

OBTAINING A COMPLEX OF 1-VINYL-1,2,4-TRIAZOLE WITH GOLD CHLORIDE AND STUDY OF ITS THERMAL AND BIOLOGICAL PROPERTIES

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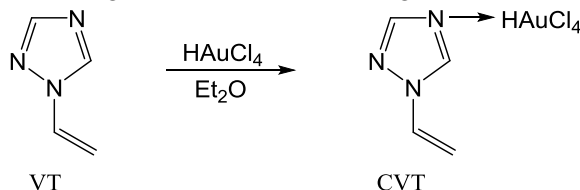
The complex (CVT) of 1-vinyl-1,2,4-triazole (VT) with HAuCl_4 was synthesized, its physicochemical characteristics were determined. It has been shown that the formation of the complex occurs through the triazole nitrogen atom N4. Using the results of thermogravimetric and elemental analyses, it has been found that regardless of the molar ratio of the starting components (VT: HAuCl_4 - 1:1; 1:2; 2:1), a complex of 1:1 composition is formed. The effect of compounds VT, HAuCl_4 , and CVT on postganglionic sympathetic nerve fibers and adrenergic receptors was studied. It has been found that the tested compounds have a weak sympatholytic and adrenomimetic effect.

Figs. 3, table 1, references 13.

The coordination properties of azoles, the complexes of which are widely used primarily as biologically active preparations for various purposes [1–7], arouse great interest of researchers both in theoretical and applied aspects.

Analysis of the literature data [8–13] devoted to this problem shows that the coordination compounds of triazoles with noble metals, in contrast to transition metal complexes [8, 11, 14], have been little studied. To fill this gap, in the present work, the interaction of 1-vinyl-1,2,4-triazole (VT) with HAuCl_4 was studied for the first time.

At room temperature, mixing of the ether solution of HAuCl_4 with the ether solution of VT instantly leads to complexation of the donor-acceptor type with the participation of nitrogen N4, which has the highest electron density [15].



The manifestation of bidentality in VT with the participation of the second nitrogen atom, as shown in [16], is unlikely.

It has been established that regardless of the molar ratio of the starting components (Established VT: HAuCl_4 - 1:1; 1:2; 2:1), a complex (CVT) of 1:1 composition is formed.

A spectral study of the obtained complex (CVT) showed that the absorption of the unsaturated substituent ($\text{C}=\text{C}$) of the initial ligand (VT) in the 1653.4 cm^{-1} region was preserved and did not undergo significant shifts in the complex (1654.3 cm^{-1}). According to published data [17], this indicates that the vinyl fragment of VT does not participate in coordination with HAuCl_4 .

Analysis of the IR spectrum of the obtained complex and comparison with the spectrum of the free ligand (VT) shows that there are noticeable short-wavelength shifts (10.2 cm^{-1}) of the absorption band related to valence oscillations of the triazole ring, which are observed in the ligand (VT) at $1509,6\text{ cm}^{-1}$, respectively. High-frequency shifts of the oscillation band of the hetero ring indicate the formation of a complex through the N4 atom [17].

In the ^1H NMR spectrum of the complex (CVT), a weak-field shift of the 3-H and 5-H ring protons is observed ($\Delta\delta$ 0.28 and 0.24). Weak-field displacements for protons of H_A , H_B , and H_C of the vinyl substituent as compared with the ligand (VT) are not observed. The results also confirm the participation of the triazole cycle in coordination [7, 17].

To assess the thermal stability and the possibility of decomposition of the complex (CVT), a thermal study was carried out under dynamic heating conditions using the [TG / MS NETZSCH STA 449 (TG) QSM403 (MS)] device (Fig. 1).

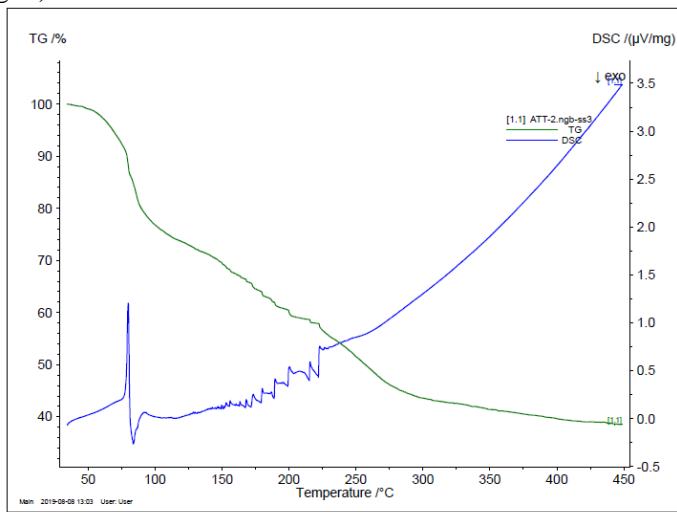


Fig. 1. Curves of thermogravimetric analysis of the complex (CVT).

It is noteworthy that the mass loss in the indicated temperature range does not affect the linear nature of the differential scanning calorimetry curve - DSC.

Intensive thermal decomposition (thermal destruction) begins at about 80°C and has a pronounced exothermic character, and its maximum value is fixed at a temperature of 90°C (DSC curve). This decay is completed at 160°C and according to the data of chromatography-mass spectroscopy analysis (Fig. 2) corresponds to the ligand splitting according to the Scheme:



The mass loss in the temperature range of 80-160°C is ~25%, which according to the calculated data (21.84) practically corresponds to the splitting of one ligand molecule.

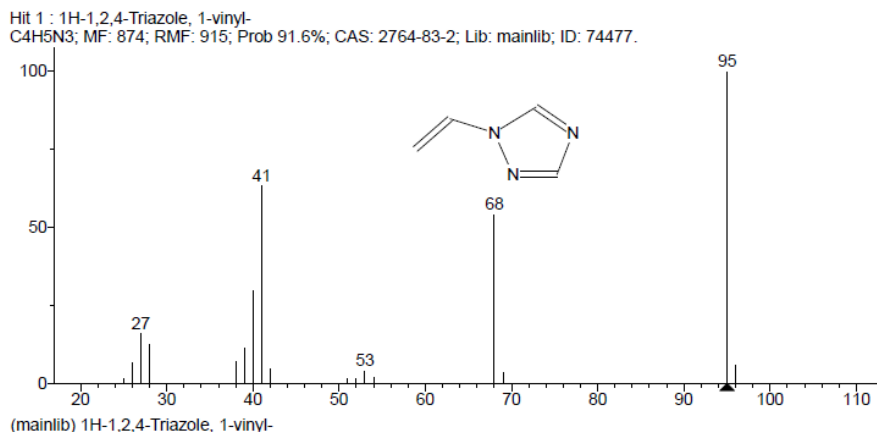


Fig. 2. Chromatography-mass spectral analysis of 1-vinyl-1,2,4-triazole released from the complex (CVT).

A further increase in temperature on the TG curve manifests as a slow mass loss and, at a temperature of ~250°C, according to the data of chromatography-mass spectral analysis (Fig. 3), the decomposition of HAuCl_4 begins according to the Scheme:

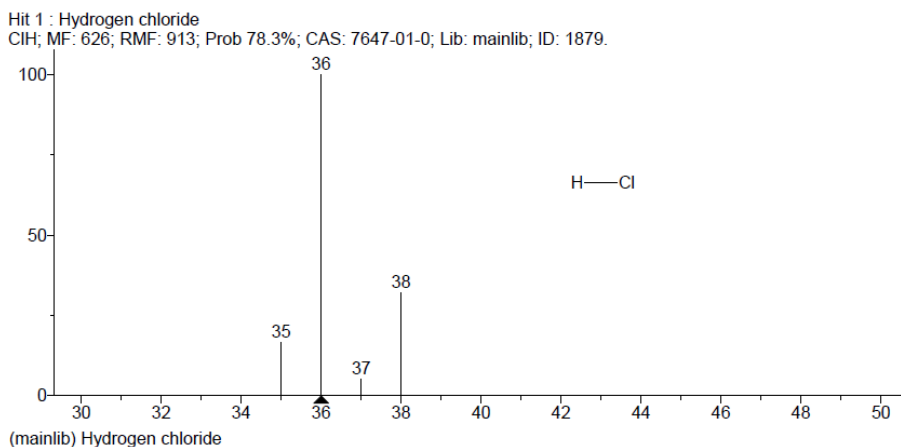
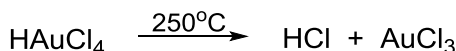


Fig. 3. Chromatography-mass spectral analysis of the released HCl from HAuCl_4 .

According to the TG curves after 325°C, the residue is approximately 44.67%, which practically corresponds to the percentage (45.28) of the gold content in the complex.

Thus, the results of thermogravimetric and elemental analyses confirm that 1-vinyl-1,2,4-triazole (VT) forms a complex (CBT) with HAuCl_4 in an equimolar ratio.

The effect of VT, HAuCl_4 , and CVT compounds synthesized at the Scientific Technological Center of Organic and Pharmaceutical Chemistry of the National Academy of Sciences of the Republic of Armenia on postganglionic sympathetic nerve fibers and adrenoreceptors was studied.

The studies were conducted in the Laboratory of Pharmacology and Histopathology in accordance with the rules for keeping and handling animals, as set out in the European Community directive (86/609/EC).

In experiments on an isolated rat vas deferens, the effect of three chemical compounds (VT, HAuCl_4 and CVT), on postganglionic sympathetic nerve fibers and adrenoreceptors, was studied.

The effect of compounds on organ contractions caused by transmural electrical stimulation (0.1 msec, 80 imp/sec, supramaximal voltage for 3 sec every 1.5 min) and norepinephrine at a concentration of $1 \cdot 10^{-6}$ g/ml was studied. Compounds were tested at a final concentration of 0.05 $\mu\text{mol/ml}$.

The effect of each compound was tested in experiments on two ducts and the arithmetic mean was determined.

Studies have shown that the tested compounds have a weak sympatholytic and adrenomimetic effect (Table).

Table

**The sympatholytic and adrenomimetic effect
of HAuCl_4 , CT and CVT compounds**

Number of experiments	Compound	Sympatholytic action: reduction of the amplitude of duct contractions caused by transmural electrical stimulation in % of control		Adrenomimetic effect: a decrease in the amplitude of duct contractions caused by $1 \cdot 10^{-6}$ g/ml in % of control	
		10 min	60 min	10 min	60 min
2	HAuCl_4	27,5	7,5	7,5	15
2	VT	15	31	17*	17
2	CVT	30	29	15	52

* increase in the amplitude of contractions (adrenomimetic effect).

Experimental Section

The IR spectra were recorded on a spectrometer “Termo Nicoletion Nexus” in vaseline oil. The ^1H and ^{13}C NMR spectra were measured on a Varian “Mercury-300VX” spectrometer in $\text{DMSO}-d_6\text{-CCl}_4$ (1:3) using TMS as internal standard. Elemental analysis was performed on a Eurovector “EA 3000” instrument. Thermogravimetric and chromatography-mass spectral analyses were performed on a “TG/MS NETZSCH STA 449 (TG) QSM403 (MS), Germany” derivatograph, heating rate 5 deg/min, temperature range 20-500°C. As starting materials, 1,2,4-triazole and HAuCl_4 manufactured by “Sigma-Aldrich” were used.

1-Vinyl-1,2,4-triazole (VT) was obtained according to the method [18]. IR spectrum, ν , cm^{-1} : 1509.6 (ring), 1653.4 ($\text{C}=\text{C}$). ^1H NMR spectrum, δ , ppm, Hz: 4.99 dd (1H, $=\text{CH}_2$, $J=8.8$ and 0.8), 5.76 dd (1H, $=\text{CH}_2$, $J=15.5$ and 0.8), 7.28 ddd (1H, $=\text{CH}$, $J=15.5$, 8.8 and 0.7), 7.84 br.s (1H, 5-H), 8.59 s (1H, 3-H). ^{13}C NMR spectrum, δ , ppm: 102.4 (CH_2), 129.3 ($\text{CH}-\text{CH}_2$), 142.7 (CH), 151.2 (CH), bp 58°C/10 mm Hg, n_D^{20} 1.5120.

Synthesis of the complex (CVT). 0.5 g (1.5 mmol) of HAuCl_4 was dissolved in 50 ml of dry ether, then 0.15 g (1.6 mmol) of VT was added. The resulting yellow crystals were filtered and dried, mp 85-125°C. The yield was 0.32 g (47%). IR spectrum, ν , cm^{-1} : 1519.8 (ring), 1654.3 ($\text{C}=\text{C}$). ^1H NMR spectrum, δ , ppm, Hz: 5.09 dd (1H, $=\text{CH}_2$, $J=8.8$ and 0.8), 5.74 dd (1H, $=\text{CH}_2$, $J=15.5$ and 0.8), 7.37 dd (1H, $=\text{CH}$, $J=15.5$ and 8.8), 8.12 s (1H, 5-H), 8.83 s (1H, 3-H). Found, %: C 11.25; H 1.18; N 9.85. $\text{C}_4\text{H}_6\text{N}_3\text{Cl}_4\text{Au}$. Calculated, %: C 11.03; H 1.37; N 9.65.

This work was supported by the State Committee of Science of the Ministry of Education and Science in the frames of research project №18T-2E151.

ՈՍԿՈՒ ՔԼՈՐԻԴՈՎ 1-ՎԻՆԻԼ-1,2,4-ՏՐԻԱԶՈԼԻ ԿՈՄՊԼԵԿՍԻ ՍՏԱՅՈՒՄԸ և ՆՐԱ ՋԵՐՄԱՅԻՆ և ԿԵՆՍԱԲԱՆԱԿԱՆ ՎԱՏԿՈՒԹՅՈՒՆՆԵՐԻ ՈՒՍՈՒՄՆԱՍԻՐՈՒԹՅՈՒՆԸ Ա. Ն. ՎԱՐԱԹՅԱՆ

Սինթեզվել է 1-վինիլ-1,2,4-տրիազոլի (ՎՏ) կոմպլեքսը HAuCl_4 -ի (ԿՎՏ) հետ, որոշվել են նրա ֆիզիկոքիմիական հատկությունները: Ցույց է տրվել, որ կոմպլեքսի առաջացումը տեղի է ունենում տրիազոլային օղակում N4 ազոտի ատոմի միջոցով: Թերմոգրավիմետրիկ և էլեմենտ անալիզների օգնությամբ պարզվել է, որ անկախ ելանյութերի մոլային հարաբերակցությունից (ՎՏ: HAuCl_4 - 1:1, 1:2, 2:1) առաջանում է 1:1 բաղադրությամբ կոմպլեքսը: Ուսումնասիրվել է ՎՏ, HAuCl_4 և ԿՎՏ միացությունների ազդեցությունը հետգանգլիոնային սիմպաթիկ նյարդային մանրաթելերի և ադրենոեցեպտորների վրա: Հայտնաբերվել է, որ փորձարկված միացություններն ունեն թույլ սիմպաթիկ և ադրենոմիմետիկ ազդեցություն:

ПОЛУЧЕНИЕ КОМПЛЕКСА 1-ВИНИЛ-1,2,4-ТРИАЗОЛА С ХЛОРИДОМ ЗОЛОТА И ИЗУЧЕНИЕ ЕГО ТЕРМИЧЕСКИХ И БИОЛОГИЧЕСКИХ СВОЙСТВ

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Синтезирован комплекс (КВТ) 1-винил-1,2,4-триазола (ВТ) с HAuCl_4 , определены его физико-химические характеристики. Показано, что образование комплекса происходит через триазольный атом азота N4. При помощи результатов термогравиметрического и элементного анализов установлено, что независимо от мольного соотношения исходных компонентов (ВТ: HAuCl_4 – 1:1, 1:2, 2:1) образуется комплекс состава 1:1. Исследовано действие соединений ВТ, HAuCl_4 и КВТ на постганглионарные симпатические нервные волокна и адренорецепторы. Установлено, что испытуемые соединения обладают слабым симпатолитическим и адrenomиметическим действием.

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