Russian Journal of Organic Chemistry, Vol. 40, No. 11, 2004, pp. 1633–1637. Translated from Zhurnal Organicheskoi Khimii, Vol. 40, No. 11, 2004, pp. 1665–1677.

Nitration of Phenylpropiolic Acid Derivatives in HSO_3F And Reactions of Vinyl Type Cations Formed Therefrom

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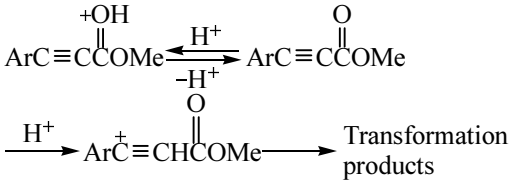
Received February 20, 2004

Abstract—Nitration of phenylpropiolic acid derivatives ArC≡CX (X=CN, CO_2Me) in HSO_3F at –75...–50°C afforded mononitro compounds, for instance, *m*-$O_2NC_6H_4C{\equiv}CX$. Vinyl type cations generated in HSO_3F from methyl 3-arylpropiolates $ArC^+{=}CHCO_2Me$ react along two pathways. The first among them results in formation of fluorosulfonates $ArC(OSO_2F){=}CHCO_2Me$, and the second one after the attack of vinyl cation on the aryl moiety of the substrate affords a dimer that on nitration is converted into a nitro product with conserved triple bond.

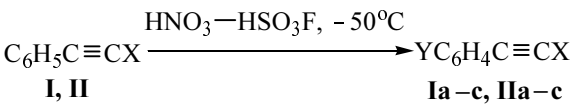
We report here on results of nitration of phenylpropiolonitrile and methyl arylpropiolates in a system HNO_3–HSO_3F performed in the framework of investigation on acetylene compounds reactions with electrophilic agents [1. 2].

In a general case the interaction of a superacid and an acetylene compound depends on the basicity of the latter and may involve a simple solvation, a formation of of variable strength hydrogen bonds, or a complete proton transfer to one of the potential basicity sites of the acetylene affording the corresponding ions.

As seen from ^1H and ^{13}C NMR spectra nitrile **I** dissolved in the superacid at –80°C does not specifically interact with HSO_3F. In contrast, many among acetylene esters under similar conditions first undergo the O-protonation at the oxygen of the carbonyl group furnishing hydroxycarbonium ions [1]. The stability of the latter and their further transformations depend not only on the temperature and the medium acidity but are crucially governed by the number, mutual position, and the character of the substituent in the aryl moiety. Ions with strong electron-withdrawing groups are the most stable in HSO_3F at –80°C (the frontier case), but at increasing number of alkyl and especially alkoxy substituents in the benzene ring the reactivity of this type ions sharply grows. Therewith irreversible changes are seen in the ^1H NMR spectra of the primary ions accompanied by appearance of the characteristic signals of –CH= groups belonging to the final products of the observed transformation. These facts should be taken into account in planning and performing reactions of acetylene compounds with electrophilic reagents.



The analysis of nitration results of compounds **I** and **II** in the system HNO_3–HSO_3F, 3:1, at –50°C (here and hereinafter molar ratios HNO_3–substance are given) has demonstrated that in both cases the reaction does not affect the triple bonds and the products contain exclusively mixtures obtained by mononitration in the benzene ring, compounds **Ia–c** and **IIa–c**. Therewith the mixture of nitro compounds **Ia–c** (yield 30%) contains isomers in the ratio *o*- : *m*- : *p*- ≈1 : 3 : 6, and for compounds **IIa–c** (yield 33%) this ratio is *o*- : *m*- : *p*- ≈1 : 3 : 2.

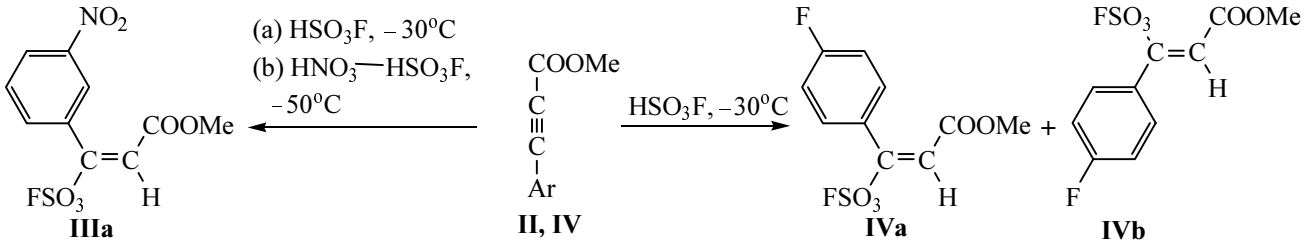


I, X = CN; **II**, X = COOMe; Y = *o*-NO_2 (**a**), *m*–NO_2(**b**), *p*-NO_2 (**c**).

Due to the strong deactivation of the benzene ring no nitration of compounds **IIa–c** occurred even at increased

reaction temperature. For instance, methyl 4-nitrophenylpropiolate (**IIc**) kept in the system HNO_3–HSO_3F at –10°C for 0.5 h was recovered unchanged.

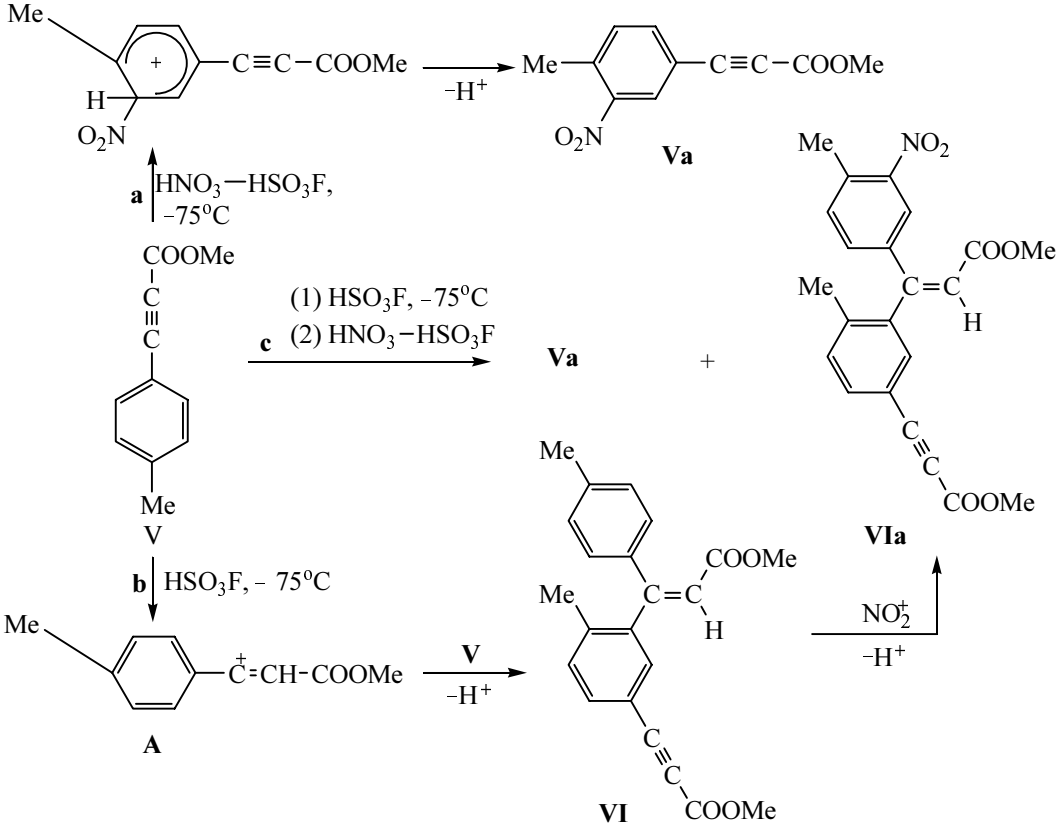
The triple bond in unsubstituted ester **II** is more basic than in nitro compounds **IIa–c**, therefore in HSO_3F already at –30°C after protonation at the acetylene C^2 atom followed by nucleophile addition it is converted into unsaturated fluorosulfonate **III**. We assigned the stereochemical structure to compound **III** basing on a close similarity of fluorosulfonate formation from phenylpropiolic acid [3]. The nitration of fluorosulfonate **III** in the system HNO_3–HSO_3F (1 h, –50°C) occurred regioselectively affording a single *meta*-nitroisomer **IIIa**.



Ar = Ph (**II**), 4-FC_6H_4 (**IV**).

Methyl 4-fluorophenylpropiolate (**IV**) in HSO_3F within 1 h at –30°C transformed into a mixture of isomeric compounds **IVa** (yield 60%) and **IVb** (yield 10%), but they did not undergo nitration in the system HNO_3–HSO_3F (1 h, –30°C).

In methyl 4-tolylpropiolate (**V**) the triple bond is more prone to protonation at the acetylene C^2 atom than in the previously mentined propiolates, and thus its nitration should be carried out at the temperature not exceeding –75°C. Therewith the order of reagents mixing becomes



of a crucial importance. To perform efficient reaction along the **a** pathway indicated on the scheme substrate **V** should be gradually added to the nitrating system HNO_3–HSO_3F cooled to –75°C. At this order of carrying out the reaction the benzene ring nitration occurs faster than the competing protonation of the triple bond into cation **A** along the pathway **b**. By this procedure it was possible to obtain nitro compound **Va** in 61% yield.

Another order of reagents mixing led to reaction along pathway ***c***. In this case substrate **V** was first dissolved in HSO_3F cooled to –75°C. Then the cooled nitrating system HNO_3–HSO_3F was added dropwise to the above solution. As a result alongside the expected product **Va** (12%) dimeric nitro compound **VIa** (17%) was isolated containing a triple bond; its structure was established by spectral data.

The nontrivial course of the process along pathway ***c*** is presumably caused by the protonation of acetylene ester **V** giving rise to relatively stable vinyl-type cation **A** that after the electrophilic attack of the aryl substituent of initial ester **V** and deprotonation affords dimer **VI** which is nitrated into the final reaction product **VIa**. To confirm this pathway we dissolved acetylene ester **V** in HSO_3F at –75°C, left standing the solution at this temperature for 0.5 h, and after treating with 20% H_2SO_4 at –60°C isolated dimer **VI** in 64% yield [2]. The regioselective nitration of only one of the two benzene rings of dimer **VI** is due to deactivation of the other ring by two electron-withdrawing groups whereas the ring undergoing nitration is linked to a single such moiety –C(Ar)=CHCO$_2$Me (cf. with nitration of fluorosulfonate **III**).

The results reported here demonstrate the new possibilities of functionalizing phenylpropiolic acid derivatives under conditions of mild low-temperature process in superacids where even in the presence of the competing protonation of the triple bond and S_E-nitration of the aryl substituent the electrophilic reaction can be efficiently directed into the desired path by varying the experimental conditions. Detailed aspects of vinyl-type cations with the "original" substrate-precursor [2] "substitute" substrates [4], and also data on regioselectivity and regiospecificity of these new reactions will be published elsewhere within the framework of the declared program [4].

EXPERIMENTAL

IR spectra were recorded on spectrophotometer Specord 75 IR from solutions of compounds in $CHCl_3$. ^1H, ^{13}C, and ^{19}F NMR spectra were registered on spectrometer Bruker AM-500 (operating frequencies 500, 125.76, and 470.7 MHz respectively) from solutions in $CDCl_3$. As internal references in the NMR spectra we used the residual signal of $CHCl_3$ (^1H, δ_H 7.25 ppm), signal of the solvent (^{13}C, δ_C 77.0 ppm), and signal of $CFCl_3$ (^{19}F, δ_F 0.0 ppm) respectively. Mass spectra were measured on MKh-1321 instrument at the ionizing electrons energy 70 eV.

GC-MS analysis of mixtures of compounds **Ia–c** and **IIa–c** was performed on Hewlett-Packard HP-5995 instrument equipped with a flame-ionization detector, ionizing electrons energy 70 eV, separator temperature 240°C, ion source temperature 250°C. Quartz capillary column 25000×0.32 mm, stationary phase Ultra-2 (95% of methylsilicone, 5% of phenylmethylsilicone) 0.53 μm. Oven temperature programmed from 100°C to 240°C, heating rate 10–20 deg/min. Carrier gas helium, flow rate 1 ml/min. The volume of probe of 3–5% solution was 2 μl.

The purity of the initial [5, 6] and obtained compounds was checked by TLC on Silufol UV-254 plates. The preparative separation of the reaction mixtures was carried out by column chromatography on silica gel Chemapol (40–100 μm) at gradient elution with 2–10% ethyl acetate solutions in hexane. Yields of the products were determined as weight of fractions obtained by chromatography.

(2-Nitrophenyl)propiolonitrile (Ia). mp 86–87°C. IR spectrum, cm^{-1}: 1340, 1525, 2275. ^1H, δ, ppm: 7.69–7.76 m ($2H_{arom}$), 7.82–7.85 m ($1H_{arom}$), 8.24–8.26 m ($1H_{arom}$). Mass spectrum, *m/z* (I_{rel}, %): 172 (22) M^+, 156 (11), 142 (11), 126 (13) $[M–NO_2]^+$, 119 (15), 114 (21), 104 (28), 100 (19), 99 (22), 90 (40), 76 (100), 63 (32), 50 (56), 44 (31). Calculated *M* 172.14.

(3-Nitrophenyl)propiolonitrile (Ib). mp 145–146°C. IR spectrum, cm^{-1}: 1345, 1540, 2265, 2285. ^1H NMR spectrum, δ, ppm: 7.65 t ($1H_{arom}$, *J* 8.0 Hz), 7.92 d.t ($1H_{arom}$, *J* 7.7, 1.1 Hz), 8.38 d.d.d ($1H_{arom}$, *J* 8.4, 2.1, 1.0 Hz), 8.47 t ($1H_{arom}$, *J* 1.6 Hz). Mass spectrum, *m/z* (I_{rel}, %): 172 (68) M^+, 126 (100) $[M–NO_2]^+$, 114 (19), 100 (39), 99 (39), 76 (18), 75 (28), 51 (35), 50 (26), 39 (11). Calculated *M* 172.14.

(4-Nitrophenyl)propiolonitrile (Ic). mp 140–142°C (publ.: mp 139–141°C [7]). ^1H NMR spectrum is consistent with the published one [7].

Methyl (2-nitrophenyl)propiolate (IIa). mp. 86–87°C. IR spectrum, cm^{-1}: 1330, 1520, 1700, 2230. ^1H NMR spectrum, δ, ppm: 3.86 s (3H, OMe), 7.61 t.d

($1H_{arom}$, *J* 7.7, 1.3 Hz), 7.66 t.d ($1H_{arom}$, *J* 7.3, 1.0 Hz), 7.77 d.d ($1H_{arom}$, *J* 7.6, 1.5 Hz), 8.16 d ($1H_{arom}$, *J* 8.1 Hz). Mass spectrum, *m/z* (I_{rel}, %): 205 (2) M^+, 174 (19) [*M*–OMe]$^+$, 147 (70), 104 (43), 102 (27), 91 (100), 89 (46), 76 (43), 74 (54), 63 (38), 59 (34). Calculated *M* 205.17.

Methyl (3-nitrophenyl)propiolate (IIb). Oily substance. IR spectrum, cm^{-1}: 1345, 1535, 1710, 2245. ^{1}H NMR spectrum, δ, ppm: 3.86 s (3H, OMe), 7.59 t ($1H_{arom}$, *J* 8.0 Hz), 7.88 d.t ($1H_{arom}$, *J* 7.7, 1.7 Hz), 8.30 d.d.d (1H arom, *J* 8.3, 2.3, 1.0 Hz), 8.43 t ($1H_{arom}$, *J* 1.8 Hz). Mass spectrum, *m/z* (I_{rel}, %): 205 (41) M^+, 174 (100) [*M*-OMe]$^+$, 147 (62), 128 (82), 116 (40), 105 (18), 101 (36), 88 (36), 77 (26), 74 (90), 50 (26). Calculated *M* 205.17.

Methyl (4-nitrophenyl)propiolate (IIc). mp 111–112°C (publ.: mp 108–111°C [8]). IR spectrum, cm^{-1}: 1345, 1520, 1710, 2240. ^{1}H NMR spectrum, δ, ppm: 3.86 s (3H, OMe), 7.74 d ($2H_{arom}$, *J* 8.6 Hz), 8.24 d ($2H_{arom}$, *J* 8.6 Hz). Mass spectrum, *m/z* (I_{rel}, %): 205 (49) M^+, 174 (100) [*M*–OMe]$^+$, 147 (65), 128(73), 116 (47), 101 (20), 100 (36), 99 (13), 98 (20), 88 (31), 77 (25), 74 (69), 62 (22), 50 (25). Calculated *M* 205.17.

***E*-Methyl 3-(3-nitrophenyl)-3-(fluorosulfonyloxy)propenoate (IIIa).** Oily substance. IR spectrum, cm^{-1}: 1210, 1235, 1350, 1555, 1665, 1730. ^{1}H NMR spectrum, δ, ppm: 3.73 s (3H, OMe), 6.41 s (1H, HC=), 7.67 t ($1H_{arom}$, *J* 8.0 Hz), 7.89 d.t ($1H_{arom}$, *J* 7.8, 1.2 Hz), 8.38 d.d.d ($1H_{arom}$, *J* 8.4, 2.3, 1.1 Hz), 8.44 t ($1H_{arom}$, *J* 1.7 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 52.57 q (*J* 148.3 Hz), 115.14 d (*J* 166.6 Hz), 124.65 d.t (*J* 170.4, 5.3 Hz), 126.27 d.t.d (*J* 170.8, 6.6, 1.0 Hz), 129.60 d (*J* 167.0 Hz), 131.06 m (*J* 6.8 Hz), 135.03 d.t (*J* 164.9, 6.0 Hz), 147.97 m (*J* 7.2 Hz), 156.62 m (*J* 5.5 Hz), 163.09 q (*J* 3.8 Hz). ^{19}F NMR spectrum, δ, ppm: 46.49 s (1F, FSO_3). Mass spectrum, *m/z* (I_{rel}, %): 305 (6) M^+, 288 (18), 274 (45) [*M*–OMe]$^+$, 206 (19) [*M*–FSO_3]$^+$, 191 (31), 174 (40), 150 (58), 104 (31), 101 (24), 89 (47), 77 (77), 76 (68), 69 (100), 63 (66), 59 (80). Found, %: C 39.15, H 2.71, N 4.30. $C_{10}H_8FNO_7S$. Calculated, %: C 39.35, H 2.64, N 4.59. *M* 305.24.

***E*- and *Z*-Methyl 3-(fluorosulfonyloxy)-3-(4-fluorophenyl)propenoates (IVa, b).** Oily substances that were separated by column chromatography on silica gel. First *E*-(**IVa**) was eluted, R_f 0.20 (hexane–ethyl acetate, 9:1). IR spectrum, cm^{-1}: 1010, 1200, 1445, 1495, 1645, 1725. ^{1}H NMR spectrum, δ, ppm: 3.70 s (3H, OMe), 6.26 s (1H, HC=), 7.14 t ($2H_{arom}$, *J* 8.6 Hz), 7.58 d.d ($2H_{arom}$, *J* 8.9, 5.2 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 52.23 q (*J* 147.5 Hz), 113.12 d (*J* 166.2 Hz), 115.67 d.d.d (*J* 165.7, 22.5, 3.0 Hz), 125.50 m (*J* 3.0 Hz), 131.78 d.d.d (*J* 164.5, 8.9, 6.8 Hz), 158.60 m (*J* 6.0 Hz), 163.63 m (*J* 4.0 Hz), 164.57 d (*J* 253.9 Hz). ^{19}F NMR spectrum, δ, ppm: –102.91 t.t ($1F_{arom}$, *J* 8.3, 5.2 Hz), 46.29 s (1F, FSO_3). Mass spectrum, *m/z* (I_{rel}, %): 278 (65) M^+, 247 (100) [*M*–OMe]$^+$, 179 (23) [*M*–FSO_3]$^+$, 147 (79), 123 (95), 120 (30), 95 (53), 69 (26), 59 (23). Then *Z*-(**IVb**) was isolated, R_f 0.10 (hexane–ethyl acetate, 9:1). ^{1}H NMR spectrum, δ, ppm: 3.84 C (3H, OMe), 6.24 s (1H, HC=), 7.17 t ($2H_{arom}$, *J* 8.5 Hz), 7.63 d.d ($2H_{arom}$, *J* 8.8, 5.2 Hz). ^{19}F NMR spectrum, δ, ppm: –102.44 t.t ($1F_{arom}$, *J* 8.2, 5.0 Hz), 50.43 s (1F, FSO_3). Mass spectrum, *m/z* (I_{rel}, %): 278 (55) M^+, 247 (100) [*M*–OMe]$^+$, 179 (15) [*M*-FSO_3]$^+$, 147 (65), 123 (87), 120 (20), 109 (15), 108 (15), 107 (15), 95 (58), 75 (29), 69 (25), 59 (18), 50 (15). Found for isomer mixture, % : C 43.30, H 3.07. $C_{10}H_8F_2O_5S$. Calculated, %: C 43.17, H 2.90. *M* 278.23.

Methyl (4-methyl-3-nitrophenyl)propiolate (Va). A solution of 26 mg (0.257 mmol) of KNO_3 in 0.5 ml of HSO_3F was cooled to –75°C, and thereto at vigorous stirring was added within 5 min 30 mg (0.172 mmol) of ester **V**. After 20 min the reaction mixture was quickly poured into 5 ml of 20% H_2SO_4 cooled to –50°C. After the usual workup [4] the residue was subjected to chromatography on silica gel. Yield 61%, mp 58–59°C. IR spectrum, cm^{-1}: 1345, 1430, 1515, 1700 (C=O), 2215, 2245 (C≡C). ^{1}H NMR spectrum, δ, ppm: 2.63 s (3H, Me), 3.85 s (3H, OMe), 7.37 d ($1H_{arom}$, *J* 7.9 Hz), 7.67 d.d ($1H_{arom}$, *J* 7.9, 1.7 Hz), 8.17 d ($1H_{arom}$, *J* 1.7 Hz). Mass spectrum, *m/z* (I_{rel}, %): 219 (38) M^+, 202 (100) [*M*–OH]$^+$, 188 (34) [*M*–OMe]$^+$, 142 (40), 130 (12), 114 (30), 102 (16), 88 (15), 77 (12), 63 (23), 51 (12). Found, % : C 60.13; H 4.31. $C_{11}H_9NO_4$. Calculated, % : C 60.27; H 4.14. *M* 219.19.

***E*-Methyl-3-(4-methyl-3-nitrophenyl)-3-(2-methyl-5-methoxycarbonylethynyl phenylpropenoate (VIa).** Yield 17%, viscous oily substance. IR spectrum, cm^{-1}: 895, 1120, 1170, 1345, 1425, 1515, 1620 (C=C), 1705, 1720 (C=O), 2225 (C≡C). ^{1}H NMR spectrum, δ, ppm: 2.12 s (3H, Me), 2.61 s (3H, Me), 3.69 s (3H, OMe), 3.83 s (3H, MeO_2CC≡), 6.08 s (1H, HC=), 7.20 d ($1H_{arom}$, *J* 7.9 Hz), 7.30 d ($1H_{arom}$, *J* 8.0 Hz), 7.37 d.d ($1H_{arom}$, *J* 8.0, 1.7 Hz), 7.41 d ($1H_{arom}$, *J* 1.6 Hz), 7.48 d.d ($1H_{arom}$, *J* 7.9, 1.6 Hz), 7.84 d ($1H_{arom}$, *J* 1.7 Hz). Mass spectrum, *m/z* (I_{rel}, %): 393 (17) M^+, 376 (100) [*M*–OH]$^+$, 375 (26), 362 (65) [*M*–OMe]$^+$, 361 (23), 346 (39), 330 (19), 310 (15), 302 (21), 287 (21), 226 (21), 215

(19), 213 (19), 202 (23), 115 (20), 59 (32). Found, %: C 66.93; H 5.01. $C_{22}H_{19}NO_6$. Calculated, % : C 67.17; H 4.87. *M* 393.39.

REFERENCES

1. Rudenko, A.P., Vasil'ev, A.V., Savechenkov, P. Yu., Sommer, Zh., Khauas, M., and Val'spurzhe, S., *Intermediaty. Sintez protonirovanie i okislenie atsetilenovykh soedinenii: Uchebnoe posobie* (Intermediates. Synthesis, Protonation, and Oxidation of Acethylene Compounds: Handbook), no. 2, St. Petersburg, 2003, p. 213.
2. Cavechenkov, P. Yu., Rudenko, A.P., and Vasil'ev, A.V., *Zh. Org. Khim.,* 2004, vol. 40, p. 1106.
3. Olah, G. A. and Spear, R. J., *J. Am. Chem. Soc.,* 1975, p. 1845.
4. Rudenko, A.P., Cavechenkov, P. Yu., and Vasil'ev, A.V., *Zh. Org. Khim.,* 2004, vol. 40, p. 1424.
5. Cavechenkov, P. Yu., Vasil'ev, A.V., and Rudenko, A.P., *Zh. Org. Khim.,* 2004, vol. 40, p. 1329.
6. Skvortsov, Yu.M., Mal'kina, A.G., Volkov, A.N., Trofimov, B.A., Oleinikova, E.B., Kazin, I.V., and Gedymin, V.V., *Izv. Akad. Nauk SSSR, Ser. Khim.,* 1978, p. 872.
7. Yadla, R., Rao, V. S., and Rao, J. M., *Indian J. Chem.*, 1982, 21B, p. 1046.
8. Shchelkunov, A.V. and Ivanova, N.N., *Fiziko-khimicheskie konstanty atsetilenovykh soedinenii* (Physicochemical Constants of Acethylene Compounds), Alma-Ata: Nauka, 1988, p. 97.