Russian Journal of Organic Chemistry, Vol. 39, No. 7, 2003, pp. 963–967. Translated from Zhurnal Organicheskoi Khimii, Vol. 39, No. 7, 2003, pp. 1024–1028.

Prototropic Rearrangement of 2-Propynyl(methyl)amino, 2-Propynyloxy, and 2-Propynylsulfanyl Derivatives of Hetarenes under Conditions of Phase-Transfer Catalysis: Mechanism and Limitations

K. Rubina, M. Fleisher, E. Abele, Yu. Popelis, and E. Lukevits

Latvian Institute of Organic Synthesis, Aizkraukles 21, Riga, LV-1006, Latvia
e-mail: kira@osi.lv

Received November 30, 2002

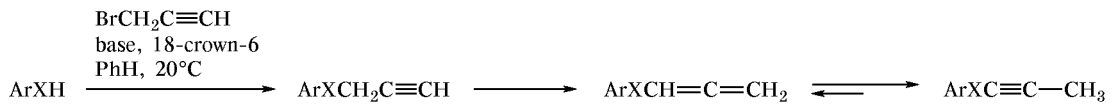
Abstract—2-Propynyl derivatives of *N*-methylaniline, phenol, benzenethiol, 2-pyridinethiol, 2-pyrimidinethiol, and 1,3-benzoxazole-2-thiol were synthesized. Under conditions of phase-transfer catalysis, phenyl 2-propynyl sulfide is converted into allenyl phenyl sulfide and phenyl 1-propynyl sulfide. The rearrangement mechanism was studied by the AM1 quantum-chemical method.

Rearrangement of 1-alkynes into 2-alkynes was usually effected in the systems KOH/EtOH [1, 2], KOEt/EtOH [3], *t*-BuOK/DMSO [4], and *t*-BuOK or EtONa/Me_2SO_4 [5]. As a rule, the triple bond migration process is reversible. For example, 2-alkynes are readily converted into 1-alkynes in the presence of *t*-BuLi [6] or BuLi/Et_2O [7]. However, both reactions require a polar solvent or organolithium base to be used. Ogawa *et al.* [8] described rearrangement of 2-propynyl sulfides into the corresponding allenes by the action of potassium bis(trimethylsilyl)amide. Most recently, Florio *et al.* [9] reported on the Wittig rearrangement of 2-propynyl ethers in the presence of butyllithium in THF. Kobychev *et al.* [10] performed a quantum-chemical study of noncatalytic acetylene–allene rearrangement of the $XCH_2C{\equiv}CH$ systems where X = H, Me, NMe_2, OMe, F, SMe.

The goal of our present study was to synthesize 2-propynyl and allenyl derivatives of aromatic and heteroaromatic thiols, alcohols, and amines under conditions of phase-transfer catalysis. The mechanism of the rearrangement of phenyl 2-propynyl sulfide into allenyl phenyl sulfide and phenyl 1-propynyl sulfide, which occurs during the phase-transfer reaction, was studied by the AM1 quantum-chemical method. 2-Propynyl(methyl)amino-, 2-propynyloxy-, and 2-propynylsulfanyl-substituted hetarenes were successfully synthesized in a two-phase system liquid–solid (Scheme 1, Table 1).

The alkylation of benzenethiol (**I**) with 2-propynyl bromide in the system solid K_2CO_3–18-crown-6–benzene at room temperature afforded a mixture of phenyl 2-propynyl sulfide (**VII**, yield 86%) and phenyl 1-propynyl sulfide (**IX**, yield 5%). By the reaction of benzenethiol with 2-propynyl bromide in the system KOH–18-crown-6–benzene at room temperature (reaction time 1 h) we obtained terminal acetylene **VII** in 52% yield. Phenyl 2-propynyl sulfide (**VII**) reacted with solid KOH under conditions of phase-transfer catalysis, yielding 60% of allene **VIII** and 40% of phenyl 1-propynyl sulfide (**IX**). Phenol (**II**) failed to react with $BrCH_2C{\equiv}CH$ in the system

Scheme 1.



I–**III**, **VII**–**XI**, Ar = phenyl; **IV**, **XII**, Ar = 2-pyridyl; **V**, **XIII**, Ar = 2-pyrimidyl; **VI**, **XIV**, Ar = 2-benzoxazolyl; **I**, **IV**–**IX**, **XII**–**XIV**, X = S; **II**, **X**, X = O; **III**, **XI**, X = NCH_3.

1070-4280/03/3907-0963 $25.00 © 2003 MAIK "Nauka / Interperiodica"

Table 1. Synthesis and mass spectra of alkynes **VII**–**XIV**

Initial comp. no.	Ar	X	Base	Reaction time, h	Product[a] (yield, %)	Mass spectrum, *m*/*z* (I_{rel}, %)
I	Ph	S	K_2CO_3 (2 equiv)	3.5	**VII** (86)	148 (M^+, 36)
					IX (5)	148 (M^+, 100)
I	Ph	S	KOH (2 equiv)	1	**VII** (52)	148 (M^+, 36)
I	Ph	S	KOH (2 equiv)	24	**VIII** (60)	146 (M^+, 27)
					IX (40)	148 (M^+, 100)
II	Ph	O	K_2CO_3 (2 equiv)	24	**X**	132 (M^+, 36)
II	Ph	O	KOH (2 equiv)	7[b]	**X** (44)	132 (M^+, 36)
III	Ph	N	K_2CO_3 (2 equiv)	16	**XI** (98)	145 (M^+, 65)
III	Ph	N	KOH (2 equiv)	10	**XI**[c]	145 (M^+, 65)
IV	2-Pyridyl	S	KOH (2 equiv)	0.25	**XII** (95)	149 (M^+, 57)
V	2-Pyrimidyl	S	KOH (2 equiv)	0.3	**XIII** (100)	150 (M^+, 98)
VI	2-Benzoxazolyl	S	KOH (2 equiv)	0.5	**XIV** (86)	189 (M^+, 88)

[a] Compounds **VII**, **VIII** [5], **X**, and **XI** [11] have already been reported.

[b] The reaction was initially accompanied by heat evolution; the mixture was then stirred for 5.5 h at room temperature and was heated for 1 h at 50°C.

[c] The product was not isolated.

Table 2. ^{1}H NMR spectra of compounds **VII**–**XIV** in $CDCl_3$, δ, ppm (*J*, Hz) (relative to HMDS)

Comp. no.	Ar	XR	CH_3	≡CH	XCH_2	$=CH_2$	XCH=	Ar
VII	Ph	$SCH_2C{\equiv}CH$	–	2.22 t (*J* = 2.5)	3.59 d (*J* = 2.5)	–	–	7.2–7.5 m
VIII	Ph	$SCH{=}C{=}CH_2$	–	–	–	4.97 d (*J* = 6.2)	5.94 t (*J* = 6.2)	7.35 m
IX	Ph	$SC{\equiv}CCH_3$	2.08 s	–	–	–	–	7.34 m
X	Ph	$OCH_2C{\equiv}CH$	–	2.50 t (*J* = 2.1)	4.67 d (*J* = 2.1)	–	–	6.98 m, 7.29 m
XI	Ph	$N(CH_2C{\equiv}CH)CH_3$	2.95 s	2.15 t (*J* = 2.3)	4.03 d (*J* = 2.3)	–	–	6.82 m, 7.26 m
XII	2-Pyridyl	$SCH_2C{\equiv}CH$	–	2.18 t (*J* = 2.6)	3.95 d (*J* = 2.6)	–	–	7.00 m, 7.18 m, 7.50 m, 8.44 m
XIII	2-Pyrimidyl	$SCH_2C{\equiv}CH$	–	2.18 t (*J* = 2.6)	4.00 d (*J* = 2.6)	–	–	6.98 m, 8.51 m
XIV	2-Benzoxazolyl	$SCH_2C{\equiv}CH$	–	2.30 t (*J* = 2.8)	4.07 d (*J* = 2.8)	–	–	7.26 m, 7.45 m, 7.62 m

solid K_2CO_3–18-crown-6–benzene. Phenyl 2-propynyl ether (**X**) was synthesized in 44% yield in the system $BrCH_2C{\equiv}CH$–solid KOH–18-crown-6–benzene. The reaction of *N*-methylaniline (**III**) with 2-propynyl bromide in the system K_2CO_3(or KOH)–18-crown-6–benzene gave 98% of *N*-methyl-*N*-(2-propynyl)aniline (**XI**) as the only product. 2-Propynyl hetaryl sulfides **XII**–**XIV** were readily obtained in 86–100% yield from the corresponding thiols by treatment with $BrCH_2C{\equiv}CH$ in the system KOH–18-crown-6–benzene at room temperature (reaction time 15–30 min). Prolonged reaction of alkynes **XII**–**XIV** with KOH leads to tarring of the mixture. Spectral parameters of compounds **VII**–**XIV** are given in Tables 1–3.

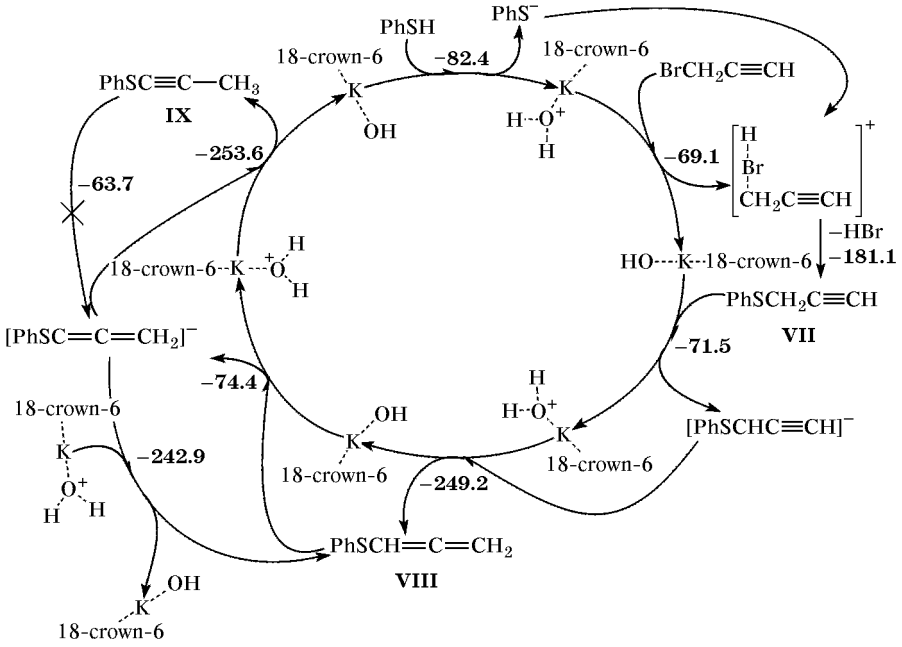
Table 3. ^{13}C NMR spectra of compounds **VII**–**XIV** in CDCl3, δ_C, ppm

Comp. no.	Ar	XR	C≡C	XCH_2	Ar[a]
VII	Ph	$SCH_2C{\equiv}CH$	71.51 (≡CH), 79.82 ($CH_2\mathbf{C}{\equiv}$)	22.55	126.95 (C^p) 128.97 (C^m) 130.06 (C^o) 134.95 (C^i)
VIII	Ph	$SCH{=}C{=}CH_2$	–	78.74 ($=CH_2$) 85.89 (XCH=)	126.45 (C^p) 128.30 (C^o) 128.93 (C^m) 135.61 (C^i) 209.35 (=C=)[b]
IX	Ph	$SC{\equiv}CCH_3$	5.19 (≡C$\mathbf{C}H_3$), 63.86 (≡$\mathbf{C}CH_3$), 95.25 (XC≡)	–	125.88 (C^o) 126.11 (C^p) 129.04 (C^m) 133.60 (C^i)
X	Ph	$OCH_2C{\equiv}CH$	75.41 (≡CH), 78.61 ($CH_2\mathbf{C}{\equiv}$)	55.69	114.87 (C^o) 121.54 (C^p) 129.45 (C^m) 157.51 (C^i)
XI	Ph	$N(CH_2C{\equiv}CH)CH_3$	38.54 (≡C$\mathbf{C}H_3$), 71.96 (≡CH), 79.28 ($CH_2\mathbf{C}{\equiv}$)	42.44	114.25 (C^o) 118.30 (C^p) 129.08 (C^m) 148.99 (C^i)
XII	2-Pyridyl	$SCH_2C{\equiv}CH$	70.42 (≡CH), 80.06 (≡C)	18.16	119.85 (C^5), 122.00 (C^3), 136.09 (C^4), 149.52 (C^6), 157.05 (C^2)
XIII	2-Pyrimidyl	$SCH_2C{\equiv}CH$	70.38 (≡CH), 79.49 (≡C)	19.15	116.77 (C^5), 157.28 (C^4, C^6), 170 (C^2)
XIV	2-Benzoxazolyl	$SCH_2C{\equiv}CH$	72.38 (≡CH), 77.86 (≡C)	20.66	109.99 (C^6), 118.67 (C^5), 124.15 (C^7), 124.40 (C^4), 141.74 (C^{7a}), 152.00 (C^{3a}), 162.99 (C^2)

[a] The ring carbon signals were assigned according to [12].
[b] The ring carbon signals were assigned according to [13].

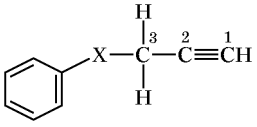
The isomerization of phenyl 2-propynyl sulfide into phenyl 1-propynyl sulfide under conditions of phase-transfer catalysis was examined by the AM1 semiempirical quantum-chemical method [14, 15]. The mechanism of the process is shown in Scheme 2. 18-Crown-6 as phase-transfer catalyst ensures transfer of $K^+ OH^-$ into the organic phase. According to the results of our calculations, the first reaction stage, deprotonation of PhSH, requires no activation energy. The heat of formation of PhS^- and water is equal to –82.4 kcal/mol. The complex $[H_2O\cdots K]^+$ reacts with 2-propynyl bromide to afford the carbocation $[H{-}Br\cdots CH_2{-}C{\equiv}CH]^+$ (ΔH = –69.1 kcal/mol). Phenyl 2-propynyl sulfide (**VII**) is formed by reaction of PhS^- ion with $H{-}Br\cdots CH_2{-}C{\equiv}CH]^+$ (ΔH = –181.1 kcal/mol). Deprotonation of alkyne **VII** yields $[PhSCHC{\equiv}CH]^-$ (ΔH = –71.5 kcal/mol) (see figure, *b*). In the initial state, the distance between the oxygen

Scheme 2.



atom of the hydroxy group and hydrogen atom on C^3 is 3.5 Å (see figure, *a*). This process is energetically more favorable than abstraction of the terminal proton from the acetylenic moiety (ΔH = –40.9 kcal/mol). The subsequent proton transfer from the complex $[H_2O\cdots K]^+$ to the terminal carbon atom (C^1, see figure, *c*; the distance bentween the C^1 atom and the corresponding proton in the complex is 2.76 Å) is characterized by a ΔH value of –249.2 kcal/mol, and it leads to formation of allenyl phenyl sulfide (**VIII**) (see figure, *d*). Allene **VIII** then reacts with OH^-, yielding $[PhSC{=}C{=}CH_2]^-$ (ΔH = –74.4 kcal/mol). Proton transfer to the terminal carbon atom C^1 gives phenyl 1-propynyl sulfide (**IX**) (ΔH = –253.6 kcal × mol^{-1}). A similar reaction heat (–242.9 kcal/mol) is typical of protonation of the C^3 atom in the carbanion $[PhSC{=}C{=}CH_2]^-$, which leads to allene **VIII**. The rearrangement of phenyl 2-propynyl sulfide (**VII**) gave a mixture of allenyl phenyl sulfide (**VIII**, 60%) and phenyl 1-propynyl sulfide (**IX**, 40%).

Table 4. Calculated charges on the X and C^1–C^3 atoms in 2-propynyl derivatives of benzenethiol, phenol, and *N*-methylaniline (compounds **VII**, **X**, and **XI**)

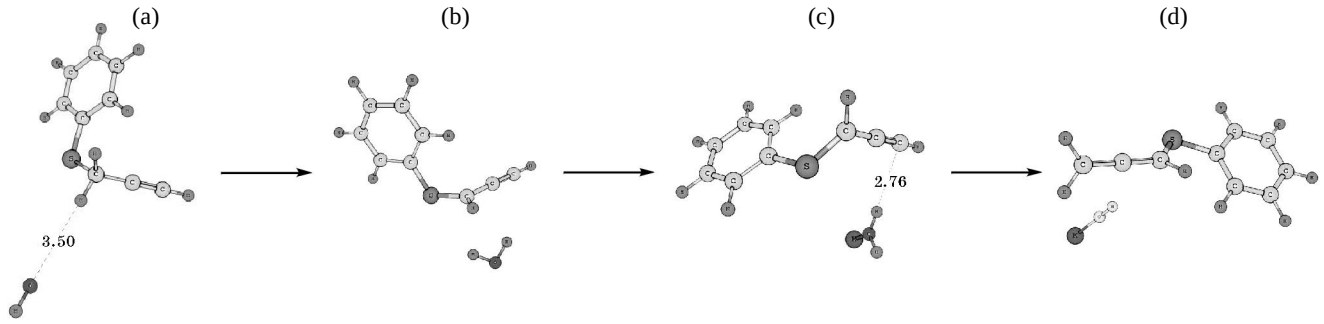


Comp. no.	X	Charge, a.u.			
		X	C^1	C^2	C^3
VII	S	0.237	–0.182	–0.182	–0.184
X	O	–0.204	–0.172	–0.210	0.087
XI	NCH_3	–0.234	–0.198	–0.207	0.048

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded on a Varian 200 Mercury spectrometer (200 and 50 MHz, respectively) using $CDCl_3$ as solvent and hexamethyldisiloxane as internal reference. The mass spectra (70 eV) were run on an HP 6890 GC–MS system. GLC analysis was performed on a Chrom-5 chromatograph equipped with a flame-ionization detector (glass column, 1.2 m × 3 mm, packed with 5% of OV-101 on Chromosorb W-HP, 80–100 mesh; carrier gas nitrogen, flow rate 60 ml/min; oven temperature was varied from 180 to 250°C, depending on the composition of the reaction mixture). Thiols, phenol, and 18-crown-6 were commercial reagents (from Acros) and were used without additional purification.

The above rearrangement does not occur with phenyl 2-propynyl ether (**X**) and *N*-methyl-*N*-(2-propynyl)aniline (**XI**). This may be explained in terms of different electronegativities of the nitrogen, oxygen, and sulfur atoms. Table 4 contains the calculated charges on the N, O, S, and C^3 atoms in compounds **VII**, **X**, and **XI**.



AM1 simulation of the rearrangement of phenyl 2-propynyl sulfide into allenyl phenyl sulfide; the distances are given in Å; for better clearness, the potassium–oxygen distance in the structures of KOH and $[H_2O\cdots K]^+$ is elongated relative to the calculated value.

2-Propynyl bromide and *N*-methylaniline were distilled prior to use.

Reaction of thiols, phenol, and *N*-methylaniline with 2-propynyl bromide. 2-Propynyl bromide, 1.33 ml (15 mmol), was added to a suspension of 10 mmol of substrate **I**–**VI**, 0.264 g (1 mmol) of 18-crown-6, and 20 mmol of powdered K_2CO_3 or KOH in 20 ml of toluene. The mixture was stirred for 0.25–24 h at room temperature, filtered through a layer of silica gel, and evaporated to isolate compounds **VII**–**IX** and **XI**. Product **X** was purified by vacuum distillation, bp 84–86°C (10 mm). Compounds **XII**–**XIV** were purified by column chromatography using toluene–hexane mixtures (at various ratios) as eluent. The reaction conditions and spectral parameters of alkynes **VII**–**XIV** are collected in Tables 1–3.

Quantum-chemical calculations. Semiempirical quantum-chemical calculations were performed with the use of MOPAC 6 software (AM1 Hamiltonian) [11, 12]. The equilibrium geometric parameters were determined by full optimization using PRECISE keyword. Insofar as MOPAC 6 lacks parametrization for potassium atom, a "sparkle" pseudospecies was used instead. Supporting information (Cartesian coordinates of all initial and optimized structures) is available from the author (Dr. chem. M. Fleisher <misha@osi.lv>).

REFERENCES

1. Jacobs, T.L., *Org. React.*, 1949, vol. 5, p. 13.
2. Jacobs, T.L., Akawie, R., and Cooper, R.G., *J. Am. Chem. Soc.*, 1951, vol. 73, p. 1273.
3. Wojtkowiak, B. and Romanet, R., *Bull. Soc. Chim. Fr.*, 1962, p. 805.
4. De Medeiros, E.F., Herbert, J.M., and Taylor, R.J.K., *Tetrahedron Lett.*, 1990, vol. 31, p. 5843.
5. Filippova, A.Kh., Frolov, Yu.L., Lyashenko, G.S., Modonov, V.B., Ivanova, N.A., Kalikhman, I.D., Voronkov, M.G., and Vyazankin, N.S., *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1986, p. 1847.
6. Magee, T.V., Stork G., and Fludzinski, P., *Tetrahedron Lett.*, 1995, vol. 36, p. 7607.
7. Klein, J. and Becker, J.Y., *Tetrahedron*, 1972, vol. 28, p. 5385.
8. Ogawa, A., Sakagami, K., Shima, A., Suzuki, H., Komiya, S., Katano, Y., and Mitsunobu, O., *Tetrahedron Lett.*, 2002, vol. 43, p. 6387.
9. Florio, S., Granito, C., Ingrosso, G., and Troisi, L., *Eur. J. Org. Chem.*, 2002, vol. 20, p. 3465.
10. Kobychev, V.B., Vitkovskaya, N.M., Klyba, N.S., and Trofimov, B.A., *Izv. Ross. Akad. Nauk, Ser. Khim.*, 2002, p. 713.
11. Ficini, J. and Barbara, C., *Bull. Soc. Chim. Fr.*, 1965, p. 2787.
12. Ewing, D.F., *Org. Magn. Reson.*, 1979, vol. 12, p. 499.
13. Kalinowski, H.-O., Berger, S., and Braun, S., *13C-NMR Spektroskopie*, Stuttgart: Georg Thieme, 1984, p. 133.
14. Stewart, J.J.P., *MOPAC, version 6.0. Quantum Chemical Program Exchange (QCPE), Program Number 455*, Bloomington, IN, 1984.
15. Stewart, J.J.P., *MOPAC, version 6.0. Manual. Program Number 455*, Bloomington, IN, 1984.