Positional Isomerism and Steric Effects in the Self-Assemblies of Phenylene Bis-Monothiooxalamides


ABSTRACT: The potential interplay of steric and substitution pattern effects of the monothiooxalamide side arms on the structure, conformational features, and self-assembly of a series of phenylene bis-monothiooxalamides was investigated. Herein we have demonstrated that phenylene bis-monothiooxalamides self-assemble in the solid state, through intermolecular hydrogen bonding as meso-helices when the thioamide NR group is 'Bu and through dispersive CO···CX (X = O, S, π), S···S, and C–H···S interactions when R is 'Bu, independently from the substitution pattern in the phenyl ring. The helical structures are exclusively developed through N=NH···O hydrogen bonding. The steric strain imposed by the ortho-substitution pattern has the effect of moving both monothiooxalyl units out of the phenyl plane enabling dimerization through strong N=CO···O intermolecular hydrogen bonds and promotes the formation of meso-helices. The steric demand of the thioamide NR group rules the conformation adopted by meta-substituted derivatives and the self-association arrangement of para-substituted derivatives. Infrared data support the blue-shifted nature of the N=NH···O hydrogen bond. NMR data in solution agree with the extensive intramolecular hydrogen bonding scheme. Results are supported by density functional theory theoretical calculations. Monothiooxalamide unit offers considerable potential as a key moiety for crystal engineering.

1. INTRODUCTION

Crystal engineering is focused on the construction of molecular architectures through noncovalent interactions. Among them, hydrogen bonding is of particular importance in the structure of biological molecules and complexes, such as in the secondary and tertiary structure of proteins, in the helical conformation of DNA, as well as in the recognition of the active sites of enzymes and biological receptor sites. The molecular shapes of self-association are determined by the use of functional groups or molecular synthons that allow the development of partnerships in the form of dimers, chains, sheets, and in some cases the construction of complex structures.

Oxalamide derivatives are flat due to the formation of intramolecular hydrogen bonds between the acidic protons of amides and the carbonyl oxygen atoms of these fragments. Thiooxalamides and oxalamides are isostructural analogues; they differ in size and polarity due to the exchange of oxygen by sulfur in one or both carboxyls. Thiooxalamides, such as oxalamides, adopt the trans disposition between the amide proton and thiocarbonyl moieties which is stabilized by the formation of intramolecular NH···S=C hydrogen bonding interactions. Differences between amides and thiocarbonyl have been attributed to the change from the electronegative oxygen atom to the larger, less electronegative sulfur atom. Thus, in the context of hydrogen bonding, the thiocarbonyl group is less polarized than the carbonyl since the electronegativities of C (2.55) and S (2.58) are almost equal. As a result, thiocarbonyls are poor hydrogen-bond acceptors (C=O vs C=S), but better hydrogen-bond donors than amides, because of resonance effects from the nitrogen atom lone pair (RAHB).

The potential use of monothiooxalamides is foreseen by their structural parallelism with oxalamides; these latter have been...
extensively used as cocrystal formers. In contrast, the use of monothiooxalamides in cocrystallization is uncommon, even though the larger acidity of the thioamide proton confers to the NCOH better hydrogen donor properties than NCSH, and the thiocarbonyl C=S sulfur atom offers the possibility to participate in the formation of long-range interactions compared to the carbonyl group. These features make monothiooxalamides attractive model compounds suitable for the study of competing hydrogen-bond donors and acceptors in the same molecule. Studies on the capacity of the oxalamides and thiooxalamides to form helical arrangements through intermolecular hydrogen bonding interactions have been reported in recent years. Nevertheless, a thorough understanding of the intermolecular interactions formed in monothiooxalamides is necessary before they can be exploited in crystal engineering.

In the other hand, N,N′-oxalamides have been widely used as ligands for metal ions, in cis or trans-conformation of the oxalyl group. This has led to the design of new magnetic materials with promising applications in nanotechnology based on a metallosupramolecular approach. In this context, it has been recently reported that thiooxalamides can be used to selectively separate silver ions.

Herein, the structure and self-association of phenylene bis-monothiooxalamides are analyzed by comparing 1,2-, 1,3-, and 1,4-phenylenebis-monothiooxalamides in cocrystallization. The compounds were chosen because of their alkyl nature and similar weight in order to avoid the participation of electronic effects and to modulate inter-vs intramolecular interactions.

Although being in close structural relation, these compounds systematically differ both in the phenyl ring substitution (1-3), m-triad, compounds 4-6, p-triad, compounds 7-9) and the amine residue (Pr-NH2, Bu-NH2, and Pr-NH3 Chart 1. These groups were chosen because of their alkyl nature and similar weight in order to avoid the participation of electronic effects and to modulate inter-vs intramolecular interactions.

Aside from their structural isomerism, the relative disposition of the carbonyl group of the amide moiety regarding the phenyl ring, as a plane of reference, gives rise to several conformers: antiperiplanar (ap) 180−150°, anticlinal (ac) 150−90°, synclinal (sc) 90−30°, and synperiplanar (sp) 30−0°. Besides, 1,2- and 1,3-phenylene-bis-monothiooxalamides are properly positioned to form a cavity, in which case, the amide carbonyl could be endo or exo. Taking into account the two thiooxalamide arms, 10 combinations are possible: three exo−exo (ap−ap, ac−ac, ap−ac), four exo−endo (ap−sc, ap−sp, ac−sc, ac−sp), and three endo−endo (sc−sc, sc−sp, sp−sp). Finally, syn or anti isomers are formed by the relative position of both thiooxalyl side arms in 1,4-phenylene-bis-monothiooxalamides.

2. EXPERIMENTAL SECTION

2.1. General. Melting points were measured on an Electrothermal IA 9100 apparatus and are uncorrected. IR spectra were recorded neat at 25 °C using a Varian 3100 FT-IR with ATR spectrum. 1H, 13C NMR, and NOE spectra were recorded either on a Bruker Avance DPX-400 (1H, 400; 13C, 100 MHz) or on Varian Mercury-300 (1H, 300.08; 13C, 75.46 MHz) spectrometers in CDCl3 solutions or DMSO-d6 with SiMe4 as the internal reference; chemical shifts are in ppm and δ(H) in hertz. Variable-temperature 1H NMR measurements were performed in the Varian Mercury-300 apparatus equipped with a temperature controller to keep the temperature constant within 0.1 °C, from 20−70 °C in 5 °C increments with a delay of 5 min for temperature stabilization. Each spectrum was recorded with 16 scans. Mass spectra were obtained in a Bruker Esquire 6000 spectrometer with an electron ionization mode. Column chromatography was performed on a silica gel.

2.2. X-ray Structure Determination. General crystallographic data for the structures in this paper have been deposited in the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 1 (1498999), 2 (1499000), 3 (1499002), 4 (1499003), 5 (1499005), 6 (1499007), 7 (1499008), 8 (1499009), and 9 (1499010). A summary of collection and refinement of the X-ray data is listed in Table S1 (Supporting Information). Single crystal X-ray diffractions data of 1, 4, and 8 were collected on an Oxford Xcalibur Ruby Gemini area detector diffractometer at 293(2) K (4, 4), 100(2) K (8) with Cu Kα radiation (λ, 1.5418 Å, and of 2, 3, 5, 6, 7, and 9 on a Bruker D8 Quest diffractometer with Mo radiation (κ, 0.7073 Å) at 100(2) K (9), 123(2) K (2, 5), 173(2) K (3, 5). The cell refinement and data reduction of 1, 6, and 8 were carried out with the CrystAlis RED software and of 2−5, 7, and 9 with SAINT. The structures were solved by direct methods using the SHELXS2014 program of the WINGX package. The final refinement was performed by full-matrix least-squares methods using the SHELXL2014 program. H atoms on C and N were positioned geometrically and treated as riding atoms with C−H 0.95−0.99 Å, Uiso(H) = 1.2 eq(C) or 1.5 eq(C); N−H = 0.88 Å, Uiso(N) = 1.2 eq(N). Platon and Mercury were used to prepare the material for publication. The disorder was analyzed using the PART command in SHELXL-2014, and the disordered sec-butyl groups were treated and refined with two independent positions, namely, A and B for compounds 8 [(A1 = 0.709(11), A2 = 0.484(11), B1 = 0.291(11), B2 = 0.516(11)), 2 [(A1 = 0.670(8), A2 = 0.818(8), A3 = 0.588(9), B1 = 0.330(8), B2 = 0.182(8), B3 = 0.412(9)], and 5 [(A = 0.540(8), B = 0.460(8)]. For
the purpose of refinement, the carbon positions for A and B are fixed at the same value. The PLATON/SQUEEZE program was used to decrease the influence of disorder of the solvent in the electronic density residual structure.

2.3. Theoretical Calculations. Geometry optimizations at the B3LYP/6-31G(d, p) level of theory were performed on compounds 1−9 without any symmetry restraints using the Gaussian 09 package. Relaxed linear potential energy surface scans of 10° each for the Ph−N bond rotation were performed using direct inversion of iterative subspace (GDIIS). The anti disposition between CO and CS groups in the NHCOCSNHR fragment was imposed. Single point calculations of the Merz−Kollman−Singh (MKZ) atomic charges

Table 1. Selected Torsion Angles, Conformation and Supramolecular Arrangement of Compounds 1−9

<table>
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<tr>
<th>triad</th>
<th>comp.</th>
<th>C2−C1−N7−C8</th>
<th>C(n)−C(n+1)−N17−C18</th>
<th>O8−C8−C9−S9</th>
<th>O18−C18−C19−S19</th>
<th>conformation</th>
<th>motif</th>
</tr>
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<tbody>
<tr>
<td>ortho</td>
<td>1</td>
<td>161.29(19)</td>
<td>107.8(2)</td>
<td>−177.62(16)</td>
<td>157.88(16)</td>
<td>exo(ap)−exo(ac)</td>
<td>helix</td>
</tr>
<tr>
<td></td>
<td>2A</td>
<td>−178.0(4)</td>
<td>80.3(4)</td>
<td>176.4(3)</td>
<td>169.2(3)</td>
<td>exo(ap)−endo(sc)</td>
<td>helix</td>
</tr>
<tr>
<td></td>
<td>2B</td>
<td>−151.9(4)</td>
<td>−66.0(4)</td>
<td>−176.3(4)</td>
<td>177.3(3)</td>
<td>exo(ac)−endo(sc)</td>
<td>dispersive</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>−145.8(3)</td>
<td>−60.9(4)</td>
<td>170.3(3)</td>
<td>−178.4(2)</td>
<td>exo(ac)−endo(sc)</td>
<td>dispersive</td>
</tr>
<tr>
<td>meta</td>
<td>4</td>
<td>22.3(3)</td>
<td>9.3(3)</td>
<td>−177.90(13)</td>
<td>176.13(14)</td>
<td>endo(sp)−endo(ap)</td>
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<tr>
<td></td>
<td>5</td>
<td>147.5(2)</td>
<td>160.9(2)</td>
<td></td>
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<td>exo(ac)−exo(ac)</td>
<td>helix</td>
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<tr>
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<td>6</td>
<td>180.0</td>
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<td>180.0</td>
<td>180.0</td>
<td>endo(sp)−exo(ap)</td>
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<td>para</td>
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<td>−163.27(9)</td>
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<td>172.6(3)</td>
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<td></td>
<td>dispersive</td>
</tr>
</tbody>
</table>

The sum 30 units to obtain the numbering of molecule 2B. n = 1 (compounds 1 and 3), 2 (compounds 4 and 6), 3 (compound 8), 31 (compound 2B). Sum 40 units to obtain the numbering of molecule 2B.

Figure 1. (a) Molecular structure of compound 1, ortep view at the 30% probability level. (b) 1D meso helix supramolecular architecture of dimers of compound 1, view along the direction of the (1 0 1) plane.
were performed at the same level of theory on those conformers closely related to the single crystal X-ray structures.

2.4. Materials. See the Supporting Information.

2.5. Synthetic Procedures. See the Supporting Information.

3. RESULTS

3.1. Synthesis and Molecular Structure. Compounds 1–9 were synthesized following the methodology reported by Zavarzin with modifications, by reacting the corresponding \(N, N'-\text{(1,4-phenylene)}\)bis(2-chloroacetamide) \((n = 2, 3, 4)\), with elemental sulfur in an excess of the corresponding amine \((\text{Pr}-\text{NH}_2, \text{Bu}-\text{NH}_2, \text{or} \ '\text{Bu}-\text{NH}_2)\).

Compounds 1–3 crystallized as yellow monoclinic crystals in the space groups \(C2/c\) with eight molecules of 1 in the unit cell, and \(P2_1/c\) with eight molecules of compound 2 (two independent molecules A and B) and four molecules of 3 in the unit cell. Compound 7 crystallized as yellow triclinic crystals, space group \(P\bar{T}\), with one molecule in the unit cell. Whereas the other compounds crystallized as yellow orthorhombic crystals in space groups \(Pbca\) (4), \(C222_1\) (5), \(Pmna\) (6), \(Pnna\) (8), and \(Pbca\) (9) with four molecules in the unit cell, except compound 4 with eight molecules because of symmetry reasons.

Compounds 1–9 have the thioxalyl arm PhNHCOCSNHHR as a common structural feature. Selected bond distances and torsion angles are listed in Table S2. The \(N-n-1\) average bond length between amide and thioamide groups is 1.535(22) Å, a value comparable to the typical value of a \(\text{Csp}^3-\text{Csp}^3\) single bond. The mean values of \(N=O=1.335(15)\) Å \((Nn-Cn+1, n = 7, 17), C=O=1.220(16)\) \((\text{Cn-On}, n = 8, 18)\), \(N=CS=1.312(16)\) Å \((Nn+1-Cn, n = 9, 19)\), and \(C=S=1.658(13)\) Å \((\text{Cn-Sn}, n = 9, 19)\) bond lengths, in compounds 1–9, are very similar to those observed in other known dithiooxalamides or monothiooxalamides. The above results are in agreement with two isolated amide and thioamide groups \((\text{C}=\text{O}=1.234(12)\) Å, \(\text{C}=\text{S}=1.681(20)\) Å\). However, it is worth noting that the mean \(N–CO\) bond length is longer than the mean \(N–CS\) bond length, in contrast to the usual mean values \((N–CO=1.325(9)\) Å, \(N–CS=1.346(2)\) Å\). This result suggests that delocalization of the corresponding nitrogen lone pair to the thiocarbonyl is more favored than to the carbonyl and therefore the contribution of the thiolate resonance form in these compounds. Nevertheless, the lone pair of the amide nitrogen is delocalized to the phenyl ring as shown by the mean \(N–Ph\) distance of 1.416(15) Å, similar to the value measured for acetonilide. Consequently, both amide and thioamide NH protons are expected to be acidic in nature.

Thiooxalamide side arms are positioned one above and the other below the plane of the aromatic ring in all compounds, as can be seen from the values of their \(C2–C1–N7–C8\) and \(C1–C2–N17–C18\) torsion angles. A summary of torsion angles and conformations of compounds 1–9 is listed in Table 1. In compounds of the \(\sigma\)-triad (1–3), molecules 2B and 3 are markedly more twisted than 1 and 2A, and their molecular structures are shown in Figures 1a, 2a, and 3a, respectively (the molecular structure of 2B is shown in Figure S1). The conformation of the \(\sigma\)-triad is dominated by the steric strain inherent to the close disposition of both thioxalyl arms in the phenyl ring. The crowding inside the cavity is independent from the \(\text{endo}(sc)\) or \(\text{exo}(ac)\) conformations of the monothioxalyl arms. Besides, the size of the bulky pendant chain has no effect of moving apart both thioxalyl arms, and this can be judged by the \(S9–S19\) distances of 5.192(2), 5.027(4), 5.942(4), and 5.512(3) Å in compounds 1, 2A, 2B, and 3, respectively.

Figure 2. (a) Molecular structure of compound 2, two independent molecules in the asymmetric unit were found, only the molecular structure of 2A is shown, ortep view at the 30% probability level. (b) Supramolecular meso-helix arrangement of compound 2, view along the direction of the \((0 \ 4 \ 0)\) axis.
The set of m-triad (4–6) is more sensitive to the steric effects from the pendant alkyl chain on the thioamide nitrogen atom than the o-triad. Their molecular structures are displayed in Figures 4a, 5a, and 6a. In compound 4, the less steric demanded compound of the triad, monothioxalamide side arms are in endo(sp)–endo(sp) conformation. The opposed conformation, exo(ac)–exo(ac), is adopted by compound 5, whereas an endo(sp)–exo(ap) conformation is adopted in compound 6 to accommodate the bulky tBu groups in the available space of the cavity given by the 1,3-substitution in the phenyl ring.

Both monothioxalamide arms are a straight angle to be almost independent from each other as well as in anti disposition in compounds of the p-triad (7–9) with C2–C1–N7–C8 torsion angle values out of the mean phenyl plane in compounds 7 and 8, but near to 180° in compound 9. Therefore, the conformation adopted by each compound of the p-triad seems to depend on both the steric demand of the NR group and the secondary intramolecular interactions imposed by the NCS-alkyl chain (vide infra). Molecular structures of compounds 7–9 are shown in Figures 7a–9a, respectively.

In all compounds, the thiocarbonyl and carbonyl groups are in anti disposition relative to each other. However, the O8–C8–C9–S9 and O18–C18–C19–S19 torsion angle values are significantly deviated from planarity in compounds 1, 2A, 5, and 8. In contrast, the monothioxalyl fragment is nearly planar in compounds 2B, 3, 4, 6, 7, and 9. This structural feature is related to the supramolecular arrangement (vide infra).

### 3.2. Intramolecular Hydrogen Bond.

The thiooxalamide side arms in compounds 1–9 are intramolecularly hydrogen bonded, displaying the typical pattern of adjacent S(S)S(X) rings formed by NCS–H···X (X = O, S) interactions, Figures 1a–9a. Depending upon the conformation and substitution pattern of the oxalyl arms in the phenyl ring, the carbonyl oxygen and thiocarbonyl sulfur atoms can form three centered interactions with CH (aryl or alkyl) hydrogen atoms. The values of the torsion angles C6–C1–N7–C8 (compounds 1, 2A, 3, 5–7, and 9), C36–C31–N37–C38 (2B), and C2–C1(3)–N7(17)–C8(18) (4 and 6) are between 0.0 and 34.1(4)°, indicating that the oxalyl arm is nearly coplanar with the phenyl plane. Therefore, C6–H6···O8, C3–H3···O18, or C2–H2···O18(18) hydrogen bonding contacts with the phenyl ring are favored, in both exo or endo conformations, describing S(6) ring motifs, Chart 2a. There are some common motifs for sulfur atoms; in the case of the pr- and ‘Bu-triads, C(sp3)–H···S contacts forming an S(S) ring motif are observed, Chart 2b, whereas for ‘Bu-triad an adamantoid [S(6)]3 system is observed, Chart 2c.

The proximity between both oxalyl arms in compounds of the o-triad allows their interlinking by N17–H17···N7, N37–H37···O58, and N7–H7···O18 hydrogen bonding in com-
pounds 1, 2B, and 3, respectively. Thus, the full hydrogen bonding pattern can be described as a series of adjacent ring motifs [S(S)]_4[5] for compound 1, [S(S)]_3[S(7)]_6[S(S)]_3 for compound 2B, and [S(6)]_3[S(S)]_3[S(7)]_6[S(S)]_3 for compound 3. The common feature of these structures is the presence of a three-centered hydrogen bond with amide NH as hydrogen bonding donor: N7···H17···S19, O58···H37···S39, and O18···H7···S9, respectively. In compound 4, a similar hydrogen bonding pattern [S(5)]_3[S(6)]_2 is formed with the participation of soft C(sp^2) donor in the three-centered hydrogen bond, O8···H2···O18.

On the other hand, in those compounds where three centered hydrogen bonding is not allowed because of the unfavored conformation, 2A, 5, and 6, or by the opposed disposition of the thiooxalyl arms, 7−9, two independent sets of intramolecular hydrogen bonding rings are formed. Two non-symmetric [S(S)]_4 and S(6)[S(S)]_3 rings in compound 2A, and two symmetric S(6)[S(S)]_3[S(S)]_3 rings in compounds 6 and 9, S(6)[S(S)]_3 in 7 and S(6)[S(S)]_3 in 8 are formed. In general, intramolecular hydrogen bonding is similar among 'Pr- and 'Bu-triads but different in the 'Bu-triad, because of the participation of cooperative [S(6)]_3 soft contacts with the alkyl chain. The geometric parameters associated with intramolecular hydrogen bonding are listed in Table S3 for 'Pr-triad, in Table S4 for 'Bu-triad, and in Table S5 for 'Bu-triad derivatives.

3.3. Supramolecular Structure. The geometric parameters associated with intermolecular interactions are listed in Table 2. Two molecules of compound 1, related by a 2-fold symmetry axis, form dimers (0D) through N17−H17···O8 hydrogen bonding interactions, described by the R_2^2(14) ring motif. The NH donor is located in the more twisted thiooxalyl arm (N17C18(O18)C19(S19)N20). The exo(ac) conformation of carbonyl C18=O18 allows the propagation of the dimers within the (1 0 1) plane through N20−H20···O18 hydrogen bonding interactions. The characteristic R_2^2(10) ring pattern, observed also for oxalamide derivatives, develops a meso-helix supramolecular arrangement with an amplitude of 26.2 Å, Figure 1b. The M and P helices are interlinked by C22−H22A···O8 soft contacts, forming a C(12) chain motif, within the (S 5 9) plane.

The supramolecular arrangement of compound 2 is very similar to that observed in compound 1, in spite of differences in the conformation of the oxalyl arms (vide supra). The two independent molecules of compound 2 are associated into dimers (0D) through N20−H20···O58 and N60−H60···O18 interactions, forming the characteristic R_2^2(10) ring pattern of compound 2. The geometric parameters associated with intermolecular hydrogen bonding are listed in Table 2 for compound 2. The NH donor is located in the more twisted thiooxalyl arm (N20C21(O21)C22(S22)N23). The exo(ac) conformation of carbonyl C21=O21 allows the propagation of the dimers within the (0 1 0) plane through N20−H20···O22 hydrogen bonding interactions. The characteristic R_2^2(10) ring pattern, observed also for oxalamide derivatives, develops a meso-helix supramolecular arrangement with an amplitude of 26.2 Å, Figure 1b. The M and P helices are interlinked by C22−H22A···O8 soft contacts, forming a C(12) chain motif, within the (S 5 9) plane.

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The supramolecular arrangement of compound 2 is very similar to that observed in compound 1, in spite of differences in the conformation of the oxalyl arms (vide supra). The two independent molecules of compound 2 are associated into dimers (0D) through N20−H20···O58 and N60−H60···O18 interactions, forming the characteristic R_2^2(10) ring pattern of
oxalamides. The more twisted arm in endo(sc) conformation (N17C18(O18)C19(S19)N20, 2A and N57C58(O58)C59-S59)N60, 2B) provides both, the thioamide hydrogen bonding NH donor and the carbonyl amid acceptor. The first dimension is given by N17—H17···O38 and N57—H57···O38 hydrogen bonds, forming an \( R_2^2(14) \) ring motif, as well as by N40—H40···S19 that develops a meso-helix with an amplitude of 22.15 Å along the (0 0 1) direction, Figure 2b. Soft C33···H33···S59 interactions link the M and P helices to rise the second dimension within the (2 0 5) plane.

Two molecules of compound 3, related by a centrosymmetric plane of symmetry, are associated into dimers (0D) through N17—H17···O8 interactions. Again, the more twisted arm in endo(sc) conformation (N17C18(O18)19(S19)N20), provides the hydrogen bonding NH donor. The first dimension is given by C24—H(24A)···Cg(1) interactions within the (3 0 0) plane. The resulting tapes are interlinked by C19—S19···N38 interactions within the (0 5 1) plane. The sulfur atoms are 3.606(4) Å apart, and this distance is below twice the van der Waals radius of sulfur atom (1.85 Å), thus in the range of strong interactions, Figure 3b. Besides, the C19—S19···N38 angle of 168.3(4)° allows sulfur atoms to be in the proper position for electrostatic interaction between positive tip and negative equatorial electrostatic potentials surrounding the S atom, similar to those described for thioureas.

Carbonyl interactions C8—O8···C19 and C8—O8···Cg(1) develop the supramolecular architecture of compound 4, within the families of planes [13 12 12], Figure 4b. Carbonyl–thiocarbonyl interaction C8—O8···C19 form dimers, with the \( R_2^2(10) \) motif, between two centrosymmetric molecules, that are further developed into columns through the C8—O8···Cg(1) interaction. Carbonyl-thiocarbonyl C8—O8···C19 interaction can be classified as a short n → \( \pi^* \) donor–acceptor electron transfer, and its geometric features are in the range reported for proline-thioamide derivatives whose energy has been calculated at least 0.27 kcal/mol, whereas C8—O8···Cg(1) is a dispersive interaction of a head-on approach toward the ring centroid. Thus, the amide O8 atom is involved in a three centered interaction, acting as an electron density donor to both thioamide carbonyl C19 and Cg(1) acceptors.

In compound 5, the characteristic \( R_2^2(10) \) ring pattern of oxalamides appears twice to develop both the first and second dimensions. The thioamide NH donor and carbonyl oxygen acceptor, N10—H10···O8, form a 10-membered ring that develops along the (0 2 0) direction as a meso-helix of 17.49 Å of amplitude, Figure 5b. The M and P helices are linked by N7—H7···S9 interactions with the participation of the amide NH donor and thio-carbonyl sulfur as the acceptor, that form the second \( R_2^2(10) \) ring pattern.
Compound 6 is stacked along the direction of the $b$ axis through several interactions, among which carbonyl−carbonyl $C8=O8⋯C18$ and carbonyl−thiocarbonyl $C8=O8⋯C19$ are highlighted. The amide oxygen is involved in a three-centered intermolecular interaction, acting as a donor to both carbonyl and thiocarbonyl carbon atoms of a neighboring molecule. Two $C12−H12C⋯S19$ soft contacts, forming an $R_{2}^{2}(28)$ motif, contribute to form the stacked columns, Figure 6b, which in turn are linked through $C13−H13A⋯O18$ interactions, developing $C(13)$ chains, within the $ac$ plane, Figure 6c. The $C−H⋯S$ interaction is in the range reported in other compounds such as thiocoumarins.\textsuperscript{23,25}

3.4. Vibrational Analysis in the Solid. The FTIR spectra in the solid state of compounds 1−9 are dominated by two strong bands corresponding to amide carbonyl and thioamide carbonyl stretching frequencies ($\nu CO$ and $\nu CS$); they are in the expected range of $1683−1669$ cm$^{-1}$ and $1525−1509$ cm$^{-1}$, respectively.\textsuperscript{32,53} The stretching frequency of both amide N$\cdot\cdot\cdot$COH and thioamide N$\cdot\cdot\cdot$CSH bonds appear well resolved for compound 4 and those compounds of $t$Bu-triad. All of them are characterized by the lack of N$\cdot\cdot\cdot$CS$\cdot\cdot\cdot$O hydrogen bonding; they are self-assembled mainly by dispersive interactions. In compound 4,
amide N\textsubscript{CO}H and N\textsubscript{CS}H stretching frequencies are at 3266 and 3241 cm\textsuperscript{-1}, respectively, whereas in compounds of \textsuperscript{1}Bu-triad, the N\textsubscript{CO}H stretching frequencies appear at 3276(±2) cm\textsuperscript{-1} as a sharp signal, and thioamide N\textsubscript{CS}H frequencies appear within the 3225–3204 cm\textsuperscript{-1} range, as a broad signal. Selected IR frequencies are listed in Table 3. The shift to higher frequencies of the N\textsubscript{CO}H vibration agrees with more planar and less involved thiooxalyl arms in intermolecular hydrogen bonding\textsuperscript{17} whereas the low shift of N\textsubscript{CS}H vibration is in agreement with its more acidic character than N\textsubscript{CO}H. In contrast, those compounds self-assembled by the participation of N\textsubscript{CS}H···O and N\textsubscript{CO}H···O hydrogen bonding, compounds 1, 7, and those compounds of \textsuperscript{1}Bu-triad showed both NH frequencies overlapped in the IR spectra; they appear in the 3266–3227 cm\textsuperscript{-1} range. Thus, the N\textsubscript{CO}H stretching frequency is red-shifted, as expected, but the N\textsubscript{CS}H frequency is unexpectedly blue-shifted as intermolecular hydrogen bonding.

3.5. NMR in Solution. The chemical shifts of NH protons in compounds of \textsuperscript{1}Bu-triad were assigned by NOE experiments. Differences between the chemical shifts in DMSO-\textit{d}_{6} and chloroform solutions (\(\Delta\delta\text{NH}\)) as well as the chemical shift gradient with temperature (\(\Delta\delta\text{NH}/\Delta T\)) in DMSO-\textit{d}_{6} solutions, for both N\textsubscript{CO}H and N\textsubscript{CS}H were measured to relate them with their mobility; the values are listed in Table 4. Thus, the \(\delta\text{N}\textsubscript{CO}H\) protons of the \textsuperscript{1}Pr and \textsuperscript{1}Bu derivatives strongly interact with the highly coordinating solvent by hydrogen bonding, whereas the N\textsubscript{CS}H protons of \textsuperscript{1}Bu derivatives are independent from the polarity of the solvent; they are at lower frequencies (9.71–9.93 in DMSO-\textit{d}_{6}) than N\textsubscript{CO}H protons. This behavior could be explained by the combined effect of steric compression and paramagnetic protection exerted by the \textsuperscript{1}Bu group. In general, in compounds 1–9, the \(\Delta\delta\text{NH}/\Delta T\) and \(\Delta\delta\text{NH}\) values are larger for N\textsubscript{CS}H than for N\textsubscript{CO}H, in agreement with the more acidic character of the former. Among the triads, \(\Delta\delta\text{NH}/\Delta T\) values for both N\textsubscript{CO}H and N\textsubscript{CS}H are the smallest for the \textsuperscript{1}Bu-triad. Particularly, values below 2.0 ppm \textsuperscript{1}K\textsuperscript{−1} are characteristic of strong intramolecular hydrogen bonding systems, such as that measured for the N\textsubscript{CO}H in \textsuperscript{1}Bu-derivatives. These results, as a whole, suggest that N\textsubscript{CO}H is compromised with intramolecular hydrogen bonding in solution, whereas N\textsubscript{CS}H is more available for an intermolecular hydrogen bonding scheme in compounds 1–9. In the case of \textsuperscript{1}Bu-derivatives, the inherent acidity of N\textsubscript{CS}H is diminished as well as its mobility because of steric hindrance exerted by the tert-butyl chain.

3.6. Theoretical Calculations. Theoretical DFT calculations at the B3LYP/6-31 G(d,p) level of theory were performed to estimate the relative stability energies (\(\Delta E\)) and the energy involved in the interconversion (\(\Delta E\text{i}\)) among the conformers of compounds 1–9, Table S6. Conformational profiles of compounds 1–9 are displayed in Figures S2–S10. Rotational barriers grow asymptotically in those angles of maximum strain in compounds of the \(\sigma\)-triaz; therefore \(\Delta E\text{i}\) and \(\Delta E\text{f}\) could not be calculated. In compounds of \(m\)-triaz, the conformer \textit{endo}(ap)–\textit{exo}(ap) is more stable by 0.56–0.58 kcal mol\textsuperscript{−1} than the \textit{exo}(ap)–\textit{exo}(ap) and by 1.04–1.05 kcal mol\textsuperscript{−1}

The chemical shifts of NH protons in solutions, for both N\textsubscript{CO}H and N\textsubscript{CS}H were measured to relate them with their mobility; the values are listed in Table 4. Thus, the \(\delta\text{N}\textsubscript{CO}H\) protons of the \textsuperscript{1}Pr and \textsuperscript{1}Bu derivatives strongly interact with the highly coordinating solvent by hydrogen bonding, whereas the N\textsubscript{CS}H protons of \textsuperscript{1}Bu derivatives are independent from the polarity of the solvent; they are at lower frequencies (9.71–9.93 in DMSO-\textit{d}_{6}) than N\textsubscript{CO}H protons. This behavior could be explained by the combined effect of steric compression and paramagnetic protection exerted by the \textsuperscript{1}Bu group. In general, in compounds 1–9, the \(\Delta\delta\text{NH}/\Delta T\) and \(\Delta\delta\text{NH}\) values are larger for N\textsubscript{CS}H than for N\textsubscript{CO}H, in agreement with the more acidic character of the former. Among the triads, \(\Delta\delta\text{NH}/\Delta T\) values for both N\textsubscript{CO}H and N\textsubscript{CS}H are the smallest for the \textsuperscript{1}Bu-triad. Particularly, values below 2.0 ppm \textsuperscript{1}K\textsuperscript{−1} are characteristic of strong intramolecular hydrogen bonding systems, such as that measured for the N\textsubscript{CO}H in \textsuperscript{1}Bu-derivatives. These results, as a whole, suggest that N\textsubscript{CO}H is compromised with intramolecular hydrogen bonding in solution, whereas N\textsubscript{CS}H is more available for an intermolecular hydrogen bonding scheme in compounds 1–9. In the case of \textsuperscript{1}Bu-derivatives, the inherent acidity of N\textsubscript{CS}H is diminished as well as its mobility because of steric hindrance exerted by the tert-butyl chain.

Table 3. Stretching IR Frequencies of Solid Powders of Compounds 1–9

<table>
<thead>
<tr>
<th>compound</th>
<th>(\sigma)-triaz</th>
<th>(m)-triaz</th>
<th>(p)-triaz</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>(\nu) N\textsubscript{CO}H (cm\textsuperscript{-1})</td>
<td>3242</td>
<td>3227</td>
<td>3275</td>
</tr>
<tr>
<td>(\nu) N\textsubscript{CS}H (cm\textsuperscript{-1})</td>
<td>3242</td>
<td>3227</td>
<td>3204</td>
</tr>
<tr>
<td>(\nu) C=O (cm\textsuperscript{-1})</td>
<td>1677</td>
<td>1677</td>
<td>1683, 1665</td>
</tr>
<tr>
<td>(\nu) C=S (cm\textsuperscript{-1})</td>
<td>1521</td>
<td>1525</td>
<td>1511</td>
</tr>
</tbody>
</table>

Figure 9. (a) Molecular structure of compound 9, ortep view at the 30% probability level. (b) C(6) chains formed by soft C—H···O interactions in the \textit{ab} plane. (c) View of zig-zagging chains along the direction of the \textit{b} axis.
than the endo(sp)—endo(sp), respectively. These results support that the preferred conformation in the solid is ruled by steric effects in this set of compounds. The rotational barrier is higher for rotation from exo to endo than in the opposite sense by \( \sim 0.6 \text{ kcal mol}^{-1} \). Calculations predict the most stable geometry with the syn-conformer is more stable than the anti by just 0.27 \( \pm 1 \text{ kcal mol}^{-1} \); thus both conformations are equally probable, whereas the rotational barrier is 4.8 \( \text{kcal mol}^{-1} \) high, similar to the calculated value for the \( m \)-triad. Calculations were not able to mark clear differences within the \( NCS^- \)-R substituents; the energy values are almost the same for \( R = \text{Pr}, \text{Bu-}, \text{and } \text{Bu} \).

MKS charge values for selected atoms of the monothiooxalyl moieties were calculated and reported as the average values of both arms; results are listed in Table 5. In general, the calculated charges are in agreement with the more acidic character of \( NCS^- \) than \( NCO^- \). However, the nature of both \( NH \) is less acidic in compounds of \( \text{Bu} \)-triad than of \( \text{Bu} \) or \( \text{Pr} \)-tris. The calculated charges on the carbonyl C and O atoms indicate that they are the best Lewis acid–base pair leading the sulfur atom as the second-best hydrogen bonding acceptor in the molecule.

Among the \( m \)-triad, the charges on C2 and H2 depend on the adopted conformation. The more positive charge for H2 atom and the more negative charge for C2 atom were calculated for compound 4 which adopts the endo(sp)—endo(sp) conformation. These results support the formation of an intramolecular three-centered hydrogen bond O···H2···O in compound 4.

### 4. DISCUSSION

#### 4.1. Structure and Intramolecular Hydrogen Bonding

The analysis of the structural features across phenylene bis-monothiooxalamides 1–9 provides interesting insights of relevance to crystal engineering involving these compounds. The key question is whether replacing one oxygen atom of oxalamides with sulfur makes substantial differences in the solid state. The structure of the thiooxalamide fragment in compounds 1–9 is consistent with those structural features observed in thioamides. First, the thiocarbonyl bond is longer than a carbonyl group, which makes thiooxalyl arms prone to get away from the phenyl ring plane. This effect is modulated by the proximity of bulky alkyl chains to the sulfur atom. Second, the thioamide carbonyl has a greater N dipole, in order to enable the formation of the medium-strength C···H bonds as has been observed in thioureas and thioamides.

The intramolecular hydrogen bonding scheme in compounds 1–9 is like that exhibited by analogous phenylene bis-oxalamides, characterized by the juxtaposition of a series of \([S(6)], [S(6)], \text{and } [S(7)]\) rings. They are formed by \( NCS^- \)-···S, \( NCS^- \)-···O, \( NCS^- \)-···H(sp²), O···HC(sp²)···O, and, in the case of \( \text{Bu} \)-triax, by \( NCS^- \)-···H(sp²)···O interactions. In general, intramolecular hydrogen bonding is similar among \( \text{Pr} \), \( \text{Bu} \), and \( \text{Bu} \)-triax. In this last set of compounds the number of pseudo rings increased because of the participation of cooperative \([S(6)]\) soft contacts with the tert-butyl chain. The proximity between both oxalyl arms allows their interlinking by
intramolecular hydrogen bonding interactions in compounds of the o-triad and in compounds of m-triad only when both arms are in endo disposition. Therefore, the substitution pattern of monothiooxalyl arms in the phenyl ring and the bulkiness of the alkyl chain seem to have a subtle influence on the intramolecular hydrogen bonding scheme displayed by compounds 1−9. Calculated charges on the atoms of the monothiooxalyl group support these findings.

4.2. Self-Assemblies in the Crystal. The self-assembly of compounds 1−9 in the crystal lattice can be categorized in three structurally based types, according to their main hydrogen bonding motifs, as helices, tapes, sheets, and others given by dispersive interactions. This leads to the question of whether the preferred arrangement in the solid is mostly due to the sulfur atom, steric effects of the alkyl chain, and the conformation of the two monothiooxalyl arms or rather to their substitution pattern in the phenyl ring.

To address this question, the analysis of the monothiooxalamide X-ray structures deposited in the CSD was included. Only six structures were found whose hydrogen bonding motifs I−V were used for self-assembly and which are depicted in Chart 3. In motifs I, III, and IV, both carbonyl NH and CO act as hydrogen donor and acceptor, respectively. Thioamide NH provides the donor to the oxygen atom of the amide carbonyl, motif II, or to a carbonyl group acceptor present in the other fragment of the molecule, motif V.

Regarding the supramolecular structure of the compounds herein reported, it is worth noting that compounds of the o-triad form discrete dimers through motif VI; among them, compounds 1 and 2 are further developed into helices through motif II, whereas the second dimension of compound 3 is formed by soft S···S and C−H···π interactions. Motif II is also involved in the organization of the helical structures of compounds 5 and 8 as well as in the unidimensional tapelike structure of compound 7. Motif VII, which involves the thio carbonyl sulfur atom as the hydrogen acceptor, also contributes to the development of the helical structure of compound 5. This behavior contrasts with the supramolecular organization in 1D of compounds 4 and 9 or in 2D of compound 6, which is ruled by C=O···A (A = CX, π; X = O, S) and C−H···XC dispersive interactions, forming dimers such as motif VIII or the three-centered interaction in motif IX. To the best of our knowledge motifs VI−IX are described for the first time in compounds bearing monothiooxalamide functionality, Chart 4.

The supramolecular structure of N-butyl-N′-phenyl-thiooxalamide (PhNHCOCSNHBu) has been reported. This molecule is almost planar and self-assembles as dimers through NCSH···O hydrogen bonding, motif II. Comparing with this molecule highlights that the second thiooxalyl arm in compounds 1−9 favors self-assembling by the increased number of hydrogen bonding donors and acceptors.

Bis-oxalamides and bis-oxalamates with the structure of benzamide (PhNHCO) were searched in CCDB. Those compounds forming helices or tapes and whose structures were developed with one or more NH···OC hydrogen bonds belonging to the oxalyl moiety were selected for comparison purposes. Compounds forming helices are gathered together;
Table 6. Geometric Parameters and Supramolecular Architectures of Reported Phenylene Bis-oxalys

<table>
<thead>
<tr>
<th>comp</th>
<th>C$<em>{5n}$−C$</em>{15}$−N−C angle (deg)</th>
<th>O−C−C−O angle (deg)</th>
<th>conformation</th>
<th>motif or interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>11-DMSO$^{26}$</td>
<td>~137.65(16)</td>
<td>178.59(15)</td>
<td>exo(ac)−exo(ac)</td>
<td>II</td>
</tr>
<tr>
<td>12$^{77,68}$</td>
<td>149.9</td>
<td>178.5</td>
<td>exo(ac)−exo(ac)</td>
<td>II</td>
</tr>
<tr>
<td>13-1,3-(OH)$_2$C$_6$H$_4$$^{17}$</td>
<td>163.3(15)</td>
<td>175.96(17)</td>
<td>exo(ap)−exo(ap)</td>
<td>II, VI (n = 16)</td>
</tr>
<tr>
<td>16$^{55}$</td>
<td>144.6</td>
<td>179.9</td>
<td>exo(ac)−exo(ac)</td>
<td>II</td>
</tr>
<tr>
<td>17$^{55}$</td>
<td>125.9</td>
<td>168.9</td>
<td>endo(sc)−endo(sc)</td>
<td>II</td>
</tr>
<tr>
<td>10$^{77-69}$</td>
<td>140.9</td>
<td>20.4</td>
<td>exo(ac)−endo(sc)</td>
<td>VI (n = 14)</td>
</tr>
<tr>
<td>12$^{70}$</td>
<td>37.1</td>
<td>167.9</td>
<td>endo(sc)−endo(sc)</td>
<td>VI (n = 16), C4</td>
</tr>
<tr>
<td>12-1,3-(OH)$_2$C$_6$H$_4$$^{16}$</td>
<td>79(1.6)</td>
<td>172.6(1.6)</td>
<td>endo(ap)−endo(ap)</td>
<td>R$_2^2$(10) cocrystal with resorcinol</td>
</tr>
<tr>
<td>13$^{55}$</td>
<td>117.0</td>
<td>167.8</td>
<td>exo(ac)−exo(ac)</td>
<td>VI (n = 16)</td>
</tr>
<tr>
<td>14$^{55}$</td>
<td>114.7</td>
<td>177.3</td>
<td>endo(sc)−exo(sc)</td>
<td>VI (n = 16), C(8)</td>
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<tr>
<td>19$^{77,68}$</td>
<td>58.0</td>
<td>162.5</td>
<td>endo(sc)−exo(sc)</td>
<td>VI (n = 16), C(8)</td>
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<td>15$^{55}$</td>
<td>104.0</td>
<td>167.4</td>
<td>endo(sc)−exo(sc)</td>
<td>VI (n = 16), C(8)</td>
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<td>18$^{55}$</td>
<td>34.07</td>
<td>166.4</td>
<td>endo(sc)−exo(sc)</td>
<td>VI (n = 16), C(8)</td>
</tr>
</tbody>
</table>

Dispersive Interactions

<table>
<thead>
<tr>
<th>comp</th>
<th>C$<em>{5n}$−C$</em>{15}$−N−C angle (deg)</th>
<th>O−C−C−O angle (deg)</th>
<th>conformation</th>
<th>motif or interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>15$^{55}$</td>
<td>179.1(3)</td>
<td>179.1(3)</td>
<td>exo(ap)−exo(ap)</td>
<td>XH−O (X = C, O, N), CO−CO, π−π</td>
</tr>
</tbody>
</table>

Hydrogen Bonded Helix

Hydrogen Bonded Tape

Dispersive Interactions

In the case of oxalyl derivatives, the methyl ester of thiooxalyl-, dithiooxalyl-, and dioxalyl of (S,S)-N,N'-bis-leucine methyl ester are known to form helical foldamers. Self-assembled helical structures are present in many biologically important macromolecules. Recently their significant role in amyloid-fibril formation has been demonstrated.52
Tapes or sheets are characterized by the following common features. (i) One NH donor of each oxalyl arm is available for hydrogen bonding: thioamide NH in thiooxalamides, amide NH in oxalamates/oxalamides. (ii) One or both oxalyl arms are in endo(sc) conformation in o- and m-substituted or in (sp) conformation in p-substituted derivatives. (iii) The duplex motif VI is developed into tapes or sheets by C(n) chains, or by motif I. It is worth noting that aliphatic bis-oxalamides of formula (R’N’HCOCONH)2R and bis-phenyl N,N’-oxalamides of formula PhNHCOSCONHPh features usually self-assemble as tapes or sheets without significant deformation of the OCCO torsion angle.

From the analysis of the reported structures of oxalamates and oxalamides with carbonyls in anti disposition and forming helices, the torsion OCCO angle is twisted out from planarity with values in the 162–170° range, Table 6, whereas in monothiooxalamides, the torsion OCCS angles are closer, in the 150–170° range. In contrast, those phenyl-bis-oxalyl (oxalamates, oxalamides, and monothiooxalamides) compounds whose supramolecular structure is built by dispersive interactions or hydrogen bonded tapes/sheets are characterized by an OCCX (X = O, S) angle close to 180°. However, discrete supramolecular arrangements are formed if NCS-H or NCO-H is not available for intermolecular hydrogen bonding because of steric hindrance or their involvement in intramolecular hydrogen bonding even when they could fulfill the additional structural requirements for helix or tape.

**4.3. Nature of Hydrogen Bonding.** Thioamide NCS-H is expected to be a better hydrogen donor than amide NCO-H and weaker hydrogen bond acceptor than amide. These expectations are supported by the calculated MKS charges and are accomplished in bis-monothiooxalamides 1–9, but they are modulated by steric hindrance from the neighboring alkyl chain and the isomerism in the phenyl ring. The question arises about the nature of hydrogen bonding, particularly about the observed blue shift of NCS-H frequencies in the IR spectra upon H-bond formation. It has been stated that the τNH in the solid state of secondary amides and thioamides depends on the acidity (NCS-H is more acidic than NCO-H), the mass of the alkyl substituent, and the geometry of the molecule.44,71 In the particular case of oxalyl derivatives, the NH stretching frequency is shifted to lower values as the weight of the entire (XC)2(NH)2 (X = O, S) fragment increases. Thus, comparison among compounds of ‘Bu- and ‘Bu-triads, of identical molecular weight, allows estimating the effect of hydrogen bonding in the NH stretching frequency. In compounds of ‘Bu-triad, that are not intermolecularly hydrogen bonded, amide NCS-H stretching frequencies appear blue-shifted in comparison to strongly hydrogen bonded compounds of ‘Bu-triad, Table 2. Further comparison with compounds whose supramolecular structures and IR frequencies in the solid are known, such as MeNHOCOCNSHMe (tape, 3240 cm−1) and the methyl ester of (S,S)-N,N’-monothiooxazyl-bis-leucine (helix, 3275 cm−1),19 follows the same trend. This last result suggests that the nature of NCS–O agrees with an “improper” blue-shifted hydrogen bond,72 in which the NH bond strengthens as hydrogen bonding. Recently, it has been proposed by theoretical calculations that the competition between covalent and ionic nature of the D–H bond is responsible for blue- or red-shifting IR frequency.73 On the other hand, it has been claimed that both the rehybridization and decrease of electron density in the NH bond in the presence of the hydrogen bonding acceptor A (N–H···A) contribute to the large NH blue shift.74

Rehybridization enhances the s-character of the hybrid orbital on D and results in the shortening of the D–H bond.75 This last approach is in accordance with RAHB and structural data found for the NCS fragment in compounds reported herein (vide supra) when they are involved in intramolecular hydrogen bonding. The magnitude of C=O → N—HCS (lone pair to σ*) has been calculated in 0.046 e, contributing with 12.03 kcal/mol to the preferred S conformation of thiourea with formula PhC(O)NHCS(NH)HR.52

1H NMR results suggest that NCS-H is compromised with intramolecular hydrogen bonding in solution, whereas NCS-H is more available for intermolecular hydrogen bonding scheme in compounds 1–9. However, in the particular case of ‘Bu-derivatives, the inherent acidity of NCS-H is diminished because of the steric demand exerted by the tert-butyl chain. The chemical shifts values of NCS-H in DMSO-d6 are very close to those recorded in CDCl3 (Δδ in the 0.23–0.34 range), implying that their intramolecular bifurcated NCS-H···O(C)···H–C(sp3) hydrogen bonding scheme is rather strong and remains even in the highly polar solvent. In addition, the values of the chemical shift gradients with temperature, Δδ(NCS-H)/ΔT, are notably smaller than those of ‘Pr- and ‘Bu-triads, in agreement with the strength of this hydrogen bonding scheme, Table 3. The thioamide sulfur atom is involved in an intramolecular bifurcated NCS-H···S=O([HC(sp3)]2 interaction. The strong intramolecular nature of NCS-H···S in ‘Bu-triad, characterized by negligible ΔNCS-H values in the 0–0.07 ppm range, and ΔNCS-H/ΔT values below 2.0 ppb K−1, is further strengthened by the participation of secondary cooperative [HC(sp3)]2−···S interactions. This adamanantoid (S(S)2), motif has been predicted by topological NBO analysis in 1-(4-chlorobenzoyl)-3-(2-methyl-4-oxopentan-2-yl) thiourea, contributing with 0.0079 e.52 The strong intramolecular hydrogen bonding scheme S(6)[S(S)2]12[S(6)3]1 proper to ‘Bu-triad compounds is stable both in solution and in the solid state. Finally, it is worth noting that the effect of single C(sp3)H···S and the steric demand of ‘Bu (87.1 Å3) and ‘Pr (69.1 Å3) groups are not able to fix the intramolecular hydrogen bonding despite their large volumes.

**5. CONCLUSIONS**

In spite of the bulkiness of the thioamide NR chair, relatively strong NCS-H···O intermolecular hydrogen bonds enable dimerization to take place in the strongly hindered ortho-phenyl isomers. The X-ray structures clearly demonstrate that the preferred conformation of the meta-phenyl bis-monothiooxalamides depends on the steric demand of the thioamide NR chain. The supramolecular architecture of this last set of compounds strongly depends on the conformation. The self-assembly patterns of the para-phenyl isomers are significantly different from each other; they only depend on the bulkiness of the thioamide NR chain. While the ‘Pr derivative forms layers of hydrogen bonded tapes, the ‘Bu derivative self-assembles in one direction to create supramolecular meso-helices through an extensive two-dimensional hydrogen bonding network developed by NCS-H···O interactions. Racemic bis-‘Bu monothio-alamides have a remarkable propensity to self-assemble as meso-helical structures independently from the substitution pattern in the phenyl ring. Steric interactions in ‘Bu derivatives preclude the formation of hydrogen bonded supramolecular aggregates. Instead, dispersive interactions such as CO···CX (X = O, S, π), S···S, and C···H···S build the crystal lattice.
When thiooxalyl arms adopt the proper conformation, hydrogen bonded *meso*-helices and tapes are developed exclusively by NH···O interactions with thioamide as the donor and amide carbonyl as the acceptor. Helices are developed when oxalyl arms are in *exoa* or *exob* conformation, with an angle below 162° in *o* and *m*-isomers, but *(sc)*—*(sc)* with an angle of 39.1° in *p*-isomers. When one or both oxalyl arms are in *endoa* conformation, in *o* and *m*-substituted, or in *(sp)* conformation, in *p*-substituted derivatives, then hydrogen bonded tapes are favored. The arrangements in helix or tape networks are accompanied by significant deformation of the OCCS angle; thus the two carbonyls are forced to deviate from planarity. Experimental structures contrast with the calculated optimal geometries in the gas phase.

IR data support a differentiated nature of the amide-carbonyl hydrogen bond, and NCOH···O agrees with a blue-shift, whereas NCOH···O agrees with red-shifted hydrogen bonding, in accordance with RAHB and structural data found for the NCS fragments. Furthermore, the thiooxalamide side arms are intramolecularly hydrogen bonded, through NH···X (X = O, S) and three centered interactions of CX (X = O, S) with CH (aryl or alkyl) hydrogen atoms, depending upon the conformation and substitution pattern of the oxalyl arms in the phenyl ring. The tBu group efficiently promotes extensive intramolecular interactions contributing to form up to 12 adjacent ring motifs ([S(n)] [S(n+1)] [S(n+2)] ; i = 1, j + i + k = 12), in contrast to eight rings in 'Bu and Pr derivatives ([S(n)] [S(n+1)] [S(n+2)] ; i = 1, j + i = 8). In solution, the chemical shifts, the chemical shift gradients with solvent and temperature of the NCOH protons of tBu derivatives are consistent with an extensive intramolecular hydrogen bonding scheme. Theoretical calculations support the experimental findings.

### ASSOCIATED CONTENT

#### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.cgd.7b00041.

Materials, synthetic procedures. Collection and refinement of X-ray data of compounds 1–9 in Table S1; selected bond lengths and torsion angles of compounds 1–9 in Table S2; the molecular structure of compound 2B in Figure S1; geometric parameters of intramolecular hydrogen bonding in Pr-triad, *Bu-triad, and *Bu-triad derivatives in Tables S3–S5; calculated relative energies (ΔEi) and interconversion barriers (ΔEi) in kcal mol⁻¹, at B3LYP/6-31G (d, p) level of theory of m-triad and p-triad compounds in several conformations in Table S6; conformational profiles of compounds 1–9 in Figures S2–S10 (PDF)

**Accession Codes**

CCDC 1498999–1499000, 1499002–1499003, 1499005, and 1499007–1499010 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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**Notes**

The authors declare no competing financial interest.

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