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Structure and photochemistry of a saccharyl thiotetrazole

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Abstract

The molecular structure and photochemistry of 5-thiosaccharyl-1-methyltetrazole (TSMT) were studied by means of matrix isolation FTIR spectroscopy, X-ray crystallography and theoretical calculations.

Calculations predict two conformers of TSMT, differing in energy by more than 15 kJ mol⁻¹. The infrared spectrum of TSMT isolated in solid argon was fully assigned based on the spectrum calculated (O3LYP/6-311++G(3df,3pd)) for the most stable conformer. In the crystal, TSMT molecules were found to assume the same conformation as for the isolated molecule, with each molecule forming four hydrogen bonds with three neighboring molecules, leading to a network of TSMT oligomers.

Upon UV (λ = 265 nm) irradiation of the matrix isolated TSMT, two photodegradation pathways were observed, both arising from cleavage of the tetrazolyl ring. Pathway (a) involves cleavage of the N₁– N₂ and N₃–N₄ bonds, with extrusion of N₂, leading to photostable diazirine and thiocarbodiimide derivatives. The photostability of the photoproduced diazirine under the conditions used precludes its rearrangement to nitrile imine, as reported by Bégué *et al* (J. Am. Chem. Soc., 134 (2012) 5339) for 5phenyltetrazole. Pathway (b) involves cleavage of the C₅–N₁ and N₄–N₃ bonds, leading to a thiocyanate and methyl azide, the last undergoing subsequent fragmentation to CNH.

Introduction

Derivatives of the heterocycles tetrazole and saccharin are widely applied in coordination chemistry, as ligands ^{1,2}. Tetrazole can coordinate through four nitrogen electron-donating atoms and may therefore act as a multidentate ligand or as a bridging building block in supramolecular assemblies. It has potential to participate in seven distinct types of coordination modes with metal ions and, as such, tetrazole-based coordination compounds are used in catalysis and in the construction of metal-organic frameworks ³⁻⁶. Similarly, saccharin and the saccharinate anion (1,2-benzisothiazole-3-one 1,1-dioxide anion; deprotonated saccharin) interact with metal centers in various ways, generating relatively strong interactions in crystalline environments, mostly through hydrogen bonding. As a polyfunctional ligand, saccharin can be engaged in N, O(C=O) or O(SO₂)-metal coordination, and can also act as a bidentate amidato-like bridging agent ⁷⁻⁹. Based on the structural features and coordination capabilities of both heterocycles we envisaged investigating the potential of saccharyl-tetrazole conjugates (Figure 1) as bridging ligands.



Figure 1. General structure of the saccharyl-tetrazole conjugates.

Synthetic routes to a small library of these target compounds were devised and optimized ¹⁰, in view of exploring their application as coordination ligands for transition metals.

Understanding the relevance of different tautomeric forms and preferred conformations of chemical systems is instrumental in predicting and exploring their properties and function. As such, the structure of selected saccharyl-tetrazole conjugates was investigated in detail, both in the isolated molecule situation,

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by matrix isolation infrared spectroscopy and contemporary methods of quantum chemistry, and in the neat crystalline phase, by X-ray crystallography and infrared and Raman spectroscopies ^{11,12}. Among the conjugates investigated, nitrogen-linked saccharinate tetrazoles (Figure 1; X = NH) proved especially challenging due to the possibility of tautomerism involving the saccharyl system ^{11,12}. For these compounds, two forms are possible, the <u>imino</u>saccharin and <u>amino</u>saccharin tautomers. If, additionally, the tetrazole ring is unsubstituted (Figure 1; X = NH; R = H), as is the case for N-(1,1-dioxo-1,2-benzisothiazol-3-yl)-amine-1*H*-tetrazole ¹¹, then four tautomers become possible, two belonging to the iminosaccharin group and other two to the aminosaccharin group. We found that the amino-linked conjugates may exhibit different structure in the crystalline and gaseous phases ^{11,12}. On the contrary, for a thio-linked saccharyl tetrazole, as is the case of the title compound, the structure simplifies, due the absence of tautomerism involving the saccharyl system. In addition, the possibility of tautomerism involving the saccharyl system 1,2-benzisothiazole 1,1-dioxo 3-(5-thio-1-methyl) tetrazole (5-thiosaccharyl 1-methyltetrazole, TSMT) (**3**: Scheme 1), in the crystalline state and in solid argon.

Scheme 1. Synthetic approach to 5-thiosaccharyl-1-methyltetrazole (TSMT)



When considering applications of saccharyl-tetrazole conjugates, assessment of photostability may be a relevant aspect. In general, the bensizothiazole moiety is known to be rather photostable, compared to the tetrazole moiety. The photochemistry of monomeric saccharin isolated in solid argon was recently investigated ¹³. A search in the literature also yields some data regarding the photochemistry of some

benzisothiazoles in solution ¹⁴⁻²³, indicating that photoreactivity is determined by the structure of the saccharyl ring, the nature of substituents and reaction media. By their turn, tetrazoles are known for their rich photochemistry, both in solution and isolated in cryogenic matrices ^{24,25}. Generally, the photochemistry of tetrazole derivatives is influenced by the chemical nature and conformational flexibility of substituents and, when the molecule exhibits tautomerism, tautomer-selective photochemistry may take place ^{25,26}.

The fact that tetrazole-saccharyl conjugates combine heterocyclic moieties with dissimilar intrinsic photoreactivity is challenging, and yet another reason to explore the photoreactivity of benzisothiazolyl-tetrazole conjugates by matrix isolation FTIR spectroscopy. This method offers several advantages for studying the photochemistry of monomeric compounds (*i.e.*: molecular diffusion is inhibited leading -in principle- only to the observation of unimolecular reactions and enabling the stabilization, detection and characterization of products and, in some cases, of intermediates)²⁵.

We report here on the UV-induced photochemistry of TSMT in solid argon. As mentioned above, in this saccharyl-tetrazole conjugate the methyl substituent on the tetrazole ring quenches the possibility of tautomerism involving the tetrazole, and the thioether linkage restricts tautomerism involving the saccharyl system, thus reducing the number of structures present on the matrix and simplifying the interpretation of the photochemical reactions. Interpretation of the experimental results is assisted by quantum chemical calculations undertaken at different levels of approximation.

Results and Discussion

Geometries and energies of TSMT

TSMT has two intramolecular rotational degrees of freedom, represented by arrows in Figure 2, which may result in different conformers. These are related with the orientations of the saccharyl and tetrazolyl rings relatively to the C–S–C plane (dihedral angles A and B, respectively).

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To identify the minimum energy conformations of TSMT, a systematic investigation on the potential energy surface of the molecule was undertaken using the B3LYP/6-31++G(d,p) method. The location of the minima on the bidimensional potential energy surface (PES) map obtained by performing relaxed scans on the PES is shown in Figure 3. In building this map, dihedral angles A (N₈–C₉–S₁₆–C₁₇) and B (C₉–S₁₆–C₁₇–N₁₈) were varied in increments of 30 degrees, while all other geometric parameters were let free during the geometry optimization. According to the calculations, TSMT may exist in two different conformers (I and II, Figure 2). The full geometry optimization of the two conformers was carried at the DFT(O3LYP)/6-311++G(3df,dpd) level of theory. The O3LYP hybrid functional was selected for these calculations because it has been shown to constitute an improvement to the B3LYP one ²⁷, particularly in the prediction of geometries and infrared spectra of derivatives of saccharin ¹³.



Figure 2. Optimized structures of the theoretically predicted conformers of TSMT. The atom numbering adopted is shown. Arrows A and B relate to the two conformationally relevant degrees of freedom.

In the most stable conformer I, the tetrazole ring is considerably rotated in relation to the C–S–C plane (*i.e.*, B is equal to $\pm 115^{\circ}$ in the two symmetry-equivalent minima corresponding to this conformer; see Figure 3), while the dihedral angle A is close to 0° (*i.e.*, the plane of the saccharyl moiety is nearly aligned with the C–S–C plane, with the C=N bond eclipsing the S₁₆–C₁₇ bond). Note that the C_s symmetry

structures with the tetrazolyl and saccharyl groups co-planar (A= 0°, B= 0° and A= 0°, B= 180°) are destabilized by steric repulsions between the closely located N₁₈ and N₈ lone-electron pairs or CH₃ group and N₈ lone-pair, respectively. In conformer I, a stabilizing interaction occurs between the nitrogen atom of the saccharyl moiety and the hydrogen of the methyl group, because in the minimum energy geometry the distance between these atoms and their relative orientation fit well the requirements for an attractive interaction (weak C–H[…]N hydrogen bond like interaction). In addition, electronic delocalization involving the lone-pairs of electrons on the sulphur atom and the π systems of the rings shall also contribute to determine this conformational preference.



Figure 3. Potential energy surface map of TSMT calculated at the B3LYP/631++G(d,p) level of theory, as function of the dihedral angles $C_9S_{16}C_{17}N_{18}$ and $N_8C_9S_{16}C_{17}$. These two dihedral angles were incrementally fixed with a step of 30 degrees while the remaining parameters were let free during geometry optimization. The position of both conformers are shown in the graph by their numbers, I and II. Each of these minima belongs to the C_1 symmetry point group and has a symmetry equivalent counterpart, also presented in the graph with quotes, I' and II'. The electronic energy of form I is chosen as relative zero. See Figure 2 for structures and atom numbering.

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The energy of conformer II was predicted to be 15 kJ mol⁻¹ higher than that of conformer I. Conformer II differs from conformer I by internal rotation about the C₉-S₁₆ bond (*i.e.*, A is equal to \pm 137°). In this conformer, a weak stabilizing intramolecular interaction of the C-H^{...}N type is present, between the nitrogen atom N₁₈ of the tetrazole ring and the hydrogen atom H₁₃ of the phenyl ring (see Figure 2). The calculated barrier for isomerization of the higher energy conformer II into the most stable conformer I is 6.1 kJ mol⁻¹ (19.4 kJ mol⁻¹ in the reverse direction; for coordinates of the transition state structure, see Supporting Information, Section "Computational Data"). According to the calculated energy difference between II and I, the population of conformer II in the gas phase, at room temperature (25° C), is only 0.2%; at the temperature used to prepare the matrices of the compound in the present investigation (100 °C), it is still below 1%. One can then anticipate that only conformer I might be trapped from the gas phase into the deposited cryogenic matrices.

Crystal structure of TSMT and IR spectrum of the crystal

The structure of crystalline TSMT, determined by X-ray, is provided in Figure 4 (packing diagram) and Figure S1 (structure of the monomeric unit in the crystal). Atomic coordinates, bond lengths, valence angles, dihedral angles, and other crystallographic data were deposited at the Cambridge Crystallographic Data Center, with the reference CCDC 1025233.

In the crystal, TSMT exists in the most stable conformation predicted for the isolated molecule (compare Figures 2 and S1). Each molecule is involved in four weak hydrogen bonds with three neighbor molecules. The methyl substituent on the tetrazolyl ring establishes two intermolecular hydrogen bonds with two neighbor molecules, one with a nitrogen atom in position 4 of the tetrazole ring (N_{18}) and another with an oxygen atom O_{14} of the SO₂ group of the saccharyl system from a second molecule, as acceptors. This same molecule establishes a third intermolecular hydrogen bond through the oxygen atom O_{14} of the SO₂ group with the methyl substituent of the previous "second" neighbor, and a fourth

hydrogen bond with a third neighbor molecule, where the nitrogen atom N_{18} acts as acceptor. In addition to these four intermolecular hydrogen bonds, a weak intramolecular interaction can also be considered between the third H atom of the methyl group and the S atom.



Figure 4. Hydrogen bonding network in the crystal of TSMT. The ORTEPII plot showing the geometry of the TSMT molecule in the crystal is provided in Figure S1 and closely resembles the theoretically predicted conformer I.

The hydrogen-bonding scheme is shown in Figure 4, and the symmetry unique short contacts are $C_{22}H_{24}\cdots N_{18}{}^{a}$: 3.486(2) Å; $C_{22}H_{25}\cdots O_{14}{}^{b}$; 3.345(2) Å; $C_{22}H_{23}\cdots S_{16}$: 3.323(2) Å, where the superscripts "a" or "b" designate atoms belonging to neighboring molecules generated by the symmetry operators a: *x*,1/2-*y*,1/2+*z*; b:1-*x*,1-*y*,1-*z*. This hydrogen bond pattern leads to the formation of TSMT oligomers. The oligomeric structure is formed from dimers of TSMT. In the dimers, the two molecules of TSMT are disposed in a head-to-tail arrangement, with the tetrazole moiety of one molecule overlapping the thioimino moiety of the other, at the inner part of the dimer, while the carbocyclic aromatic rings are

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directed to the extremities. The oligomeric structure results from an intricate network of weak hydrogen bonds formed between consecutive dimers (with involvement of both molecules of the dimer) and adjacent dimers. Weak π - π interactions between tetrazole rings and thioimino moieties, as well as S-O^{$--\pi$} interactions (short contacts of 4.65 Å and 3.01 Å, respectively), may also play a role in the stabilization of the observed supramolecular structure.

A comparison between the geometrical parameters of the TSMT monomer I, calculated at the O3LYP/6-311++G(3df,3pd) level of theory, and those determined for the compound in the crystal (Table S1), reveals an excellent correlation between the two sets of data, although in the crystal the dihedral angles A and B (see Figure 2) appear slightly rotated (*i.e.*, the A dihedral is equal to -10.5° and B to -108.8°) compared to those obtained from theory for the isolated molecule (A dihedral equal to -3.3° and B to -115.3°), as a result of the intermolecular interactions.

The infrared spectrum of neat crystalline TSMT at room temperature is provided as Supporting Information (Figure S2). The calculated spectrum of conformer I is also shown in this figure, for comparison. Proposed assignments for the spectra are given in Table S2. The good general description of the experimental spectra of the crystal by the calculated spectra of the isolated monomer is an indication that the intermolecular interactions present in the solid do not perturb substantially the intramolecular potential.

Infrared spectra of matrix-isolated TSMT

As described in the experimental section, a sample of crystalline TSMT was sublimated *in vacuo* (at ~100 °C), the vapors of the compound were mixed with argon (*ca.* 1:1000 molar ratio), and the mixture was deposited onto a substrate kept at 15 K. Figure 5 shows the spectrum of TSMT isolated in an argon matrix prepared by this way.

The detailed analysis of the infrared spectrum for matrix-isolated TSMT doubtlessly shows that only conformer I is present in the matrix, as anticipated taken into account the predicted relative energies of the two conformers and their estimated populations in the gas phase equilibrium before deposition. This is particularly noticeable in the low frequency region where, according to the calculations, the spectra of the two conformers are clearly differentiable (see Figure 6).



Figure 5. Infrared spectrum of matrix isolated TSMT (Ar matrix; 15 K) and O3LYP/6-311++G(3df,3pd) calculated infrared spectrum for the most stable conformer. The calculated spectra were simulated by Lorentzian functions centered at the calculated frequency scaled by 0.992 and with FWHM (full width at half maximum) equal to 2 cm⁻¹. Please note also that the peak intensities in the calculated spectrum differ from the calculated intensity values; in the figure the calculated intensities correspond to the areas of the peaks.



Figure 6. Low-frequency region of the infrared spectrum of matrix isolated TSMT (Ar matrix; 15 K) and O3LYP/6-311++G(3df,3pd) calculated infrared spectra for the two conformers of the compound in the same spectral range. The calculated spectra were simulated by Lorentzian functions centered at the calculated frequency scaled by 0.992 and with FWHM (full width at half maximum) equal to 2 cm⁻¹. Please note also that the peak intensities in the calculated spectrum differ from the calculated intensity values; in the figure the calculated intensities correspond to the areas of the peaks.

UV-induced photochemistry of matrix-isolated TSMT

In order to investigate the photochemical reactions of TSMT, the deposited matrix was irradiated with UV light, as described in experimental section. The sample was monitored after each irradiation, by recording its infrared spectrum. The wavelengths used for irradiation have been chosen according to the UV-Vis spectrum of TSMT in ethanol, at room temperature, which shows the absorption maximum at 263 nm.

Upon irradiation at 265 nm, the bands due to TSMT decreased in intensity, indicating that the compound was being consumed and, simultaneously, new bands appeared in the spectrum, due to photoproduced species. The changes are particularly noticeable in the 2300-1700 cm⁻¹ spectral region, presented in Figure 7, where the results of irradiation at λ = 265 nm for 1 h are shown. In this figure, the calculated spectra of the proposed photoproducts (see also Scheme 2), in the same spectral range, are also shown for comparison. The observation that the changes in the intensities of the various new bands in the 2300-1700 cm⁻¹ spectral range follow different patterns with time of irradiation indicates that these bands originate in different products.

For the interpretation of the photochemical results, it must be noticed that TSMT is a molecule composed of 25 atoms, 15 of them belonging to the rigid benzisothiazole ring. Thus, 39 out of 69 vibrational modes are related with this benzisothiazole ring. This ring is unaffected by irradiation under the experimental conditions used, which results in an extensive overlap of the bands of TSMT with those of the photoproducts, complicating interpretation of the data. The strong overlap between the spectra of some of the proposed photoproducts and between these and the spectrum of TSMT can be clearly noticed in Figure S3, where the calculated infrared spectra for the relevant species are shown. As it can be seen in that figure, such superposition is particularly noticeable in the case of the most intense bands appearing in the low frequency spectral range (below 1700 cm⁻¹), where most of the bands due to the benzisothiazole moiety appear. However, the most characteristic bands of the photoproducts are observed in the 2300-

1700 cm⁻¹ spectral region, which is a clean spectroscopic window; this allowed us to doubtlessly identify these species, as described in detail below.



Figure 7. *Top*: IR spectra in spectral region 2300-1700 cm⁻¹ of TSMT after irradiation of the matrix with UV light (λ = 265 nm) for 1 h, showing peaks due to the photolysis products. The peak at 1754 cm⁻¹ is assigned to the N=C stretching vibration in diazirine **5**, the peak at 2139 cm⁻¹ is assigned to the N=C=N anti-symmetrical stretching of the thiocarbodiimide **6**, the peak at 2090 cm⁻¹ is assigned to the N=N=N anti-symmetric stretching of methyl azide **8**, the peak at 2050 cm⁻¹ is assigned to the CN stretching of CNH **9**, and the peak at 2265 cm⁻¹ is assigned to the C=N stretching of the observed photoproducts. The intensities of the individual spectra were multiplied by different factors to obtain a better simulation of the experimental spectra. Theoretical wavenumbers were scaled by a factor of 0.978 and bands were broadened by Lorentzian functions with FWHM equal to 4 cm⁻¹.

The band appearing at 2139 cm⁻¹ (Figure 7) fits nicely the predicted frequency for the NCN antisymmetric stretching vibration of the thiocarbodiimide **6** (Scheme 2). The observation of carbodiimides, resulting from photolysis of matrix-isolated tetrazole derivatives has been reported ^{28–30}. Additionally, the bands appearing around 1754 cm⁻¹ fit well the predicted frequencies for the vC=N stretching vibration of diazirine **5**. Formation of diazirines (including of 1,3-substituted diazirines) from photochemically induced cleavage of the tetrazole ring has also been reported ^{25,29}.

The identification of bands assigned to thiocarbodiimide **6** and diazirine **5** suggests photocleavage of the N_{18} – N_{19} and N_{20} – N_{21} bonds (see Figure 2 for atom numbering) with extrusion of molecular nitrogen. Note that the broad profile of the band around 1754 cm⁻¹ may be due to the presence in the matrix of different conformers of diazirine **5**. Actually, this molecule has two rotational axes, S– $C_{(saccharin)}$ and S– $C_{(diazirine)}$ and calculations predict the existence of two conformers with relative energies differing only by 2.9 kJ mol⁻¹. The two conformers have similar IR spectra, but the calculated frequencies for the vC=N mode are different enough (1722 cm⁻¹ and 1740 cm⁻¹) to result in the observed broad band.

Note also that in the case of the carbodiimide **6**, the calculated spectrum does not coincide so much with those of the reactant molecule and other photoproducts. As seen in Figure 8, several bands observed in the low frequency range in the spectra of the photolysed matrix doubtlessly confirm this species as one of the dominant photoproducts of TSMT. Moreover, it shall also be noticed that the carbodiimide **6**, as well as the diazirine **5**, are formed since the very beginning of the irradiation, being already present in significant amounts after only 30 s of irradiation (see Figure 8).

The band observed around 2100 cm⁻¹ is likely to be due to methyl azide **8** (vNNN anti-symmetric stretching), which can be formed by photocleavage of the N_{17} – N_{21} and N_{18} – N_{19} bonds of the tetrazole ring of TSMT upon irradiation, concomitantly with the thiocyanate 7. Under the used irradiation conditions, methyl azide has been found to partially react to yield, as final main product, CNH ³¹ (together with H₂ and N₂), in a process where methylenimine (CH₂=NH) acts as intermediate ³¹⁻³⁴. Indeed, the photochemistry of methyl azide 5 in an argon matrix has been studied in the past and, for example, the



Figure 8. (Top; violet): infrared difference spectrum obtained by subtracting the spectrum of the deposited TSMT matrix from that resulting from irradiation of the matrix ($\lambda = 265$ nm) during 30 s; (Bottom): DFT calculated (wavenumbers scaled) spectra for TSMT (blue trace, bands pointing down), thiocarboidiimide 6 (red trace) and diazirine 5 (magenta trace).

production of radicals such as CN has been safely excluded ³². According to the available knowledge on the photochemistry of methyl azide ³¹⁻³⁴, one can then expect that formation of this compound from photolysis of TSMT should essentially result in the accumulation of CNH. In consonance with such expectations, a product band was observed around 2050 cm⁻¹, which shall correspond to the vCN stretching mode of CNH, observed by Milligan and Jacox ³¹ upon photolysis of matrix-isolated methyl azide at nearly this frequency (2032 cm⁻¹). In the present study, CNH is formed together with other products and is, with all probability, interacting in the matrix cage with other species. Because of that, the frequencies may shift somewhat. Nevertheless, the assignment of the band at 2050 cm⁻¹ to CNH seems to be doubtless. It is unfortunate that the other two additional bands due to CNH reported by Milligan and Jacox (at ca. 535 and 3583 cm⁻¹) ³¹ could not be ascribed with certainty in the present study, though a product band at 536 cm⁻¹ (almost coincident with a band of TSMT) seems also to be present in the spectra of the photolysed matrix. However, the large spectral noise below ca. 600 cm⁻¹ in the spectra of the photolysed matrix makes this observation uncertain. On the other hand, the band observed by Milligan and Jacox ³¹ at 3583 cm⁻¹ is due to the NH stretching mode of CNH and can be expected to be extensively broadened due to intermolecular interactions (H-bonding) between CNH and other species present in the matrix cage (several bumps in the baseline are present in the spectra of the photolysed TSMT matrix in the high frequency region; however, no band could be safely assign to this mode). It shall also be noticed that no spectroscopic evidence of presence of methylenimine in the photolysed matrix could be found, specifically in the CH and C=N stretching spectral regions, where putative bands due to this compound appearing in a relatively less congested spectral region by bands due to other species should be observed. However, in the present experiments this species can be expected to be present only in very low amounts, due to its expected prompt fragmentation into CNH and H₂ ³¹⁻³⁴ and, since its infrared spectrum is characterized by bands of very low intensity ³², its successful observation would be very improbable.

The bands observed around 2265 cm⁻¹ correspond to typical frequency values for C=N stretching modes ^{35,36} and can be assigned to the vC=N vibrational mode of thiocyanate 7, which is the photoproduct that can be expected to be formed together with methyl azide **5** (see Scheme 2). The calculated intensity of this band for the thiocyanate in gas phase is small, but it is possible that it intensifies in some extent in the matrix due to polarization effects induced by the medium. Very unfortunately, most of the other thiocyanate bands with significant predicted intensity are expected to be superimposed with bands due to the diazirine **5** and TSMT (see Figure S3). Since the direct evidence for identification of the thiocyanate **7** is mainly in the observation of the feature in the ~2265 cm⁻¹ region, it must be considered as tentative. However, this assignment is strongly suggested from the mechanistic point of view, since, as already mentioned, the thiocyanate is the product that can be expected to be formed simultaneously with methyl azide.

Scheme 2. Proposed reaction pathways resulting from irradiation of TSMT monomer isolated in argon

matrix.



A schematic drawing summarizing the proposed photochemistry of matrix-isolated TSMT is presented in Scheme 2. As mentioned above, according to the identified photoproducts, two photodegradation pathways can be postulated, both arising from cleavage of the tetrazolyl ring: the dominant **Pathway** *a* involves photoinduced cleavage of the N₁₈–N₁₉ and N₂₀–N₂₁ bonds, with extrusion of molecular nitrogen, leading to production of diazirine **5** and thiocarbodiimide **6**. A nitrene-type intermediate can be postulated to be involved in this processes, ^{28,29} though we could not experimentally observe it. The concentrations of both the thiocarbodiimide **6** and diazirine **5** increased continuously with time, with no apparent sign of their further chemical transformations. The minor **Pathway** *b* involves photoinduced cleavage of the C₁₇–N₂₁ and N₁₈–N₁₉ bonds of the tetrazole ring, leading to formation of thiocyanate **7** and methyl azide **8**; the thiocyanate remains photostable, while methyl azide undergoes subsequent decomposition into CNH **9**.

An additional note shall here be made in relation with the observed photostability of the diazirine5. The recent study of Nunes *et al.* on the photolysis of the predominant 2*H* tautomeric form of matrix

isolated 5-methyltetrazole, with light of λ = 222 and ~328 nm, demonstrated that elimination of molecular nitrogen leads to the initial production of a nitrile imine, after a few seconds of irradiation, which can then isomerize to a 1*H*-diazirine, this species undergoing subsequent photoconversion into a carbodiimide 29 . In the present work, no evidence of formation of a nitrile imine was found, while the photoproduced diazirine revealed to be photostable even after 1 h of irradiation (λ = 265 nm). This might indicate, as suggested by Begué et al.²⁸, that the photochemistries of 1*H*- and 2*H*- tautomers of substituted tetrazoles might be different. Indeed, the present results on TSMT shall be compared more directly with those reported by the last authors ²⁸ on 5-phenyl-1*H*-tetrazole, since TSMT is also a 1-substituted tetrazole derivative. Begué *et al.* observed that, upon photolysis (λ = 254 nm) of 5-phenyl-1*H*-tetrazole, this tautomer did not produce the nitrile imine directly, contrarily to what was observed for the 2*H*-tautomer 28 (and also in the case of the 2*H*-tautomer of 5-methyltetrazole 29 , as mentioned above). The suggested route for production of the nitrile imine starting from the 1*H*-tautomer of 5-phenyltetrazole considered by Begué et al. implies the initial production of a diazirine intermediate, despite they were not able to observe this species (see Scheme S1) 28 . The present observation of diazirine 5 as a stable photoproduct seems to confirm the proposition of Begué et al.²⁸. The photostability of **5** is, probably, due to both the stabilizing effect of the electron rich sulphur substituent of the tetrazole ring and presence of the methyl substituent, which preclude the photoinduced rearrangement of the diazirine 5 under the experimental conditions used.

Conclusions

A combined matrix isolation FTIR and theoretical study of the molecular structure and photochemistry of 5-thiosaccharyl 1-methyltetrazole was performed. The conformational preferences of TSMT in both matrix isolated situation and in the crystalline phase were also investigated.

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According to the performed DFT calculations, TSMT has two conformers, I and II. However, the higher energy form (II) has a relative energy of *ca*. 15 kJ mol⁻¹ and only conformer I is significantly populated in the gas phase. As it could be expected, this conformer was found to be the only detectable in the cryomatrices (15 K) prepared from the vapor of the compound at 100 °C. The infrared spectrum of matrix isolated TSMT was fully assigned based on the O3LYP/6-311++G(3df,3pd) spectra calculated for conformer I.

In the crystal, TSMT was also found to exist in form I. In the crystalline phase, each molecule of TSMT forms four hydrogen bonds with three neighbor molecules, and a network of TSMT dimers is clearly observed. In the dimers, the two molecules of TSMT are disposed in a head-to-tail arrangement, with the tetrazole moiety of one molecule overlapping the thioimino moiety of the other (and vice versa), at the inner part of the dimer, while the aromatic rings are directed to the extremities. Formation of dimers is possibly due to π - π interactions between complementary tetrazole ring and thioimino moieties. The oligomeric structure results from an intricate network of weak hydrogen bonds formed between consecutive dimers (with involvement of both molecules of the dimer) and adjacent dimers.

Upon irradiation of the matrix isolated compound with UV light (λ = 265 nm), two photodegradation pathways were observed, both arising from cleavage of the tetrazolyl ring: *Pathway (a)* involves photoinduced cleavage of the N₁-N₂ and N₃-N₄ bonds, with extrusion of molecular nitrogen, leading to production of diazirine **5** and thiocarbodiimide **6**. The concentration of these two photoproducts increases with time, and there is no apparent sign of their photodegradation, even after almost complete consumption of the reagent (TSMT). The observed photostability of the photoproduct diazirine **5** under the conditions used is possibly ascribable to a stabilizing effect of the electron-rich sulphur substituent and the presence of the 1-methyl substituent. *Pathway (b)* involves photoinduced cleavage of the C₃-N₁ and N₄-N₃ bonds, leading to thiocyanate **7** and methyl azide **8** as primary photoproducts. Thiocyanate **7** remains photostable while methyl azide **8** originates CNH **10**, in a secondary photoreaction.

Experimental Section

General Methods

A convergent synthetic approach was followed to prepare TSMT, as depicted in Scheme 1. Solvents for extraction were of technical grade. When required, solvents were freshly distilled from appropriate drying agents before use. Melting points were recorded and are uncorrected. Mass spectra were obtained by electron ionization (EI) at 70 eV. NMR (400 MHz) spectra were measured using TMS as the internal reference ($\delta = 0.0$ ppm).

Preparation of 3-chloro-1,2-benzisothiazole 1,1-dioxide

Saccharyl chloride (3-chloro-1,2-benzisothiazole-1,1-dioxide, **2**) was obtained from saccharin (10.2 g; 56 mmol) and phosphorus pentachloride (14.0 g; 66 mmol), heated at 180 °C, using a procedure reported previously ³⁷: colorless needles (7.00 g; 63% yield); ¹H NMR (400 MHz, CDCl₃): δ 7.95-7.82 (m, 4H); elemental analysis: C, 41.5%, H, 2.0%, N, 6.9% (found), C, 41.7%, H, 2.0%, N, 7.0% (calculated for C₇H₄NO₂SCl).

Preparation of 1,2-benzisothiazole 1,1-dioxo 3-(5-thio-1-methyl) tetrazole (TSMT)

A mixture of anhydrous 5-mercapto-1-methyltetrazole **1** (0.30 g; 2.56 mmol) and 3-chloro-1,2benzisothiazole 1,1-dioxide **2** (0.53 g, 2.56 mmol) in dry THF (20 mL) was stirred at 60 °C, under a nitrogen atmosphere. The reaction was monitored by TLC (toluene/acetone; 5:3). After 24 h, the solvent was evaporated under reduced pressure and the remaining solid was dried under vacuum at room temperature. Crystallization from chloroform/THF (2:1) yielded the required product as colorless crystals (0.6 g; 83% yield), m.p. 222–224 °C. ¹H NMR (400 MHz, CDCl₃): δ 7.98–7.96 (m, 1H), 7.91–7.79 (m,

3H), 4.22 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 170.35, 165.77, 139.44, 135.13, 134.35, 128.84, 123.34, 122.94, 35.26; MS (EI): m/z 281 [M]⁺.

Matrix preparation, infrared spectroscopy and irradiation experiments

The matrix was prepared by co-deposition, onto the cooled CsI substrate of the cryostat, of the matrix gas (argon 99.9998%, obtained from Air Liquid) and vapors of TSMT produced by sublimation in a specially designed temperature variable mini-oven assembled inside the cryostat. The temperature of the mini-oven used for sublimation of TSMT was *ca*. 100 °C. The cryogenic system was based on a close-cycle helium refrigeration system with a DE-202A expander. The temperature of the CsI substrate during deposition was 15 K.

The infrared spectra of matrix-isolated TSMT were obtained using a Fourier transform infrared spectrometer equipped with a deuterated triglycinesulphate (DTGS) detector and a Ge/KBr beam splitter, with 0.5 cm⁻¹ spectral resolution. The room-temperature IR spectrum (4000-400 cm⁻¹) of solid polycrystalline TSMT in a KBr pellet was obtained using a Fourier Transform spectrometer equipped with a DTGS detector and Zn/Se optics. Data collection was performed with 128 scans and 4 cm⁻¹ spectral resolution.

The matrix was irradiated through the outer quartz window of the cryostat, with the frequency-doubled signal beam of the Quanta-Ray MOPO-SL pulsed (10 ns) optical parametric oscillator (FWHM \sim 0.2 cm⁻¹, repetition rate 10 Hz, pulse energy \sim 5.8 mJ) pumped with a pulsed Nd:YAG laser.

Crystallografic analysis

X-ray diffraction data were collected using a small single crystal. The crystallographic structure was solved by direct methods using SHELXS-97 ³⁸. Refinements were carried out with the SHELXL-97 package ³⁹. All refinements were made by full-matrix least-squares on F^2 with anisotropic displacement parameters for all non-hydrogen atoms (see Table S3 for details). All hydrogen atoms could be located on

a difference Fourier synthesis; their positions were refined as riding on parent atoms with an isotropic temperature factor using SHELXL-97 defaults that constrain these atoms to idealized positions. X-ray data collection and processing parameters for TSMT are presented in Table S3.

Computational methods

Quantum chemical calculations were performed at the DFT level of theory using either the valence double- ζ polarized 6-31+++G(d,p) or the extended valence triple- ζ polarized 6-311+++G(3df,3pd) basis set ⁴⁰⁻⁴³ and the B3LYP or O3LYP functionals ^{44,45}. Inclusion of both diffuse and polarization functions in the basis sets is required for a more accurate approximation to the calculated infrared spectra, since vibrational modes involving hypervalent S atoms (in particular the >SO₂ stretching and bending modes) are known not to be correctly predicted at a lower level of approximation ^{46,47}. The use of the DFT/B3LYP or O3LYP method with the 6-311+++G(3df,3dp) basis set was found to be appropriate to attain reliable results at moderate computational effort ^{12,13,46,47}. Geometries were optimized using the Direct Inversion in the Iterative Subspace (DIIS) method ⁴⁸. The transition state was located using the synchronous transit quasi-Newton method (QST3 implementation)^{49,50}. The optimization of geometries was followed by harmonic vibrational calculations undertaken at the same theory level. The nature of the obtained stationary points was checked through analysis of the corresponding Hessian matrix. The calculated harmonic vibrational frequencies (scaled by the factor 0.978 for the B3LYP functional ⁵¹ and by the factor 0.992 for the O3LYP functional ¹³) were used to assist the analysis of the experimental spectra. All calculations were performed with the Gaussian 09 suite of programs ⁵².

Associated Content

Supporting Information: Figures showing ¹H NMR and ¹³C NMR spectra of TSMT, the X-ray and IR spectrum of the TSMT crystal and calculated infrared spectra for TSMT and relevant photoproducts, and

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Tables with experimental (X-ray, single crystal) details of the crystallographic studies and calculated geometrical parameters of TSMT, including Cartesian coordinates, electronic energies and calculated infrared spectra for all optimized structures, at the B3LYP/6-311++G(3df,3pd) and O3LYP/6-311++G(3df,3pd) levels are provided as supporting information. This material is available free of charge via the Internet at http://pubs.acs.org.

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