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M. S. MUKANOVA[1], YE. S. SYCHEVA[1], T. M. SEILKHANOV[2], V. K. YU[1]

[1]JSC «A.B. Bekturov Institute of Chemical Sciences», Almaty, Republic of Kazakhstan Kazakhstan,
[2]Sh. UalikhanovKokshetau State University, Kokshetau, Republic of Kazakhstan Kazakhstan.
E-mail: chem_mukan@mail.ru

SYNTHESIS OF DITHIOACETYLENIC PIPERAZINE DERIVATIVES

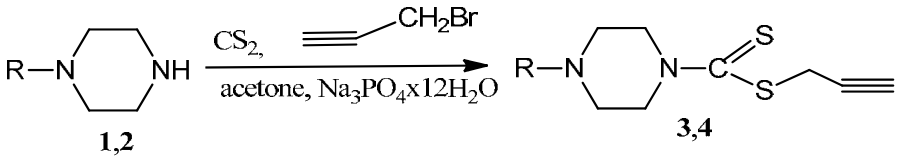
Abstract. The conditions for the three-component one-pot synthesis of dithioacetylenic piperazine derivatives was developed. As a result prop-2-yn-1-yl-4-methylpiperazin-1-carbodithioate (73,4%) and prop-2-yin-1-yl-4-diphenylmethyl piperazine-1-carbodithioate (93,6%) were synthesized. Structure of dithioacetylenic piperazine derivatives was established based on IR and NMR(^{1}H and ^{13}C) spectroscopic data.

Keywords: one-pot synthesis, 1-methylpiperazine, 1-diphenylmethylpiperazine, carbon disulfide, dithioacetylenic derivatives.

As it is known, N,N'-substituted piperazines possess a wide range of biological activity. Compounds having a piperazine ring showed antimicrobial, neurotropic, antihemolytic, atypical antipsychotic activity and evaluated as potential herbicides and plant growth regulators [1–6].

In order to synthesize biologically active piperazine containing compounds, one-pot synthesis of dithioacetylenic piperazine derivatives was studied. The reactivity of N-substituted piperazines was studied in a three-component system: amine–carbon disulfide–alkyl halide. The conditions for the three-component one-pot synthesis of dithioacetylenic piperazine derivatives were developed. The reaction of the interaction of the heterocyclic amines (1-methylpiperazine, 1-diphenylmethylpiperazine) with carbon disulfide and propargyl bromide was carried out in acetone in the presence of sodium phosphate at room temperature for 1,5–2 hours. As a result prop-2-yn-1-yl-4-methylpiperazin-1-carbodithioate (**3)** (73,4%) and prop-2-yin-1-yl-4-diphenylmethyl piperazine-1-carbodithioate (**4)** (93,6%) were synthesized.

The composition and individuality of the synthesized compounds (**3,4**) was confirmed by the elemental analysis TLC and IR spectroscopy.



1,2 **3,4**

R = CH_3 (**1,3**); $(Ph)_2CH$ (**2,4**)

In the IR spectra of dithioacetylenic piperazine derivatives (**3,4**) are found absorption bands of stretching vibrations of the C=S groupin the region

ν1146 – 1139 cm^{-1}. The absorption band of stretching vibrations of the C–S bond is found in the regionν 705–660 cm^{-1}. The stretching vibrations of the C≡CH bond appear as a narrow intense absorption band in the region ν 3250, 3291 cm^{-1}.

The structure of dithioacetylenic piperazine derivatives (**3**,**4**) was established based on the ^{1}H and ^{13}C NMR spectra (table).

In the^{1}HNMR spectra of compound (**4**) the protons of the methylene groups of the piperazine cycle resonate in the strong field region δ 2,49 ppm in the form of a broadened singlet and for compound (**3**) in the form of weakly split triplet (J = 4,0 Hz) in the region δ 2,44 ppm. In the specta of compound (**3**) the chemical shift of the methyl group is found as a singlet at δ 2,27 ppm. Singlet signal for the protons of the methylene group, bound to the sulfur atom, is shifted to the weak field region δ 4,05, 4,11 ppm. The signal of the methine group protons of compound (**4**) as a singlet is also shifted to the weak field region δ 4,27 ppm. The chemical shift for the proton of the terminal acetylene bond is foundas a triplet in the region δ 2,21, 2,24 ppm. In the spectra of compound (**4**) chemical shifts for the equivalent protons of two phenyl groups are foundin the weak fieldregion δ 7,21– 7,42 ppm.

Analysis of the ^{13}C NMR spectra of the compounds (**3**,**4**) (table) confirms the structure of the synthesized compounds. Chemical shifts for the cyclic carbon atoms of the piperazine cycle are found as a singlet signal in the region δ 51,41, 54,41 ppm. The carbon atom of the methyl group of compound (**3**) resonates in the weak field region δ 45,72 ppm. The chemical shift of the methylene group carbon atom associated with the sulfur atom is located in the region δ 26,03, 26,06 ppm. The signals in the region δ 71,80– 78,60 ppm were assigned to the carbon atoms of the acetylene bond. The chemical shifts of the equivalent carbon atoms of the two phenyl groups of the compound (**4**) are found in the form of double signals in the weak field region δ 127,46– 141,91 ppm. The carbon atom C=S bonds resonates in the weak field region δ 194,35, 197,57 ppm.

^{1}H and ^{13}C NMR (δ, ppm) spectral data of the compounds (**3**,**4**)

#	^{1}H NMR (δ, ppm, J (Hz)					
	CH_3	CH_2 (pip.)	SCH_2	≡CH	CH	C_6H_5
3	2,27	2,44 (J=4.0)	4,05	2,21 (J=4.0)	–	–
4	–	2,49	4,11	2,24 (J=4.0)	4,27	7,21 т (J=8,0), 7,30 т (J=8,0), 7,42 д (J=8,0)

#	^{13}C NMR (δ, ppm)						
	CH_3	CH_2 (pip)	SCH_2	≡C	≡CH	C_6H_5	C=S
3	45,72	54,41	26,06	78,46	78,60	–	194,57
4	–	51,41	26,03	71,83	71,80	127,46 (Pho); 127,93 (Php); 128,84 (Phm); 141,91 (Phi)	194,35

EXPERIMENTAL

Control of the reaction was carried out by TLC on Silufol UV-254 plates, eluent ethanol - benzene (1:3). IR spectra of synthesized compounds are recorded on a Nicolet 5700 device in KBr tablets. ^{1}H and ^{13}C NMR spectra were obtained on a JNM-ECA 400 (JEOL) spectrometer in $CDCl_3$ solution.

Prop-2-yn-1-yl-4-methylpiperazine-1-carbodithioate (3). A solution of carbon disulfide (2,28g, 0,03mol) was added dropwise to a solution of 1-methylpiperazine(1,0g, 0,01 mol) and Na_3PO_4 x $12H_2O$ (2,28g, 0,006 mol) in 40 ml of acetone. Then, after 20 minutes of stirring, propargyl bromide (1,31g, 0,011 mol) was added dropwise to the reaction mixture and was stirred for 1 hour. Then the precipitate was filtered, the solvent was distilled off in a water jet pump vacuum. The yield was 1,57g (73.4%). M.p. 43-45^{0}C. R_f = 0,12.

Prop-2-in-1-yl-4-diphenylmethyl-piperazine-1-carbodithioate (4) was synthesized by the similar procedure. The yield was 3,43g (93.6%). M.p. 82-84 °C. R_f = 0,43.

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Резюме

М. С. Мұқанова, Е. С. Сычева, Т. М. Сейілханов, В. К. Ю

ПИПЕРАЗИННІҢ ДИТИОАЦЕТИЛЕНДІ
ТУЫНДЫЛАРЫН СИНТЕЗДЕУ

Пиперазиннің дитиоацетиленді туындыларының үшкомпонентті бір реакторлық синтездеу жағдайлары жасалынды. Нәтижесінде проп-2-ин-1-ил-4-метилпиперазин-1-карбодитиоат (73,4%) және проп-2-ин-1-ил-4-дифенилметилпиперазин-1-карбодитиоат (93,6%) синтезделінді. Пиперазиннің дитиоацетиленді туындыларының құрылысы ЯМР ^{1}Н және ^{13}С спектроскопиялық мәліметтері негізінде анықталынды.

Түйін сөздер: бір реакторлық синтезі, 1-метилпиперазин, 1-дифенилметилпиперазин, көміртегі дисульфиді, дитиоацетиленді туындылар.

Резюме

М. С. Муканова, Е. С. Сычева, Т. М. Сейлханов, В. К. Ю

СИНТЕЗ ДИТИОАЦЕТИЛЕНОВЫХ
ПРОИЗВОДНЫХ ПИПЕРАЗИНОВ

Разработаны условия трехкомпонентного однореакторного синтеза дитиоацетиленовых производных пиперазинов. В результате синтезированы проп-2-ин-1-ил-4-метилпиперазин-1-карбодитиоат (73,4%) и проп-2-ин-1-ил-4-дифенилметилпиперазин-1-карбодитиоат (93,6%). Структура дитиоацетиленовых производных пиперазинов установлена на основании данных спектроскопии ЯМР ^{1}Н и ^{13}С.

Ключевые слова: однореакторный синтез, 1-метилпиперазин, 1-дифенилметилпиперазин, сероуглерод, дитиоацетиленовые производные.