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[2+2]-PHOTOCYCLOADDITION OF (*E*)-2-(3,4-DIMETHOXYSTYRYL)PYRIMIDINE AND ITS SALTS IN CRYSTALS

V. A. Karnoukhova[1]*, A. E. Saifutairova[1,2], O. A. Fedorova[1,2], and A. V. Vologzhanina[1]

Crystal structures of two salts of (*E*)-2-(3,4-dimethoxystyryl)pyrimidinium ($HDmsPy^+$) are studied: $(HDmsPy)Cl\cdot H_2O$ and $(HDmsPy)Cl\cdot 0.5C_6H_4(OH)_2$. (*E*)-2-(3,4-dimethoxystyryl)pyrimidinium chloride is photoinert. Upon UV irradiation, the (*E*)-2-(3,4-dimethoxystyryl)pyrimidinium cocrystal with catechol as well as pure (*E*)-2-(3,4-dimethoxystyryl)pyrimidine (DmsPy) are involved in the [2+2]-photocycloaddition reaction with crystal destruction. Structures of solid phase reaction products and a similar photocycloaddition reaction in the solution are analyzed by ^1H NMR spectroscopy.

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Keywords: diazines, styryl derivatives, dimerization, [2+2]-photocycloaddition, crystal structure.

INTRODUCTION

The [2+2]-photocycloaddition reaction of non-symmetric alkenes in solutions is known to lead, as a rule, to the formation of a mixture of eleven possible stereoisomers of 1,2,3,4-tetrasubstituted cyclobutane (Fig. 1). In crystals, the reaction takes place not always, and if it does, then towards only one (rarer two) possible reaction products, depending on the arrangement of molecules. Photocycloaddition is known to be possible in a solid if the distance *d* between C=C bonds does not exceed 4.2 Å [1, 2]; the coplanar and parallel arrangements of these fragments are desirable, too [3].

We have recently synthesized and structurally characterized three isomeric derivatives of styryldiazine [4], and only in one of them – (*E*)-2-(3,4-dimethoxystyryl)pyrimidine (DmsPy, **1**, Scheme 1) – the molecular arrangement corresponds to the above criteria of the possible occurrence of the photoreaction with the expected reaction product, namely 2,2′-((1R,2R,3S,4S)-2,4-bis(3,4-dimethoxyphenyl)cyclobutane-1,3-diyl)bipyrimidine (**X**, Fig. 1). Therefore, the search for other solid forms (salts, cocrystals, polymorphs) $HDmsPy^+$ and/or DmsPy can become promising for preparing other isomers of 1,2,3,4-tetrasubstituted cyclobutane obtained by dimerization of styrylpyrimidine **1**.

In this work, we report data on the synthesis and crystal structure of two salts of 2-(3,4-dimethoxystyryl)pyrimidine: $(HDmsPy)Cl\cdot H_2O$ (**2**) and $(HDmsPy)Cl\cdot 0.5C_6H_4(OH)_2$ (**3**). We compared the products of the solid phase photoreaction in salts and initial crystalline compound DmsPy (**1**) and in the solution.

[1]Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, Moscow, Russia; *v_a_k_h_h@mail.ru. [2]Mendeleev Russian Chemical Technological University, Moscow, Russia. Original article submitted August 27, 2021; revised October 25, 2021; accepted October 26, 2021.

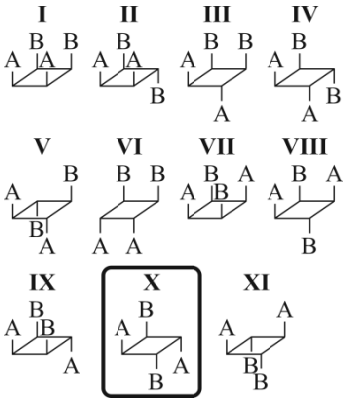
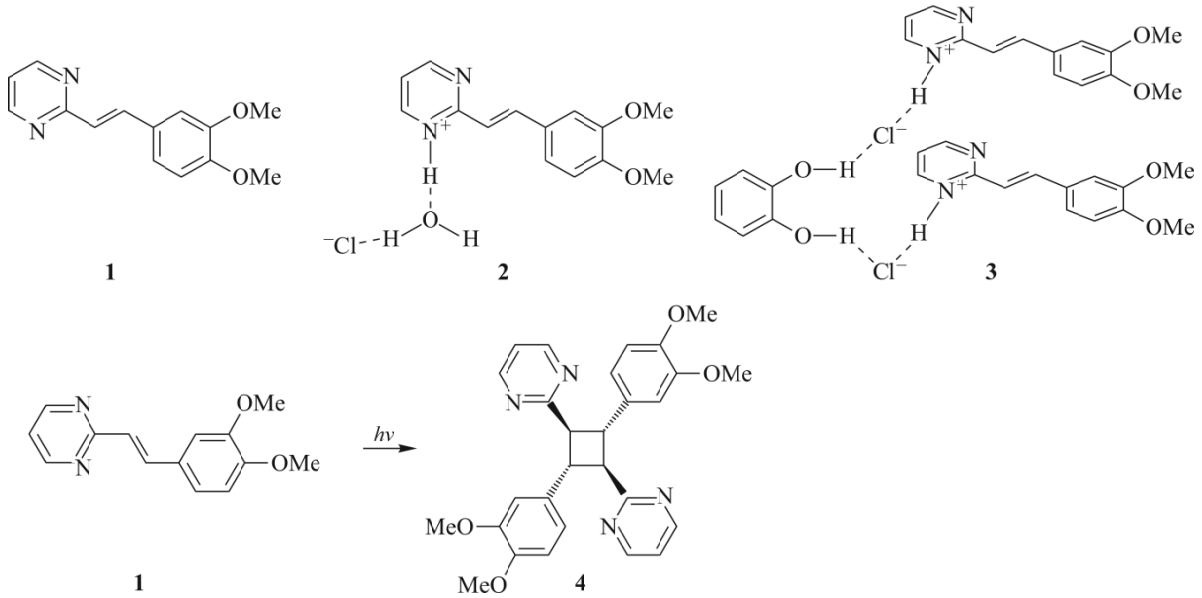


Fig. 1. Schematic structure of possible [2+2]-photocycloaddition reaction products of styrylpyrimidine **1** (A is the heterocyclic fragment, B is the 3,4-dimethoxyphenyl substituent).



Scheme 1. Objects **1**-**4** and the [2+2]-photocycloaddition process studied in this work.

EXPERIMENTAL

Synthesis of the compounds. (*E*)-2-(3,4-dimethoxystyryl)pyrimidine compound (**1**) was obtained by the previously described procedure [5].

(*E*)-2-(3,4-Dimethoxystyryl)pyrimidin-1-ium chloride monohydrate (**2**) was synthesized by dissolving styryl derivative **1** in acetonitrile with the addition of a 10% HCl solution followed by slow evaporation of the obtained mixture until the formation of crystals. M.p. 193-195 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): 3.98 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 6.93-6.96 (d, 1H, H5, ^{3}J = 8.3), 7.27 (s, 1H, H2), 7.34-7.37 (d, 1H, H6, ^{3}J = 8.4), 7.51 (t, 1H, H11), 7.59-7.64 (d, 1H, Ha, ^{3}J = 15.7), 8.42-8.48 (d, 1H, Hb, ^{3}J = 15.5), 8.94-8.96 (d, 2H, H10, H12, ^{3}J = 4.1); ^{13}C NMR ($CDCl_3$, 101 MHz, 25 °C) δ: 56.13 (2C,OMe), 110.32 (C2), 111.11 (C5), 115.21 (Ca), 117.94 (C6), 124.94 (C11), 127.00 (C1), 147.88 (Cb), 149.51

(2C, C10, C12), 152.78 (2C, C3, C4), 160.11 (C8). Found (%): C 69.12, H 6.21, N 11.51. $C_{14}H_{15}N_2O_2$. Calculated (%): C 69.41, H 6.82, N 11.56. Mass spectrum of the solution (ESI-MS) in acetonitrile, *m*/*z*: 243.29 $[\mathbf{2}]^+$.

A cocrystal of the salt with catechol of the composition $(HDmsPy)Cl{\cdot}0.5C_6H_4(OH)_2$ (**3**) was synthesized by dissolving 0.01 g of styryl derivative **1** and 0.03 g of catechol in a 0.1 M HCl solution.

The crystal samples were irradiated by a Shimadzu L9588-4 xenon lamp (unfiltered light, 40% intensity of the maximum passport power) for 8 h. The powder formed during irradiation of single crystals of **1** was purified by flash chromatography on SiO_2; the eluent was a hexane:ethylacetate gradient mixture, $1{:}0 \rightarrow 0{:}1$. 2,2′-(2,4-Bis(3,4-dimethoxyphenyl)cyclobutane-1,3-diyl)bipyrimidine compound (**4**) was obtained. Yield: 4.0 mg (90%); m.p. 100-102°C. ^{1}H NMR ($CDCl_3$, 600 MHz, 25 °C): 3.76 (s, 6H, OCH_3), 3.79 (s, 6H, OCH_3), 4.90 (m, 2H, Ha, Ha′), 5.04 (m, 2H, Hb, Hb′), 6.65-6.67 (d, 2H, H5, H5′, ^3J = 8.2), 6.71 (s, 2H, H2, H2′), 6.82-6.84 (d, 2H, H6, H6′, ^3J = 8.3), 7.01 (t, 2H, H11, H11′), 8.58-8.59 (d, 4H, H10, H10′, H12, H12′, ^3J = 2.6); ^{13}C NMR ($CDCl_3$, 151 MHz, 25 °C) δ: 44.7 (2C, Cb, Cc), 46.5 (2C, Ca, Cd), 55.7 (4C, OCH3), 110.4 (2C, C5, C5′), 111.3 (2C, C2, C2′), 118.4 (2C, C11, C11′), 119.9 (2C, C6, C6′), 132.5 (2C, C1, C1′), 147.2 (2C, C4, C4′), 148.2 (2C, C3, C3′), 156.6 (4C, C10, C10′, C12, C12′), 169.5 (2C, C8, C8′). Found (%): C 69.41, H 5.82, N 11.56. $C_{28}H_{28}N_4O_4$. Calculated (%): C 69.38, H 5.78, N 11.83. Mass spectrum of the solution (ESI-MS) in acetonitrile, *m*/*z*: 485.40 $[\mathbf{4}+\mathbf{H}]^+$.

Single crystal X-ray diffraction (XRD) analysis. XRD studies of compounds **2** and **3** were carried out on an automated Bruker D8 Quest diffractometer (graphite monochromator, $\lambda(MoK_\alpha) = 0.71073$ Å, φ- and ω-scanning). Intensities were integrated using the SAINT program [6]. Absorption correction and systematic error correction were applied semi-empirically using the SADABS program [7] with the intensities of equivalent reflections. The structure of **2** was a twin and for it the intensities of overlapping reflections were corrected by algorithms implemented in the PLATON software [8]. The calculated BASF parameter was 0.21. The structures were solved by the dual space method implemented in the SHELXT software [9] and refined by the full-matrix least squares method against F^2_{hkl} in the anisotropic approximation for all non-hydrogen atoms (except a minor component of the disorder in the structure of **2**, which was refined in the isotropic approximation with a common thermal parameter). Hydrogen atoms bonded to heteroatoms were localized from Fourier difference maps and refined in the isotropic approximation (except the minor component of the disorder of the **2** structure). The other hydrogen atoms were placed in geometrically calculated positions and refined in the riding model with isotropic thermal parameters U_{iso}(H) exceeding 1.5 times the equivalent isotropic thermal parameters U_{eq}(X) of carbon atoms of methyl groups and 1.2 times of the other atoms. In the structure of **2**, the $HDmsPy^+$ cation was partially disordered over two positions with relative occupancies of 0.88:0.12; the minor component was refined using the SAME instruction. To refine and analyze the geometric parameters we employed the SHELXL software [10]. The main crystallographic data and refinement parameters are listed in Table 1.

The structures have been deposited with the Cambridge Crystallography Data Center (CCDC) under numbers CCDC 2105326-2105327 and can be received at www.ccdc.cam.ac.uk/structures.

RESULTS AND DISCUSSION

In this work, the objects of the study were crystals of stilbene derivatives in both free form (**1**) and products of its interaction with hydrochloric acid (**2**) and catechol in the presence of hydrochloric acid (**3**) (Scheme 1). In the previously studied [4] crystal structure of **1**, (*E*)-2-(3,4-dimethoxystyryl)pyrimidine forms centrosymmetric dimers with parallel and coplanar arrangements of double bonds (Fig. 2*a*). The distance between carbon atoms of olefin moieties (3.896(2) Å) indicates that the solid-phase photocycloaddition reaction can occur. Here the substituents are located antiparallel, and hence, the expected reaction product, as well as in the solution, must be bipyrimidine **4** (Scheme 1).

Unfortunately, during UV irradiation single crystals of **1** (0.35×0.20×0.15 mm) completely decompose to powder in 20 min. After irradiation of solid **1** for 8 h, the reaction completeness and the structure of the reaction product were controlled

TABLE 1. Main Crystallographic Parameters and Refinement Parameters for **1**-**3** Structures

Structure	**1**, [4]	**2**	**3**
CCDC	-	2105326	2105327
Chemical formula	$C_{14}H_{14}N_2O_2$	$C_{14}H_{17}ClN_2O_3$	$C_{17}H_{18}ClN_2O_3$
Molecular weight	242.27	296.74	333.78
T, K	120	296	296
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_1/n$	$P2_1/c$	$C2/c$
Z / Z'	4 / 1	4 / 1	8 / 1
a, b, c, Å	12.4701(9), 5.7175(4), 16.5799(12)	7.1580(15), 16.469(4), 12.436(3)	29.576(2), 7.3168(5), 17.9209(14)
β, deg	93.054(2)	103.061(5)	124.223(2)
V, Å^3	1180.43(15)	1428.1(6)	3206.6(4)
d_{cal}, g/cm^3	-	1.380	1.383
μ, cm^{-1}	-	2.76	2.55
$2\theta_{max}$, deg	-	52	52
Number of reflections measured / independent / with $I > 2\sigma(I)$ (R_{int})	-	12201 / 2778 / 1789 (0.0650)	17092 / 3133 / 2480 (0.0748)
Number of refined parameters	-	240	218
R_1, wR_2	-	0.0576, 0.1530	0.0606, 0.1951
$GOOF$	-	1.036	1.043
Residual electron density, (ρ_{max} / ρ_{min}), e/Å^3	-	0.206 / –0.224	0.577 / –0.548

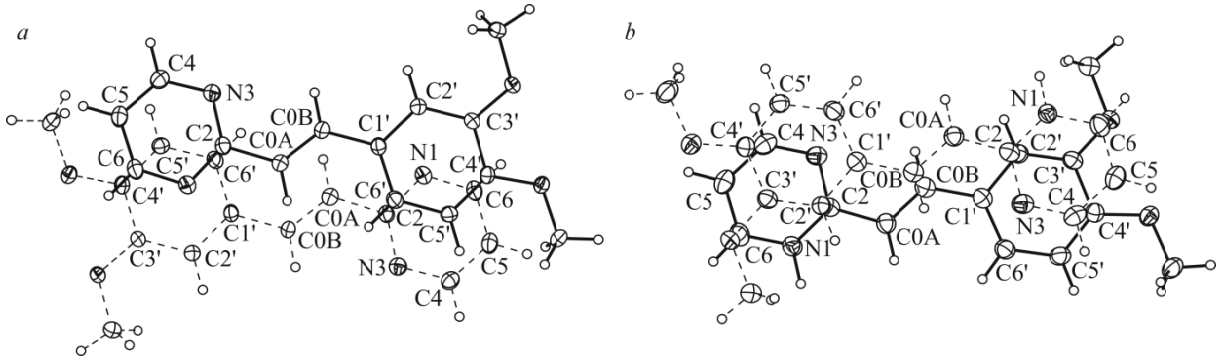


Fig. 2. Dimers DsmPy (p = 50%) (*a*) and HDmsPy$^+$ (p = 30%) (*b*) formed by stacking interactions in the structures of **1** and **3**; projection on the mean square plane of the lower molecule.

by ^{1}H NMR spectroscopy (Fig. 3). Photocycloaddition product **4** was also isolated using flash chromatography and its structure was determined by a set of physicochemical methods (see EXPERIMENTAL). As expected, the single reaction product was compound **4**. Its yield was 90% and did not change during further irradiation of the compound.

Thus, both in solution and solid state, the structure of the [2+2]-photocycloaddition reaction product of styrylpyrimidine **1** is governed by the mutual antiparallel arrangement of molecules in the head-to-tail fashion, which is due to the dipole interaction of the donor (phenyl) part of one molecule and the acceptor (pyrimidine) of the second molecule. In this case, the synthesis of new solid forms of styrylpyrimidine **1** can be one of the ways to obtain other isomers of (bis(3,4-dimethoxyphenyl)-cyclobutanediyl)bipyrimidin, especially (3,4-bis(3,4-dimethoxyphenyl)cyclobutane-1,2-diyl)bipyrimidines (**VI**) and (**VII**), for the preparation of which the coplanar arrangement of molecules in the head-to-head fashion is needed.

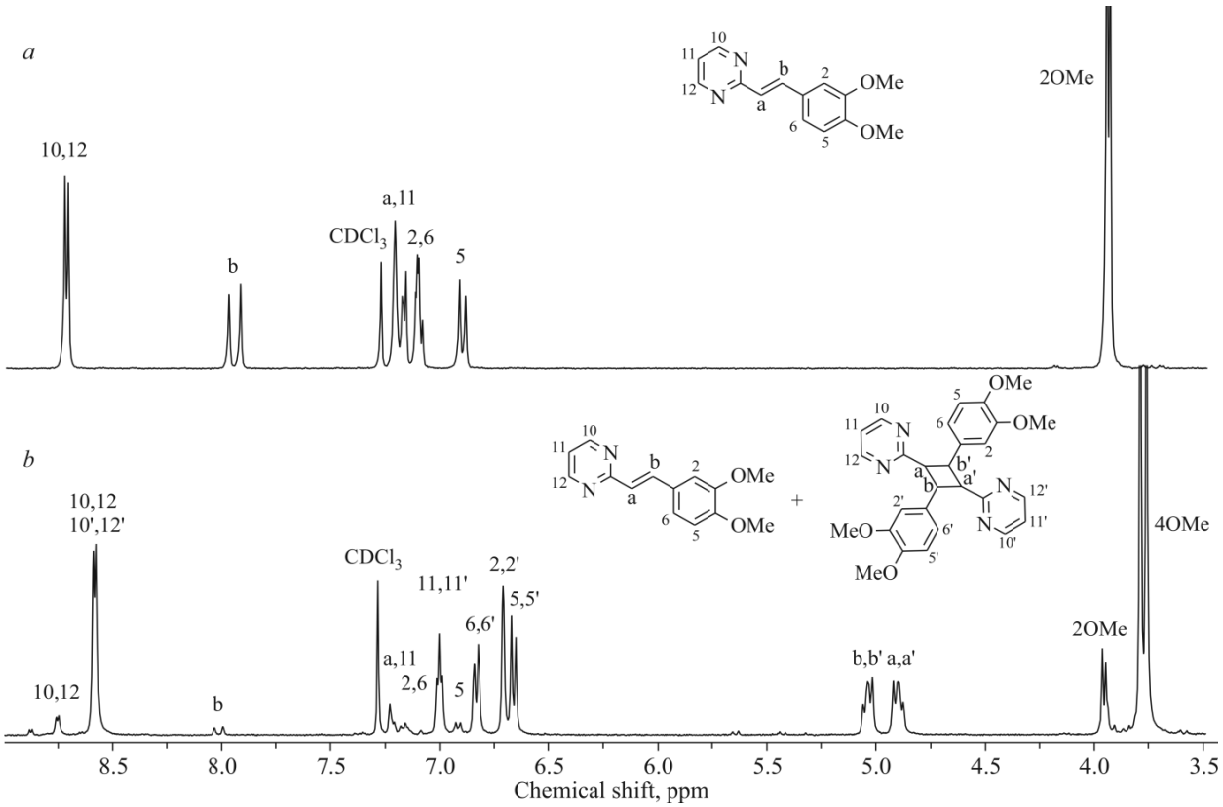


Fig. 3. ^{1}H NMR spectra ($CDCl_3$, 400 MHz): compound **1** (*a*); mixture of compounds **1** and **4** after xenon lamp irradiation of the crystals of **1** for 8 h (*b*).

The most popular way to organize the head-to-head molecular packing via strong intermolecular interactions is to use hydrogen bonds [11, 12]. The molecular structure of pure compound **1** does not imply the formation of hydrogen bonds, however, as well as bipyrimidine, it can cocrystallize with molecules – donors of hydrogen bonds (e.g., bipyridines crystallize with catechol with the formation of parallel dimers [13]) or act as a donor of hydrogen bonds in the interaction with acids, such as $HDmsPy^+$ or H_2DmsPy^{2+} cations.

The obtained molecular structures of **2** and **3** are presented in Fig. 4. Unfortunately, we failed to obtain crystals from the solution of **1** in 0.1 M HNO_3 within six months because of the extremely high solubility of $(HDmsPy)(NO_3)$ salt.

Both structures as well as compound **1** crystallize in centrosymmetric space groups ($P2_1/c$ and $C2/c$ respectively). The $HDmsPy^+$ cation, the chloride anion, and the water molecule are in general positions in the structure of **2**, and the cation is disordered over two positions in the 0.88:0.12 ratio. The asymmetric unit of the **3** structure contains only one cation, one chloride anion, and half of the catechol molecule. The main geometric parameters (bond lengths, bond and torsion angles) are close to the expected values for similar fragments of the known compounds, which is confirmed by the analysis with the Mogul program [14]. The spatial structure of the cations is, in general, similar to that of the initial neutral molecule: average deviations of cation non-hydrogen atoms in the **2** and **3** structures from the respective atoms in the **1** structure are 0.34 Å and 0.22 Å. Here the cations are more planar than the neutral molecule, and the main distinctions correspond to the rotation angle of the dimethoxyphenyl ring relative to the olefin moiety. In the molecule of **1**, it is 17.5(2)°, and in the cations it does not exceed 7.4(7)°, while the rotation of the pyrimidine ring relative to the olefin moiety in **1-3** varies in the range of 1.4(6)-4.3(2)°.

Associates formed by hydrogen bonds in the **2** and **3** structures are depicted in Fig. 5. In both cases, the cation is a donor of one hydrogen bond, the chloride anion is an acceptor of two hydrogen bonds, and the third molecule (water or catechol) is a bridge linking two cations and two anions into discrete ensembles via hydrogen bonds (three and two respectively). In salt **2**, the N…O_{aq} distance and the NHO angle for the major/minor components of the disorder are

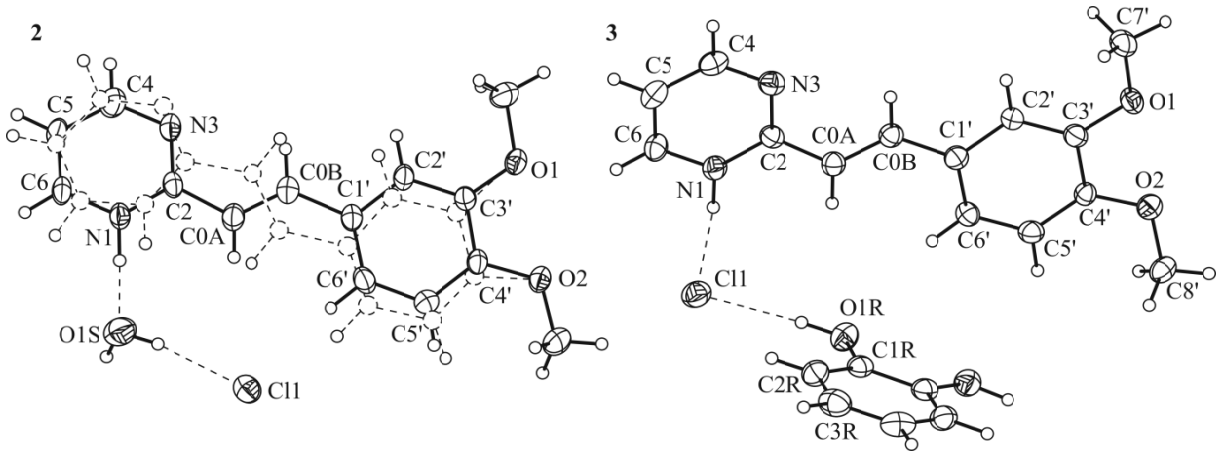


Fig. 4. General view of the crystal structures of **2** and **3**; non-hydrogen atoms are shown by thermal ellipsoids (p = 30%), atoms of the asymmetric unit are designated. The minor component of the disorder in the structure of **2** and hydrogen bonds are shown by dashed lines.

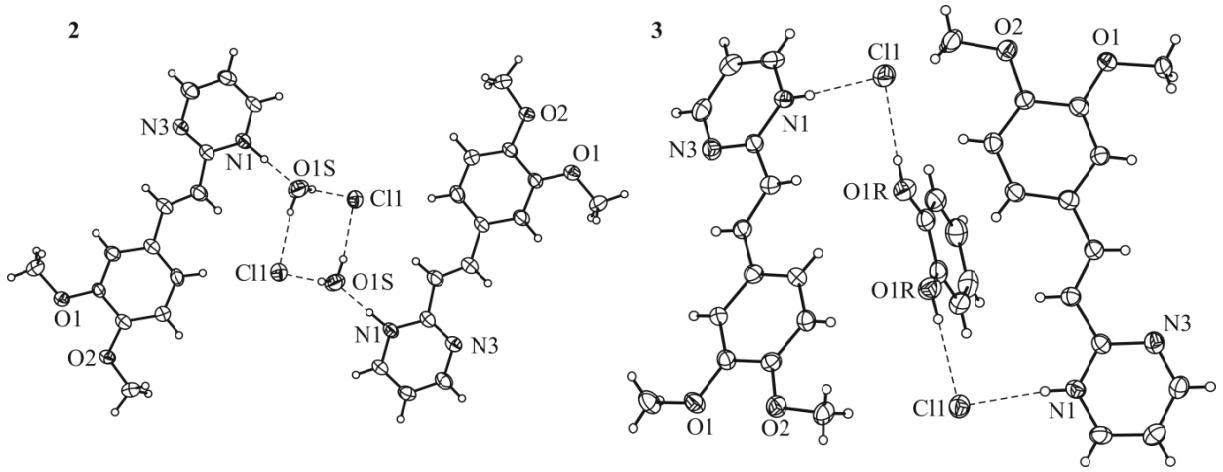


Fig. 5. Hydrogen-bonded associates in the structures of **2** (minor component of the disorder is omitted) and **3**. Hydrogen bonds are shown by dashed lines.

2.602(5)/2.91(2) Å and 174(4)/160.8° respectively, and the O_{aq}…Cl distances are 3.071(4) Å and 3.076(4) Å; the OHCl angles are 166(5)° and 171(4)°. In the crystals of **3**, the N…Cl and O…Cl distances are 3.016(2) Å and 3.097(2) Å and the NHCl and OHCl angles are 172(3)° and 177(3)°.

Unfortunately, we failed to obtain the parallel head-to-head packing of cations via hydrogen bonds, however, the planar structure of molecules allows the parallel packing due to stacking interactions. In the structure of **2**, the molecular packing does not imply the possibility of solid phase reactions because the nearest environment of olefin moieties contains only methoxy groups and pyrimidine rings. In the structure of **3**, it is possible to distinguish centrosymmetric dimers with a distance between carbon atoms of the olefin moieties of 3.648(3) Å (Fig. 2*b*). Compound **3** exists as a salt, and this is manifested in a shift of proton signals from the heterocyclic fragment to the strong field in the ^{1}H NMR spectra (Fig. 6*a*). During UV irradiation the crystals of **3** (0.53×0.21×0.05 mm) completely decompose, as well as in the case of **1**. The data of ^{1}H NMR spectroscopy and high efficiency liquid chromatography (HELC) indicate that only one photoprocess proceeds efficiently in the crystal of styrylpyrimidine **3** - photodimerization with the formation of **4** (Fig. 6). The degree of conversion for compound **4** was 12%. By means of HELC we managed to prove that photoisomerization typical of styryl heterocycles [15, 16] does not occur (Fig. 7) because of the inclusion of catechol molecules between pairs of styryl heterocycles. From

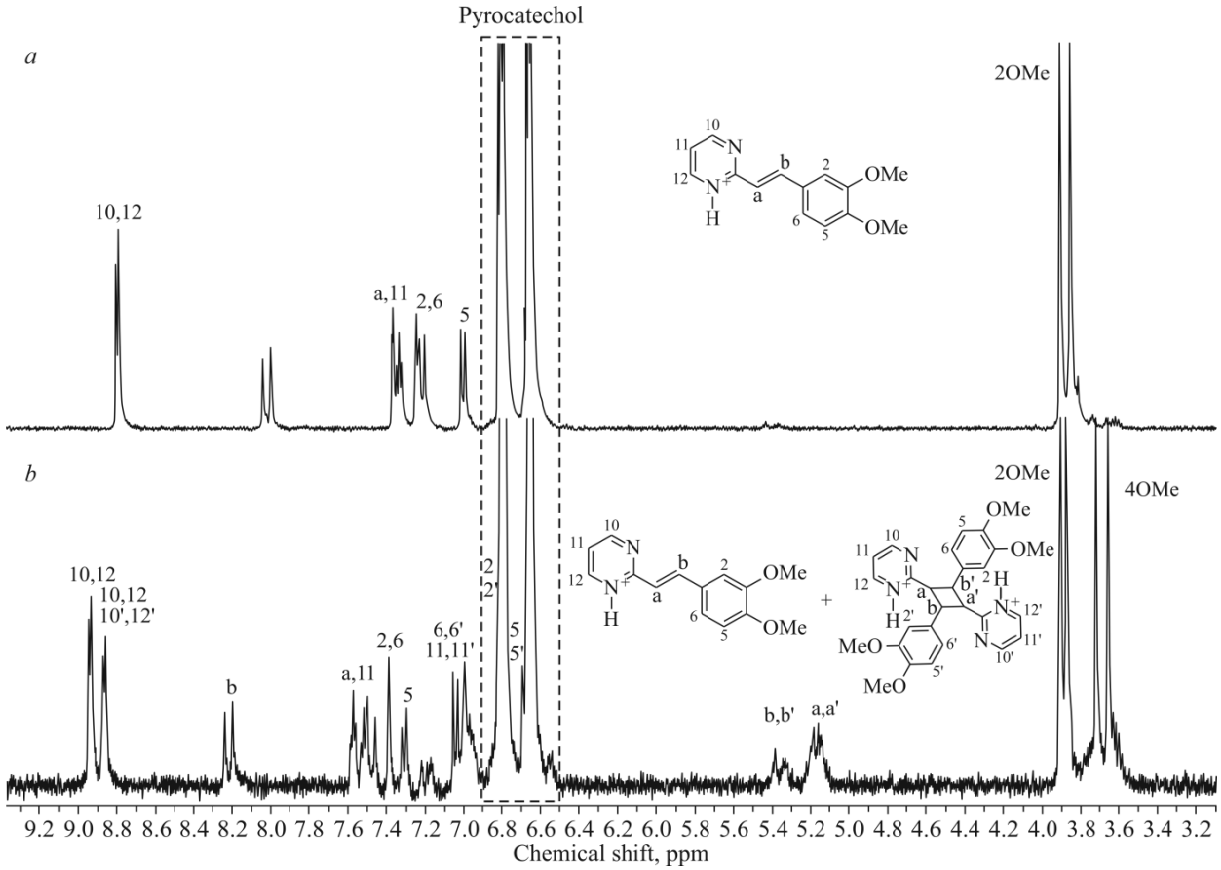


Fig. 6. ^{1}H NMR spectra (acetone-d_6, 400 MHz) of compound **3** before irradiation (*a*) and after irradiation with a xenon lamp for 8 h (*b*).

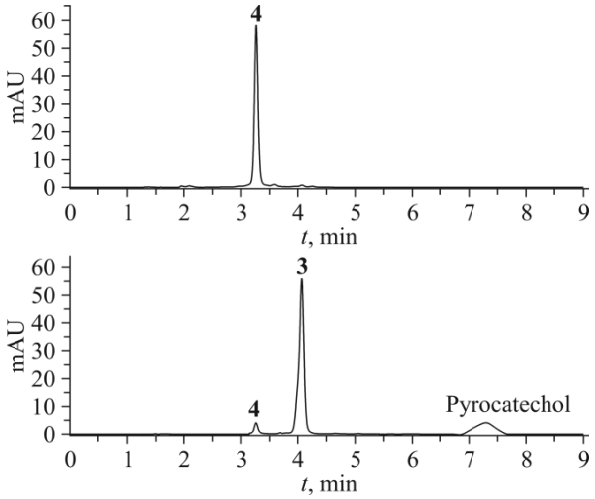


Fig. 7. HELC chromatogram of cyclobutane **4** obtained by flash chromatography after xenon lamp irradiation of the crystals of **1** for 8 h (*a*); HELC chromatogram of the solution of **3** after xenon lamp irradiation of the crystals of **3** for 8 h, which shows the presence of compound **3**, catechol, and cyclobutane **4** (*b*) in the mixture; acetonitrile:water = 65:35.

Fig. 6*b* and the analysis of the ^{1}H NMR spectrum it is possible to conclude that in the cyclobutane derivative the heterocyclic part also remains protonated.

CONCLUSIONS

Thus, unlike previously studied styrylquinolines and styrylquinoxalines [15, 16], styrylpyrimidines undergo only [2+2]-photocyclization rather than the intramolecular isomerization reaction. The formation of head-to-tail dimers in a solid results in a regio- and stereoselective photodimerization process and the formation of one of eleven possible isomers of cyclobutane (isomer **X**, Fig. 1).

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CONFLICT OF INTERESTS

The authors declare that they have no conflicts of interests.

REFERENCES

1. M. D. Cohen and G. M. J. Schmidt. *J. Chem. Soc*., **1964**, 1996-2000. https://doi.org/10.1039/jr9640001996
2. G. M. J. Schmidt. *Pure Appl. Chem*., **1971**, *27*(4), 647-678. https://doi.org/10.1351/pac197127040647
3. K. Gnanaguru, N. Ramasubbu, K. Venkatesan, and V. Ramamurthy. *J. Org. Chem*., **1985**, *50*(13), 2337-2346. https://doi.org/10.1021/jo00213a027
4. A. E. Saifutiarova, V. A. Karnoukhova, E. N. Gulakova, O. A. Fedorova, and I. V. Fedyanin. *J. Struct. Chem*., **2021**, *62*(4), 527-536. https://doi.org/10.1134/S002247662104003X
5. T. M. Aliyeu, D. V. Berdnikova, O. A. Fedorova, E. N. Gulakova, C. Stremmel, and H. Ihmels. *J. Org. Chem*., **2016**, *81*(19), 9075-9085. https://doi.org/10.1021/acs.joc.6b01695
6. SAINT, v8.40B. Madison, Wisconsin, USA: Bruker AXS Inc., **2019**.
7. L. Krause, R. Herbst-Irmer, G. M. Sheldrick, and D. Stalke. *J. Appl. Crystallogr*., **2015**, *48*, 3-10. https://doi.org/10.1107/S1600576714022985
8. A. L. Spek. *Acta Crystallogr*., *Sect. E: Crystallogr. Commun*., **2020**, *76*, 1-11. https://doi.org/10.1107/S2056989019016244
9. G. M. Sheldrick. *Acta Crystallogr*., *Sect. A: Found. Adv*., **2015**, *71*, 3-8. https://doi.org/10.1107/S2053273314026370
10. G. M. Sheldrick. *Acta Crystallogr*., *Sect. C: Struct. Chem*., **2015**, *71*, 3-8. https://doi.org/10.1107/S2053229614024218
11. L. G. Kuz′mina, A. I. Vedernikov, S. P. Gromov, and M. V. Alfimov. *Crystallogr. Rep*., **2019**, *64*(5), 691-712. https://doi.org/10.1134/S1063774519050122
12. M. Nagarathinam, A. M. P. Peedikakkal, and J. J. Vittal. *Chem. Commun*., **2008**, 5277-5288. https://doi.org/10.1039/b809136f

13. G. S. Papaefstathiou, A. J. E. Duncan, and L. R. MacGillivray. *Chem Commun*, **2014**, *50*(100), 15960-15962. https://doi.org/10.1039/C4CC07747D
14. I. J. Bruno, J. C. Cole, M. Kessler, J. Luo, W. D. S. Motherwell, L. H. Purkis, B. R. Smith, R. Taylor, R. I. Cooper, S. E. Harris, and A. G. Orpen. *J. Chem. Inf. Comput. Sci.*, **2004**, *44*(6), 2133-2144. https://doi.org/10.1021/ci049780b
15. O. A. Fedorova, A. E. Saifutiarova, E. N. Gulakova, E. O. Guskova, T. M. Aliyeu, N. E. Shepel, and Y. V. Fedorov. *Photochem. Photobiol. Sci.*, **2019**, *18*(9), 2208-2215. https://doi.org/10.1039/C9PP00028C
16. E. N. Gulakova, D. V. Berdnikova, T. M. Aliyeu, Y. V. Fedorov, I. A. Godovikov, and O. A. Fedorova. *J. Org. Chem.*, **2014**, *79*(12), 5533-5537. https://doi.org/10.1021/jo500696n