cooling from the ether extract precipitated colorless crystals of compound **VII**. ¹H NMR spectrum (δ, ppm): 2.14 s (3H, CH₃), 6.01 s (2H, CHCN), 7.32–7.45 m (14H, H arom).

Reaction of P-zwitterion XII with isocyanates.

An equimolar mixture of P-zwitterion XII and an appropriate aryl isocyanate (2 mmol each) in 2 ml of CH_2Cl_2 was maintained in dry nitrogen atmosphere at room temperature for 24 h. The solvent was removed, and the residue was crystallized from pentane-ether mixture. At the use of cyclohexyl isocyanate the latter was taken in 3-fold excess, and the reaction mixture was kept at 20°C for a week. Afterwards the solvent was removed, and the residue was crystallized from acetone.

Compound XIV. ^1H NMR spectrum (δ , ppm): 0.92 t (9H, CH_3 , J 7.3 Hz), 1.23–2.22 m (24H, CH_2 , CH_3COC^- , CH_3CON), 5.09 br. signal (1H, CHPh), 7.28–7.35 m (5H, Ph).

Compound XV. ^1H NMR spectrum (δ , ppm): 0.85 t (9H, CH_3 , J 7.3 Hz), 0.93–1.9 m (18H, CH_2), 2.04 s (3C, CH_3COC^-), 2.52 s (3C, CH_3CON), 4.18 br. signal (1H, CHPh), 7.15–7.34 m (10H, 2Ph).

Compound XVI. ^1H NMR spectrum (δ , ppm): 0.84 t (9H, CH_3 , J 7.1 Hz), 0.96–1.89 m (18H, CH_2), 1.85 s (3C, CH_3COC^-), 2.36 s (3C, CH_3CON), 5.08 br. signal (1H, CHPh), 7.06–7.70 m (10H, 2Ph).

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