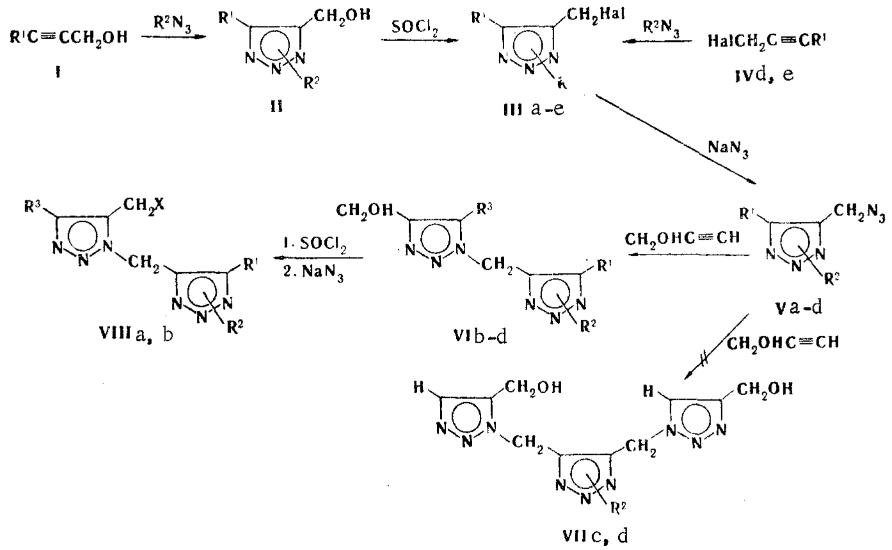
SYNTHESIS OF NONCONDENSED POLYNUCLEAR VICINAL TRIAZOLES

L. G. Tikhonova, E. S. Serebryakova,
A. V. Maksikova, G. A. Gareev,
and L. I. Vereshchagin

UDC 547.791.07

The reaction of propargyl alcohol and butynediol with organic mono- and diazides gave N-alkyl-C-hydroxymethyl-1,2,3-triazoles, the hydroxy group of which was transformed successively to a halo group and an azide fragment. Two- and three-ring triazole structures that are crosslinked at the C and N atoms by methylene bridges were synthesized by the subsequent addition of a second molecule of the acetylenic alcohol.

In one of our previous communications [1] we demonstrated the possibility of the synthesis of polynuclear triazoles by the addition of organic azides to the triple bond of propargyltriazoles. In a search for new substances that are potential pesticides and plant growth regulators from polynitrogen heterocyclic compounds [2-4] we examined another method that makes it possible to obtain polynuclear vicinal triazoles by means of ethynylcarbinols and butynediol as the starting acetylenic components [5, 6]. The hydroxy group of triazoles IIa-d synthesized by this method is quite easily transformed by successive treatment with thionyl chloride and sodium azide to an azide fragment and then to triazole heterocycle VI. Experiments show that the stepwise joining together of triazole rings to form chains can be realized in this way. In place of acetylenic alcohols I, in the reaction with azides one can quite satisfactorily use their halo derivatives, viz., propargyl halides or dichlorobutyne (IVd, e).



I, II a $R^1=H$, $R^2=CH_2C_6H_5$; b $R^1=H$, $R^2=C_7H_{15}$; c $R^1=CH_2OH$, $R^2=CH_2C_6H_5$; d $R^1=CH_2OH$, $R^2=C_5H_{11}$; III a $R^1=H$, $R^2=CH_2C_6H_5$, Hal=Cl; b $R^1=H$, $R^2=C_7H_{15}$, Hal=Cl; c $R^1=CH_2Cl$, $R^2=CH_2C_6H_5$, Hal=Cl; d $R^1=CH_2Cl$, $R^2=C_5H_{11}$, Hal=Cl; e $R^1=H$, $R^2=CH_2C_6H_5$, Hal=Br; IV d $R^1=CH_2Cl$, Hal=Cl; e $R^1=H$, Hal=Br; V a $R^1=H$, $R^2=CH_2C_6H_5$; b $R^1=H$, $R^2=C_7H_{15}$; c $R^1=CH_2N_3$, $R^2=CH_2C_6H_5$; d $R^1=CH_2N_3$, $R^2=C_5H_{11}$; VI b $R^1=R^3=H$, $R^2=C_7H_{15}$; c $R^1=CH_2N_3$, $R^2=CH_2C_6H_5$, $R^3=H$, d $R^1=CH_2N_3$, $R^2=C_5H_{11}$, $R^3=H$; VIII a $R^1=R^3=H$, $R^2=C_7H_{15}$, X=Cl; b $R^1=R^3=H$, $R^2=C_7H_{15}$, $X=N_3$

The use of dichlorobutyne or butynediol in the reaction with azides makes it possible to obtain 4,5-bis(azidomethyl)-1,2,3-triazoles (Vc-d) and, consequently, should open up a

---

Irkutsk State University. Institute of Petrochemical and Coal-Chemical Synthesis, Angarsk 665813. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1685-1688, December, 1981. Original article submitted October 20, 1980; revision submitted February 18, 1981.

0009-3122/81/1712- 1241$07.50

TABLE 1. Characteristics of the Triazoles Obtained

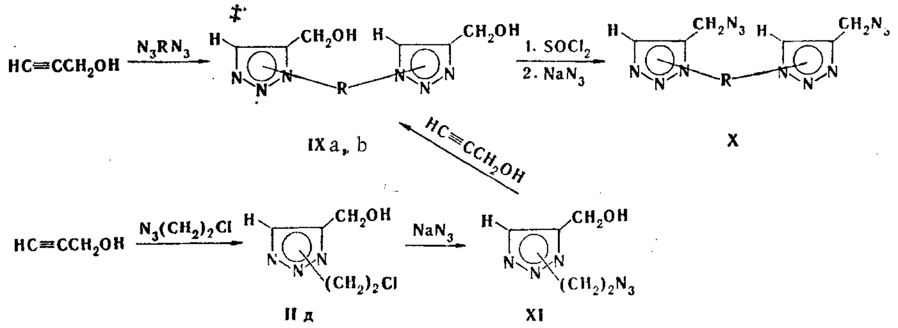
Compound	mp (°C) or n_D^{23}	Found, %				Empirical formula	Calculated, %				Yield, %
		C	H	Cl	N		C	H	Cl	N	
IIIa	64—65* 116—117	57,8	4,9	16,9	19,9	$C_{10}H_{10}ClN_3$	57,9	4,8	16,9	20,3	73
IIIb	1,5028	55,6	8,3	16,8	19,0	$C_{10}H_{18}ClN_3$	55,8	8,4	16,3	19,5	57
IIIc	1,5216	52,1	4,5	27,0	16,8	$C_{11}H_{11}Cl_2N_3$	51,5	4,3	27,7	16,4	43
IIId	1,5163	46,1	6,5	30,1	17,5	$C_9H_{15}Cl_2N_3$	45,7	6,4	30,1	17,8	55
Va	1,5761	56,2	4,8	—	39,1	$C_{10}H_{10}N_6$	56,1	4,7	—	39,2	91
Vb	1,4892	54,0	8,1	—	37,2	$C_{10}H_{18}N_6$	54,0	8,1	—	37,8	56
Vc	1,5515	50,8	4,4	—	47,0	$C_{11}H_{11}N_9$	49,1	4,9	—	46,8	51
Vd	1,5058	43,2	6,4	—	50,4	$C_9H_{15}N_9$	43,4	6,0	—	50,6	56
VIb	108—109	55,8	7,8	—	30,3	$C_{13}H_{22}N_6O$	56,1	7,9	—	30,2	70
VIc	1,5715	50,1	4,9	—	37,9	$C_{14}H_{15}N_9O$	51,7	4,6	—	38,7	—
VId	1,5422	47,5	6,1	—	41,2	$C_{12}H_{19}N_9O$	47,2	6,2	—	41,3	44
VIIIb	86—87	50,9	6,4	—	42,6	$C_{13}H_{21}N_9$	51,5	6,9	—	41,6	48
XX†	—	38,6	5,0	—	54,0	$C_{10}H_{14}N_{12}O$	37,8	4,1	—	53,0	31

---

*The melting points of the two isomeric compounds are indicated. †A colored, viscous, undistillable liquid. IR spectrum, cm^{-1}: 920, 970, 1070, 1140, 1430, 1585 (triazole ring); 2190 (N_3); 3070 (triazole =C—H).

pathway to the joining together of triazole rings simultaneously at two active centers. However, we found that the reaction of diazidotriazoles V with acetylenic alcohols requires prolonged heating at temperatures above 120°C, in which case only 1 mole of propargyl alcohol adds to one of the azide groups. The IR spectra of azidomethyltriazolyltriazoles VIc-d contain intense absorption bands of azido and hydroxy groups (2110 and 3400-3450 cm^{-1}) and bands that are characteristic for the triazole ring at 900-910, 1070-1120, 1470-1480, and 1550-1580 cm^{-1}. An increase in the number of triazole links in the chain that are separated by methylene bridges decreases the solubility of the compounds in organic solvents appreciably. The subsequent reaction of azidotriazoles VI with propargyl alcohol was therefore carried out in dimethylformamide (DMF), which, in addition, made it possible to raise the reaction temperature. After the reaction mixture is heated at 120-130°C for several hours, the absorption bands of the azido group (2110 cm^{-1}) vanish, and this constitutes evidence for completion of the reaction; however, with respect to their elementary compositions, the isolated products do not correspond to the formula of the expected structure (VII). A similar pattern was observed in the case of the reaction of azidomethylthiazole VIIIb with propargyl alcohol.

In the examined method the joining together of triazole rings to form chains is realized through the methylene group at the C—N atoms of the heteroring. Crosslinking of the rings at the N—N atoms is possible by synchronous cycloaddition of diazides to acetylenes [7] or by addition to the latter of hydroxy- or chloroethyl azide with subsequent conversion of the hydroxy group or the chlorine atom to an azido group and then to a triazole ring via the scheme:



IXa R=(CH$_2$)$_2$; IXb, X R=(CH$_2$)$_2$O(CH$_2$)$_2$

As expected, a mixture of several difficult-to-separate regioisomers of triazoles, the presence of which is determined by means of the PMR spectra from the chemical shift of the free proton of the triazole ring and the protons of the methylene groups (7.68-7.98 and 4.66-4.76 ppm, respectively). It must be noted that the low solubility of the bistriazoles in organic solvents limits the use of the NMR method for the identification of these compounds. The principal physical characteristics and the results of elementary analysis of the synthesized compounds are presented in Table 1.

EXPERIMENTAL

The PMR spectra of the compounds were recorded with a Varian H-100 spectrometer with hexamethyldisiloxane as the internal standard. The IR spectra were recorded with a UR-20 spectrometer. The course of the reaction was monitored by means of thin-layer chromatography on plates with a loose layer of aluminum oxide (activity II). The compounds were purified with chromatographic columns filled with aluminum oxide. The eluting mixture consisted of diethyl ether and petroleum ether in ratios of 1:1 and 3:1 with added ethanol. The organic mono- and diazides [8], bis(azidomethyl)-1,2,3-triazole (Vc) [9], propargyl halides (IV) [11], N-substituted 1,2,3-triazoles (II) [10], and bis[4(5)-hydroxymethyl-1,2,3-triazolyl]-alkanes (IX) [7] were obtained by known methods.

Chloromethyl-1,2,3-triazoles (IIIb-d). A) These compounds were obtained by chlorination of 0.4-0.5 mole of hydroxymethyl-1,2,3-triazoles IIb-d with thionyl chloride in dioxane in the presence of an equimolar amount of pyridine, as in the synthesis of IIIa [1]. In contrast to the indicated method, the reaction products were purified by elution through a layer of aluminum oxide. The principal characteristics of the chloromethyltriazoles are presented in Table 1.

B) A solution of 0.01 mole of propargyl bromide (IVe) or dichlorobutyne (IVd) and 0.011 mole of the organic azide in 20 ml of toluene was stirred with heating to 110°C for 10 h (30 h for IVd). At the end of the reaction, the solvent was removed at reduced pressure, and the residue was eluted through a column filled with aluminum oxide. Bromomethyltriazole IIIe was used for the synthesis of azidotriazole Va without special purification and analysis. Bis(chloromethyl)-1,2,3-triazole IIId was identical with respect to the analytical data and its refractive index to triazole IIId obtained by chlorination of bis-(hydroxymethyl)-1,2,3-triazole IId.

Azidomethyl-1,2,3-triazoles Va-d. These compounds were synthesized by refluxing a suspension of 0.1 mole of the corresponding chloromethyl-1,2,3-triazoles IIIa-d and 0.11 or 0.22 mole of sodium azide in ethanol for 2 h. The subsequent isolation of the azidotriazoles was carried out as in [5]. The IR spectra of triazoles Va-d contain absorption bands that are characteristic for a heteroaromatic ring at 3080-3150, 1550-1580, 1410-1450, 1075-1145, and 900-910 cm^{-1} and absorption bands of an azide fragment at 2090-2160 cm^{-1}. The analytical data for azides Va-d are presented in Table 1.

Reaction of Azidotriazoles V with Propargyl Alcohol. A solution of 0.01 mole of the acetylenic alcohol and 0.11 mole of azidotriazole V in 15-20 ml of toluene was heated with stirring for 40-50 h, after which it was treated with ether, and the precipitated bistriazole VI was removed by filtration and crystallized from aqueous alcohol. The reaction of diazidotriazoles Vc, d with propargyl alcohol was carried out similarly. Azidomethylbistriazoles VIc, d were purified by elution through a column filled with aluminum oxide. The yields of the reaction products and the principal characteristics are presented in Table 1.

1-Heptyl-4(5)-methyl-4(5)-azidomethyl-1,2,3-triazol-1-yl-1,2,3-triazole (VIIIb). A 6-ml sample of pyridine was added dropwise to a cooled (to 3-5°C) solution of 0.011 mole of hydroxymethyltriazolyl-1,2,3-triazole VIb and 0.012 mole of thionyl chloride in 10 ml of dioxane with chloroform, and the mixture was stirred for 5-7 h, initially with cooling and then at 20-25°C. The solvent and gaseous reaction products were removed by heating the reaction mixture at reduced pressure. The concentrate containing chloromethyltriazole VIIIa was passed through a layer of aluminum oxide, after which a suspension of 0.0024 mole of the VIIIa concentrate and 0.03 mole of sodium azide in 5 ml of ethanol was refluxed with stirring for 3 h. The solvent was evaporated, and the crystalline residue was washed successively with water and ether to give 0.5 g (48%) of azidomethyltriazolyl-1,2,3-triazole VIIIb. IR spectrum: 910 (C=C), 1580 (C=C), and 2250 cm^{-1} (N_3).

1,5-Bis[5(4)-azidomethyl-1,2,3-triazol-1(3)-yl]-3-oxapentane (X) was similarly obtained from 1,5-bis[3(4)-hydroxymethyl-1,2,3-triazol-1(3)-yl]-3-oxapentane (IXb). The reaction of 1-(β-chloroethyl)-4(5)-oxamethyl-1,2,3-triazole (IIe) gave 1-(β-azidoethyl)-4(5)-hydroxymethyl-1,2,3-triazole (XI), which, after elution through a column filled with aluminum oxide, was used for the synthesis of dihydroxymethyl-1,2,3-triazole (X). The principal constants of the substances obtained are presented in Table 1.

LITERATURE CITED

1. L. I. Vereshchagin, A. V. Maksikova, L. G. Tikhonova, S. R. Buzilova, and G. V. Sakovich, Khim. Geterotsikl. Soedin., No. 5, 688 (1981).
2. Japanese Patent No. 21599; Ref. Zh. Khim., 9N562P (1973).
3. British Patent No. 1353699; Ref. Zh. Khim., 90458P (1975).
4. Japanese Patent Nos. 7021833 and 7021834; Chem. Abstr., 73, 77256, 77257 (1970).
5. G. I. Tsypin, T. N. Timofeeva, V. V. Mel'nikov, and V. V. Gidaspov, Zh. Org. Khim., 11, 1395 (1975).
6. S. S. Novikov, V. M. Brusnikina, and V. A. Rudenko, Izv. Akad. Nauk SSSR, Ser. Khim., 474 (1961).
7. L. G. Tikhonova, L. S. Serebryakova, A. V. Maksikova, G. V. Chernysheva, and L. I. Vereshchagin, Zh. Org. Khim., No. 7, 1401 (1981).
8. E. Lieber, T. S. Chao, and C. N. Rao, J. Org. Chem., 22, 238 (1957).
9. L. G. Tikhonova, A. V. Maksikova, E. S. Serebryakova, and L. I. Vereshchagin, Zh. Org. Khim., 16, 730 (1980).
10. L. Brandsma (editor), Preparative Acetylenic Chemistry (1971), p. 157.
11. A. V. Maksikova, L. G. Tikhonova, E. S. Serebryakova, and L. I. Vereshchagin, Khim. Geterotsikl. Soedin., No. 12, 1688 (1980).

REARRANGEMENTS IN THE HALOALKOXY(THIO,AMINO)-sym-TRIAZINE SERIES.

10. SYNTHESIS AND REARRANGEMENT OF 2-DIMETHYLAMINO-4-(2-ACYLHYDRAZINO)-6,7-DIHYDROOXAZOLO[3,2-a]-sym-TRIAZINES

V. V. Dovlatyan, N. Kh. Khachatryan,
T. A. Gomktsyan, and S. M. Saakyan

UDC 547.873'787'781.07:542.952

2-Dimethylamino-4-(2-acetylhydrazino)- and 4-(2-benzoyl)hydrazino-6,7-dihydrooxazolo[3,2-a]-sym-triazines were synthesized. It was established that when these compounds are heated, they undergo rearrangement to the corresponding 2-dimethylamino-6,7-dihydroimidazo[2,1-a]-sym-triazines. Deacylation of the latter gives the N-amino derivative.

We have shown [1] that 2-(2-chloroethoxy)-4-dialkylamino-6-(1-methyl-2-acethylhydrazino)-sym-triazine undergoes intramolecular cyclization to give a substituted triazinotriazine derivative when it is heated.

It was of interest to study a similar reaction in the case of 2-dimethylamino-4-(2-chloroethoxy)-6-(2-acylhydrazino)-sym-triazine, which, inasmuch as it has labile hydrogen atoms in the α and β positions of the hydrazine fragment, may form both an oxazolo- or imidazotriazine and a triazinotriazine in the case of thermolysis.

We established that the reaction of quaternary salt Ia with ethylene chlorohydrin in the presence of alkali at low temperature gives, instead of the expected 2-chloroethoxy derivative, dihydrooxazolo-sym-triazine IIa, which upon heating (200°C) undergoes rearrangement to dihydroimidazo-sym-triazine IIIa.

Compound Ib reacts with ethylene chlorohydrin in the presence of alkali at low temperatures to give a mixture of dihydrooxazolo- and dihydroimidazo-sym-triazines in a ratio of 4:3. When this mixture is heated in xylene, the dihydrooxazolotriazine is converted to the more stable dihydroimidazotriazine IIIb.

Strongly hygroscopic amine IV, which was identified in the form of Schiff base V, is formed in the deacylation of IIIa, b.

Armenian Agricultural Institute, Yerevan 375009. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, 1689-1692, December, 1981 Original article submitted December 9, 1980.

0009-3122/81/1712-1244$07.50