ISSN 1070-3632, Russian Journal of General Chemistry, 2009, Vol. 79, No. 7, pp. 1467–1472. © Pleiades Publishing, Ltd., 2009.
Original Russian Text © K.V. Turov, E.B. Rusanov, B.S. Drach, 2009, published in Zhurnal Obshchei Khimii, 2009, Vol. 79, No. 7, pp. 1110–1115.

Biphilic Properties of Substituted Triphenylphosphoranylideneacetonitriles Bearing 4,5-Di(arylsulfonyl)-1,3-thiazol-2-yl Fragments at the Ylide Center

K. V. Turov[a], E. B. Rusanov[b], and B. S. Drach[a]

[a] *Institute of Bioorganic and Petroleum Chemistry, National Academy of Sciences of Ukraine, ul. Murmanskaya 1, Kiev-94, 02660 Ukraine*
e-mail: drach@bpci.kiev.ua

[b] *Institute of Organic Chemistry, National Academy of Sciences of Ukraine, Kiev, Ukraine*

Received February 2, 2009

Abstract—Phosphonium ylides stabilized by nitrile and 4,5-di(arylsulfonyl)-1,3-thiazol-2-yl fragments show biphilic reactivity. They react with aromatic aldehydes upon heating revealing a noticeable activity of ylide center and are condensed with typical nucleophiles at C^4 center of the thiazole ring with the elimination of arylsulfonyl group under mild conditions. New 1,3-thiazole derivatives were obtained whose structures were proved by chemical, spectal and X-ray structural investigations.

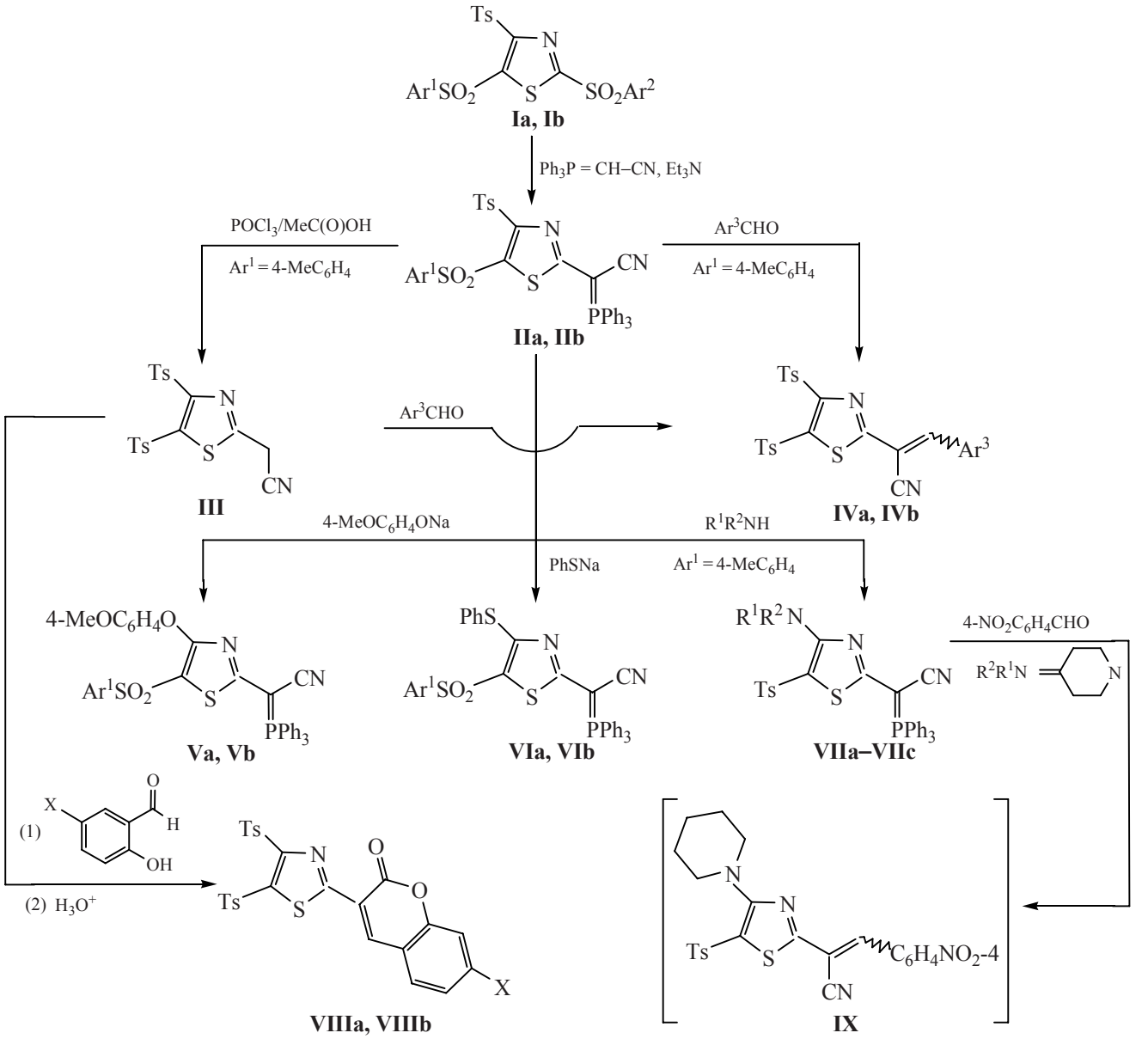
DOI: 10.1134/S107036320907010X

In the recently initiated investigation of nucleophilic substitution reactions of 2,4,5-tri(arylsulfonyl)-1,3-thiazoles [1,2] we found that accessible polycentric electrophilic substrates **I** reacted readily with triphenylphosphoranylideneacetonitrile at the C^2 center of thiazole ring with the formation of earlier unknown stable phosphonium ylides **II**. In turn, on this basis we successfully synthesized a series of new functional thiazole derivatives **III**–**IX**, as shown in the scheme and in Table 1.

It is noteworthy that despite the presence of three strong electron-acceptor substituents, ylides **II** enter Wittig reaction upon heating to 140ºC with excess benzaldehyde or *p*-fluorobenzaldehyde (see pathway **II** → **IV**). On the other hand, the ylide center of substrates **II** can be involved into acidic dephosphorylation **II** → **III**; the mechanism of this reaction has been considered earlier [3, 4].

In such transformations the nucleophilic character of polycentric substrates **II** is clearly seen. Nevertheless, they display even more pronounced electrophilic properties, as seen from the pathways **II** → **V**, **II** → **VI** and **II** → **VII** proceeding under very mild conditions. A high regioselectivity of these processes of nucleophilic substitution at the C^4 center of thiazole ring was mainly established by ^{1}H NMR spectroscopy that allowed the unequivocal identification of both leaving and remaining arylsulfonyl groups at varied substituents in 4 and 5 positions of the thiazole ring (Table 2). However, for establishing the structure of the product of reaction between substrate **IIa**, Ar^1 = Ts, and piperidine we had to apply the X-ray diffraction analysis. The general view of molecule **VIIa** and its principal geometric parameters are shown in the figure.

Thiazole heterocycle $S^1N^2C^{21–23}$ has usual bond lengths and bond angles. The thiazole ring is practically planar: the maximal deviation of atoms from the mean square plane is not greater than 0.016(1) Å. Bond C^{19}–C^{21} length is 1.428(3) Å, that is noticeably less than the value 1.48 Å characteristic of a single C(sp^2)–C(sp^2) bond [5]. The bond P^1–C^{19} 1.743(2) Å also is noticeably shorter than P–C bond with phenyl substituents (average value 1.798 Å) indicating conjugation in the P^1–C^{19}–C^{21} system and ylide character of P^1–C^{19} bond. The length of C^{19}–C^{20} bond is 1.408(3) Å, namely, it is shortened to the typical value of aromatic systems and indicates the



Ar^1 = 4-MeC_6H_4 (**Ia, IIa, Va, VIa**), 4-ClC_6H_4 (**Ib, IIb, Vb, VIb, VIIb**); Ar^2 = 4-MeC_6H_4 (**Ia**), Ph (**Ib**); Ar^3 = Ph (**IVa**), 4-FC_6H_4 (**IVb**); X = H (**VIIIa**), OH (**VIIIb**); R^1R^2N = N (**VIIa**), O N (**VIIb**), $PhCH_2NH$ (**VIIc**).

Table 1. Yields, constants and the data of elemental analyses of compounds **II**–**VIII**

Comp. no.	Yield, %	mp, °C (solvent)	Found, %		Formula	Calculated, %	
			Cl (P)	S		Cl (P)	S
IIa	83	154–155 (EtOH–CH_3CN, 10:1)	(4.45)	14.04	$C_{37}H_{29}N_2O_4PS_3$	(4.49)	13.88
IIb	74	164–165 (CH_3CN)	4.81 (4.38)	13.05	$C_{36}H_{26}ClN_2O_4PS_3$	4.97 (4.34)	13.49
III	79	164–165	–	22.34	$C_{19}H_{16}N_2O_4S_3$[a]	–	22.24
IVa	42	156–157 (EtOH)	–	18.61	$C_{26}H_{20}N_2O_4S_3$[b]	–	18.48

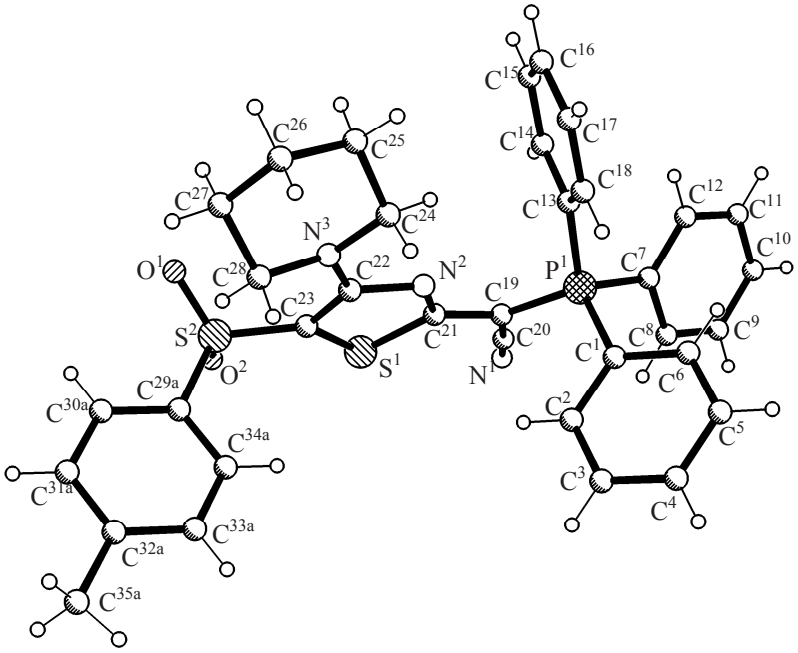
Table 1. (Contd.)

Comp. no.	Yield, %	mp, °C (solvent)	Found, %		Formula	Calculated, %	
			Cl (P)	S		Cl (P)	S
IVb	47	225–226 (EtOH)	–	17.54	$C_{26}H_{19}N_2FO_4S_3$[c]	–	17.86
Va	78	195–196 (EtOH)	(4.64)	9.68	$C_{37}H_{29}N_2O_4PS_2$	(4.69)	9.71
Vb	82	181–182 (EtOH)	4.93 (4.49)	9.56	$C_{36}H_{26}ClN_2O_4PS_2$	5.20 (4.55)	9.41
VIa	73	225–226 (EtOH)	(4.74)	14.69	$C_{36}H_{27}N_2O_2PS_3$	(4.79)	14.87
VIb	77	194–195 (EtOH)	5.07 (4.57)	14.70	$C_{35}H_{24}ClN_2O_2PS_3$	5.31 (4.64)	14.42
VIIa	81	210–211 (EtOH)	(4.93)	10.37	$C_{35}H_{32}N_3O_2PS_2$	(4.98)	10.31
VIIb	74	226–227 (EtOH)	(4.92)	10.30	$C_{34}H_{30}N_3O_3PS_2$	(4.97)	10.28
VIIc	83	238–239 (EtOH)	(4.76)	9.89	$C_{37}H_{30}N_3O_2PS_2$	(4.81)	9.96
VIIIa	87	271–272 (EtOH)	–	17.69	$C_{26}H_{19}NO_6S_3$[d]	–	17.89
VIIIb	82	266–267 (EtOH)	–	17.42	$C_{26}H_{19}NO_7S_3$[e]	–	17.37

[a] Found, %: S 52.41; H 3.95. Calculated, %: S 52.76; H 3.73. [b] Found, %: S 59.63; H 4.02 Calculated, %: S 59.98; H 3.87. [c] Found, %: S 57.53; H 3.80 Calculated, %: S 57.98; H 3.56. [d] Found, %: S 57.85; H 3.73 Calculated, %: S 58.09; H 3.56. [e] Found, %: S 56.17; H 3.80 Calculated, %: S 56.41; H 3.46.

Table 2. Spectral data of the synthesized compounds **II–VIII**

Comp. no.	^{1}H NMR spectrum, δ, ppm (DMSO-d_6)
IIa	2.33 s (3H, CH_3), 2.46 s (3H, CH_3), 7.03–7.05 m (4H$_{arom}$), 7.42–7.44 m (2H$_{arom}$), 7.53–7.62 m (12H$_{arom}$), 7.76–7.79 m (3H$_{arom}$), 7.93–7.95 m (2H$_{arom}$)
IIb	2.32 s (3H, CH_3), 6.95–7.10 m (4H$_{arom}$), 7.45–7.60 m (14H$_{arom}$), 7.70–7.85 m (3H$_{arom}$), 8.00–8.15 m (2H$_{arom}$)
III	2.46 s (3H, CH_3), 2.52 s (3H CH_3), 4.57 s (2H, CH_2), 7.40–7.42 m (2H$_{arom}$), 7.50–7.52 m (2H$_{arom}$), 7.72–7.74 m (2H$_{arom}$) 7.98–8.00 m (2H$_{arom}$)
IVa	2.43 s (3H, CH_3), 2.50 s (3H, CH_3), 7.39–7.41 m (2H$_{arom}$), 7.51–7.58 m (5H$_{arom}$), 7.73–7.75 m (2H$_{arom}$), 8.01–8.04 m (4H$_{arom}$), 8.40 s (1H CH)
IVb	2.43 s (3H, CH_3), 2.50 s (3H, CH_3), 7.35–7.40 m (4H$_{arom}$), 7.50–7.52 m (2H$_{arom}$), 7.72–7.74 m (2H$_{arom}$), 7.98–8.00 m (2H$_{arom}$), 8.13–8.15 m (2H$_{arom}$), 8.41 s (1H CH)
Va	2.42 s (3H, CH_3), 3.67 s (3H, OCH_3), 6.32–6.34 m (2H$_{arom}$), 6.46–6.48 m (2H$_{arom}$), 7.34–7.54 m (14H$_{arom}$), 7.68–7.71 m (3H$_{arom}$), 7.76–7.78 m (2H$_{arom}$)
Vb	3.68 s (3H, OCH_3), 6.34–6.36 m (2H$_{arom}$), 6.47–6.49 m (2H$_{arom}$), 7.40–7.60 m (14H$_{arom}$), 7.69–7.72 m (3H$_{arom}$), 7.88–7.90 m (2H$_{arom}$)
VIa	2.39 s (3H, CH_3), 6.77–6.85 m (4H$_{arom}$), 6.97–7.05 m (1H$_{arom}$), 7.31–7.57 m (14H$_{arom}$), 7.67–7.75 m (3H$_{arom}$), 7.82–7.85 m (2H$_{arom}$)
VIb	6.81–6.83 m (3H$_{arom}$), 7.34–7.65 m (16H$_{arom}$), 7.68–7.70 m (3H$_{arom}$), 7.97–7.99 m (2H$_{arom}$)
VIIa	1.06 s (4H$_{piperidine}$), 1.30 s (2H$_{piperidine}$), 2.42 s (3H, CH_3), 2.83 s (4H$_{piperidine}$), 7.31–7.33 m (2H$_{arom}$), 7.55–7.65 m (14H$_{arom}$), 7.71–7.73 m (3H$_{arom}$)
VIIb	2.36 s (3H, CH_3), 2.84 s (4H$_{morph}$), 3.15 s (4H$_{morph}$), 7.37–7.39 m (2H$_{arom}$), 7.57–7.67 m (14H$_{arom}$), 7.73–7.76 m (3H$_{arom}$)
VIIc	2.36 s (3H, CH_3), 3.76 m (2H CH_2), 6.73–6.76 m (3H$_{arom}$), 6.98–7.01 m (3H$_{arom}$), 7.29–7.32 m (3H$_{arom}$), 7.49–7.71 m (15H$_{arom}$)
VIIIa	2.42 s (3H, CH_3), 2.49 s (3H CH_3), 7.37–7.51 m (6H$_{arom}$), 7.77–7.82 m (3H$_{arom}$), 7.99–8.07 m (3H$_{arom}$), 9.04 s (1H CH$_{coumarin}$)
VIIIb	2.41 s (3H, CH_3), 2.49 s (3H CH_3), 6.80–6.88 m (3H$_{arom}$), 7.36–7.88 m (2H$_{arom}$), 7.45–7.47 m (2H$_{arom}$), 7.78–7.80 m (2H$_{arom}$), 7.97–7.99 m (2H$_{arom}$), 8.89 s (1H CH$_{coumarin}$), 11.13 s (1H, OH)

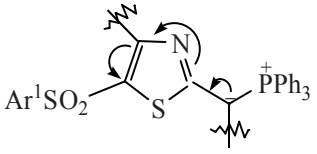


General view of **VIIa** molecule, principal bond lengths and bond angles: P^1–C^1 1.803(2), P^1–C^7 1.802(2), P^1–C^{13} 1.790(2), P^1–C^{19} 1.743(2), C^{19}–C^{21} 1.428(3), C^{19}–C^{20} 1.408(3), S^1–C^{21} 1.727(2), S^1–C^{23} 1.750(2), N^2–C^{21} 1.320(3), N^2–C^{22} 1.369(3), C^{22}–C^{23} 1.397(3), N^1–C^{20} 1.142(3), N^3–C^{22} 1.358(3), S^2–C^{23} 1.714(2) Å; $C^{21}S^1C^{23}$ 89.15(10), $N^2C^{21}S^1$ 114.74(15), $C^{21}N^2C^{22}$ 112.29(18), $N^2C^{22}C^{23}$ 114.08(19), $C^{22}C^{23}S^1$ 109.68(15), $N^2C^{21}C^{19}$ 123.65(18), $C^{21}C^{19}$ P^1 119.57(15), $S^2C^{23}S^1$ 114.68(13)°.

conjugation of the π-system with the ylide center; the cyano group itself lies in the plane of thiazole heterocycle [torsion angle C^{20}–C^{19}–C^{21}–S^1 is only 6.7(3)°]. Note that P^1–C^{19} bond length 1.743(2) Å in the structure **VIIa** is close to the respective values 1.753 and 1.743 Å found for the ylides $Ph_3P{=}C(CN)_2$ and $PhMe_2P{=}C(CN)_2$ [6, 7].

Short contacts in the crystal of compound **VIIa** are not revealed.

Thus, at the action of piperidine, like, by the way, of the other hard and soft nucleophiles, on the substrates **IIa**, **IIb** predominantly occurs the substitution of arylsulfonyl group in the 4 position of thiazole ring, while the neighboring electrophilic center is not practically affected, owing probably to its deactivation by conjugation with ylide center, as shown below.



Note in conclusion that the products of reaction of accessible biphilic substrates **II** with electrophilic and nucleophilic agents, substituted thiazoles **III**–**VII**, turned out to be useful for further transformations. Thus, the stabilized ylides **V**–**VIII** enter Wittig reaction with aromatic aldehydes but with strong tarring that hampers isolation of compound **IX** and its analogs. On the other hand, compound **III** was without problems transformed into the derivatives of 3-(1,3-thiazol-2-yl)coumarin (**VIII**). Other transformations of the polycentric compounds **II**–**VII** will be considered in future.

EXPERIMENTAL

The ^{1}H NMR spectra were registered on a Varian Mercury-400 instrument from solutions in DMSO-d_6 with internal TMS.

The X-ray structural investigation of a single crystal of compound **VIIa** with linear dimensions 0.04×0.32×0.62 mm was carried out at room temperature on a Bruker Smart Apex **II** diffractometer (λMoK_α radiation, graphite monochromator, θ_{max} 28.41°, the sphere segment was $-11 \le h \le 11$, $-9 \le k \le 12$, $-26 \le l \le 28$). Total array contained 21328 reflexes of which 7726 were independent (average *R*-factor 0.0372). The crystals of compound **VIIa**, $C_{35}H_{32}N_3O_2PS_2$, M 621.73, are triclinic, space group $P2_1/c$

(no. 14), *a* 8.7930(7), *b* 9.2612(7), *c* 21.1879(17) Å, α 79.412(4), β 85.798(5), γ 68.942(4)º, V 1582.7(2) Å^3, *Z* 2, d_{calc} 1.305 g cm^{-3}, μ 0.255 mm^{-1}, *F*(000) 652. The structure was solved by the direct method and refined by the least-squares method in full-matrix anisotropic approximation using SHELXS97 and SHELXL97 programs [8, 9]. For the refinement were used 4909 reflexes with $I > 2\sigma(I)$, (430 of refined parameters, 11.4 reflexes per a parameter, weight scheme $w = 1/[\sigma^2(Fo^2) + (0.046P)^2 + 0.4482P]$, where $P = (Fo^2 + 2Fc^2)/3$ is applied, the ratio of maximal (average) shift to error in the final cycle is 0.009 (0.003). Corrections for extinction were introduced with SADABS program (the minimal/maximal correction ratio T_{min}/T_{max} = 0.607). The carbon atoms C^{29}–C^{35} of tosyl group as well as the respective hydrogen atoms are disordered over two positions A and C with occupancies 53 and 47%, respectively. All hydrogen atoms were located geometrically. Final divergence factors are: $R1(F^2)$ = 0.094, $R_W(F^2)$ = 0.123, *GOF* = 1.034 over all reflexes and $R1(F)$ = 0.051 $R_W(F^2)$ = 0.106, *GOF* = 1.034 over the reflexes with $I > 2\sigma(I)$. Residual electron density from differential Fourier synthesis after the final refinement cycle is 0.32 and –0.34 e Å^{-3}.

Elemental analyses and constants of newly synthesized compounds are listed in Table 1, their spectral data are collected in Table 2.

2,4,5-Tritosyl-1,3-thiazole (Ia) is synthesized in accordance with [1].

4-Tosyl-2-phenylsulfonyl-5-*p*-chlorophenylsulfonyl-1,3-thiazol (Ib) is prepared by known procedure [2].

2-[(4,5-Ditosyl)-1,3-thiazol-2-yl]triphenylphosphoranylideneacetonitrile (IIa) and 2-[(4-tosyl-5-*p*-chlorophenylsulfonyl)-1,3-thiazol-2-yl]triphenylphosphoranylilideneacetonitrile (IIb). To a solution of 0.5 mmol of compound **Ia** or **Ib** in 10 ml of THF was added 1 mmol of triphenylphosphoranylideneacetonitrile and 1 mmol of triethylamine. The mixture was heated for 10 h at 60ºC, the solvent was removed in a vacuum and to the residue was added 5 ml of ethanol, the precipitate was filtered off and compound **IIa** was purified by recrystallization from a mixture of ethanol and acetonitrile (10:1), compound **IIb**, from acetonitrile.

2-(2,4-Ditosyl-1,3-thiazol-2-yl)acetonitrile (III). To a suspension of 0.7 mmol of compound **IIa** in 6 ml of acetic acid was added 0.14 mmol of phosphorus oxychloride. The mixture was heated at 100ºC for 15 min, the solvent was removed in a vacuum, to the residue was added 5 ml of ethanol, the precipitate was filtered off and used further without purification.

2-(4,5-Ditosyl-1,3-thiazol-2-yl)-3-phenyl(*p*-fluorophenyl)acrylonitrils (IVa, IVb). To 0.7 mmol of compound **IIa** was added 7 mmol of an appropriate aldehyde. The mixture was heated for 10 h at 140ºC, cooled to 20ºC, 5 ml of ethanol was added, the precipitate was filtered off and purified by crystallization from ethanol.

2-[5-Arylsulfonyl-4-(*p*-methoxyphenyloxy)-1,3-thiazol-2-yl]triphenylphosphoranylideneacetonitriles (Va, Vb). To a solution of 0.7 mmol of compound **IIa**, **IIb** in 5 ml of THF was added 0.7 mmol of sodium *p*-methoxyphenoxide, the mixture was left for 24 h at 20ºC, the solvent was removed in a vacuum, 5 ml of ethanol was added, the precipitate was filtered off and purified by crystallization from ethanol.

2-[5-Arylsulfonyl-4-(phenylthio)-1,3-thiazol-2-yl]-triphenylphosphoranylilideneacetonitriles (VIa, VIb). To a solution of 0.7 mmol of compound **IIa**, **IIb** in 5 ml of THF was added 0.7 mmol of sodium thiophenoxide, the mixture was left for 24 h at 20ºC, the solvent was removed in a vacuum, 5 ml of ethanol was added, the precipitate was filtered off and purified by crystallization from ethanol.

2-[4-Piperidino (morpholino, benzylamino)-5-tosyl-1,3-thiazol-2-yl]triphenylphosphoranylideneacetonitriles (VIIa–VIIc). A mixture of 0.7 mmol of compound **IIa** and 7 mmol of an appropriate nitrogen base was heated for 10 h at 120ºC, cooled to 20ºC, 5 ml of ethanol was added, precipitate was filtered off and purified by crystallization from ethanol.

3-(4,5-Ditosyl-1,3-thiazol-2-yl)-2*H*-chromen-2-one (VIIIa). To a solution of 0.7 mmol of compound **III** in 10 ml of ethanol was added 0.8 mmol of salycilic aldehyde and 1 drop of piperidine. The mixture was heated to 40ºC for 1 h and left at 20ºC for 24 h, the solvent was removed in a vacuum, 10 ml of sodium carbonate and then 2 ml of concn. hydrochloric acid was added, and the mixture was refluxed for 1 h. The precipitate formed was filtered off and purified by crystallization from a mixture of ethanol and DMF (10:1).

7-Hydroxy-3-(4,5-ditosyl-1,3-thiazol-2-yl)-2*H*-chromen-2-one (VIIIb). To a solution of 0.7 mmol of compound **III** in 10 ml of ethanol was added 0.8 mmol of 2,4-dihydroxybenzaldehyde and 1 drop of piperidine. The mixture was heated to 40ºC for 1 h and left

at 20ºC for 24 h, then the solvent was removed in a vacuum, 10 ml of sodium carbonate and then 2 ml of concn. hydrochloric acid was added, and the mixture was refluxed for 1 h. The precipitate formed was filtered off and purified by crystallization from ethanol.

3-*p*-Nitrophenyl-2-(4-piperidino-5-tosyl-1,3-thiazol-2-yl)acrylonitrile (XI). To 0.7 mmol of compound **IIa** was added 7 mmol of *p*-nitrobenzaldehyde. The mixture was heated for 4 h at 140ºC, 10 ml of ethanol was added, and the presence of triphenylphosphine oxide and the product of Wittig reaction **XI** was revealed by TLC. Alongside these substances a mixture of several products was formed that considerably hampered the separation of individual compound **XI**.

REFERENCES

1. Turov, K.V., Babii, S.B., Zyabrev, V.S., and Drach, B.S., *Zh. Obshch. Khim*., 2006, vol. 76, no. 10, p. 1757.
2. Turov, K.V. and Drach, B.S., *Zh. Obshch. Khim*., 2008, vol. 78, no. 14, p. 648.
3. Smolii, O.B., Panchishin, S.Ya., Romanenko, E.A., and Drach, B.S., *Zh. Obshch. Khim*., 1995, vol. 75, no. 4, p. 583.
4. Smolii, O.B., Panchishin, S.Ya., Pirozhenko, V.V., and Drach, B.S., *Zh. Obshch. Khim*., 2001, vol. 71, no. 11, p. 1830.
5. Burke-Laing, M. and Laing, M., *Acta Crystallogr. B*, 1976, vol. 32, no. 7, p. 3216.
6. Richter, R., Hartung, H., and Deresch, S., *Z. Anorg. Allgem. Chem*., 1980, vol. 469, no. 10, p. 179.
7. Dreissig, W., Hecht, H.J., and PLieth, K., *Z. Kristallogr.*, 1973, vol. 137, no. 2/3, p. 132.
8. Sheldric, G.M., *SHELXS97. Program for the Solution of Crystal Structure*, University of Gottingen, Germany, 1997.
9. Sheldric, G.M., *SHELXL97. Program for the Refinement of Crystal Structures*, University of Gottingen, Germany, 1997.