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**Supplementary Information**

# Isosteric O/S exchange in carbonyl(thio)ureides: molecular interactions, structure, and bioactivity assays

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## Crystallographic Supplementary Information

**Table S1.** Crystal data and structure refinement results for compounds **I** and **II**.

| Compound | **I** | **II** |
|---|---|---|
| Chemical formula | $C_{13}$ $H_{18}$ $N_2$ $O_2$ S | $C_{13}$ $H1_8$ $N_2$ $O_3$ |
| Formula weight | 266.35 | 250.29 |
| Temperature (K) | 297(2) | 297(2) |
| Wavelength (Å) | 0.71073 | 0.71073 |
| Crystal system | Monoclinic | Monoclinic |
| Space group | *P* $2_1$/*c* | *P* $2_1$/*c* |
| Unit cell dimensions: | | |
| *a*(Å) | 6.3789(3) | 4.8639(2) |
| *b*(Å) | 23.739(1) | 15.2441(7) |
| *c*(Å) | 9.2761(5) | 18.5621(8) |
| *β*(º) | 98.122(5) | 96.637(4) |
| Volume (Å$^3$) | 1390.6(1) | 1367.1(1) |
| *Z* | 4 | 4 |
| Density (calculated, Mg/m$^3$) | 1.272 | 1.216 |
| Absorption coeff. (mm$^{-1}$) | 0.229 | 0.087 |
| F(000) | 568 | 536 |
| Crystal color | Colorless | Colorless |
| Crystal size (mm$^3$) | 0.324 x 0.078 x 0.061 | 0.402 x 0.110 x 0.079 |
| *ϑ*-range (º) for data collection | 3.226 to 28.752 | 3.468 to 29.025 |
| Index ranges | -8≤h≤8, -13≤k≤30, -12≤l≤10 | -6≤h≤6, -20≤k≤20, -23≤l≤24 |
| Reflections collected | 5746 | 12946 |
| Independent reflections | 3009 [*R*(int) = 0.0362] | 3150 [*R*(int) = 0.0446] |
| Obs. reflections [*I*>2*σ*(*I*)] | 1932 | 1672 |
| Completeness (%) | 99.9 (to *ϑ* = 25.242°) | 99.8 (to *ϑ* = 25.242°) |
| Refinement method | Full-matrix least-squares on $F^2$ | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 3009 / 0 / 235 | 3159 / 3 / 165 |

| | | |
|---|---|---|
| Goodness-of-fit on $F^2$ | 1.027 | 1.027 |
| Final $R$ indices[a] [$I > 2\sigma(I)$] | R1 = 0.0515, wR2 = 0.1021 | $R1$ = 0.0785, $wR2$ = 0.2118 |
| $R$ indices (all data) | R1 = 0.0937, wR2 = 0.1205 | $R1$ = 0.1448, $wR2$ = 0.2587 |
| Larg. diff. peak / hole (e.Å$^{-3}$) | 0.161 / -0.239 | 0.472 / -0.335 |

[a] $R1=\Sigma||F_o|-|F_c||/\Sigma|F_o|$, $wR2=[\Sigma w(|F_o|^2-|F_c|^2)^2/\Sigma w(|F_o|^2)^2]^{1/2}$

**Table S2.** Bond lengths [Å] and angles [°] in compound (**I**).

| | |
|---|---|
| C(1)-O(1) | 1.361(2) |
| C(1)-C(6) | 1.378(3) |
| C(1)-C(2) | 1.379(3) |
| C(2)-C(3) | 1.373(3) |
| C(3)-C(4) | 1.389(3) |
| C(4)-C(5) | 1.379(3) |
| C(4)-C(8) | 1.482(3) |
| C(5)-C(6) | 1.377(3) |
| C(7)-O(1) | 1.416(3) |
| C(8)-O(2) | 1.224(2) |
| C(8)-N(1) | 1.369(3) |
| C(9)-N(2) | 1.319(3) |
| C(9)-N(1) | 1.394(3) |
| C(9)-S | 1.665(2) |
| C(10)-N(2) | 1.458(3) |
| C(10)-C(11) | 1.506(3) |
| C(11)-C(12) | 1.525(3) |
| C(12)-C(13) | 1.510(4) |
| O(1)-C(1)-C(6) | 124.8(2) |
| O(1)-C(1)-C(2) | 115.5(2) |
| C(6)-C(1)-C(2) | 119.7(2) |
| C(3)-C(2)-C(1) | 120.5(2) |
| C(2)-C(3)-C(4) | 120.5(2) |
| C(5)-C(4)-C(3) | 118.2(2) |
| C(5)-C(4)-C(8) | 117.8(2) |
| C(3)-C(4)-C(8) | 123.9(2) |
| C(6)-C(5)-C(4) | 121.6(2) |
| C(1)-C(6)-C(5) | 119.5(2) |
| O(2)-C(8)-N(1) | 121.5(2) |
| O(2)-C(8)-C(4) | 121.4(2) |
| N(1)-C(8)-C(4) | 117.1(2) |
| N(2)-C(9)-N(1) | 116.4(2) |
| N(2)-C(9)-S | 124.4(2) |
| N(1)-C(9)-S | 119.1(2) |
| N(2)-C(10)-C(11) | 110.7(2) |
| C(10)-C(11)-C(12) | 111.4(2) |
| C(13)-C(12)-C(11) | 113.0(3) |
| C(8)-N(1)-C(9) | 128.8(2) |
| C(9)-N(2)-C(10) | 123.9(2) |
| C(1)-O(1)-C(7) | 118.4(2) |

**Table S3.** Bond lengths [Å] and angles [°] in compound **II**.

| | |
|---|---|
| C(1)-O(1) | 1.363(4) |
| C(1)-C(2) | 1.378(5) |
| C(1)-C(6) | 1.372(4) |
| C(2)-C(3) | 1.371(5) |
| C(3)-C(4) | 1.385(4) |
| C(4)-C(5) | 1.374(4) |
| C(4)-C(8) | 1.481(4) |
| C(5)-C(6) | 1.381(4) |
| C(7)-O(1) | 1.419(4) |
| C(8)-O(2) | 1.222(3) |
| C(8)-N(1) | 1.371(3) |
| C(9)-O(3) | 1.232(3) |
| C(9)-N(2) | 1.320(4) |
| C(9)-N(1) | 1.393(4) |
| C(10)-N(2) | 1.443(4) |
| C(10)-C(11) | 1.490(7) |
| C(11)-C(12) | 1.361(10) |
| C(12)-C(13) | 1.509(12) |
| O(1)-C(1)-C(2) | 116.0(3) |
| O(1)-C(1)-C(6) | 124.7(3) |
| C(2)-C(1)-C(6) | 119.3(3) |
| C(1)-C(2)-C(3) | 120.7(3) |
| C(2)-C(3)-C(4) | 120.7(3) |
| C(5)-C(4)-C(3) | 117.9(3) |
| C(5)-C(4)-C(8) | 124.8(2) |
| C(3)-C(4)-C(8) | 117.3(3) |
| C(6)-C(5)-C(4) | 121.8(3) |
| C(5)-C(6)-C(1) | 119.6(3) |
| O(2)-C(8)-N(1) | 121.8(3) |
| O(2)-C(8)-C(4) | 121.2(2) |
| N(1)-C(8)-C(4) | 117.1(2) |
| O(3)-C(9)-N(2) | 123.3(3) |
| O(3)-C(9)-N(1) | 118.1(3) |
| N(2)-C(9)-N(1) | 118.5(2) |
| N(2)-C(10)-C(11) | 112.6(3) |
| C(12)-C(11)-C(10) | 119.3(7) |
| C(11)-C(12)-C(13) | 111.2(13) |
| C(8)-N(1)-C(9) | 127.8(2) |
| C(9)-N(2)-C(10) | 122.0(3) |
| C(1)-O(1)-C(7) | 118.0(2) |

**Table S4.** Torsion angles [°] in **I**.

| | |
|---|---|
| O(1)-C(1)-C(2)-C(3) | 179.58(19) |
| C(6)-C(1)-C(2)-C(3) | -0.2(4) |
| C(1)-C(2)-C(3)-C(4) | 0.0(3) |
| C(2)-C(3)-C(4)-C(5) | 0.5(3) |

| | |
|---|---|
| C(2)-C(3)-C(4)-C(8) | 177.69(19) |
| C(3)-C(4)-C(5)-C(6) | -0.8(3) |
| C(8)-C(4)-C(5)-C(6) | -178.1(2) |
| O(1)-C(1)-C(6)-C(5) | -179.8(2) |
| C(2)-C(1)-C(6)-C(5) | 0.0(4) |
| C(4)-C(5)-C(6)-C(1) | 0.6(4) |
| C(5)-C(4)-C(8)-O(2) | 13.0(3) |
| C(3)-C(4)-C(8)-O(2) | -164.2(2) |
| C(5)-C(4)-C(8)-N(1) | -168.2(2) |
| C(3)-C(4)-C(8)-N(1) | 14.7(3) |
| N(2)-C(10)-C(11)-C(12) | -174.2(2) |
| C(10)-C(11)-C(12)-C(13) | 173.8(3) |
| O(2)-C(8)-N(1)-C(9) | 6.3(3) |
| C(4)-C(8)-N(1)-C(9) | -172.52(19) |
| N(2)-C(9)-N(1)-C(8) | -1.2(3) |
| S-C(9)-N(1)-C(8) | 178.18(18) |
| N(1)-C(9)-N(2)-C(10) | -178.7(2) |
| S-C(9)-N(2)-C(10) | 2.0(3) |
| C(11)-C(10)-N(2)-C(9) | 164.5(2) |
| C(6)-C(1)-O(1)-C(7) | 0.8(4) |
| C(2)-C(1)-O(1)-C(7) | -179.0(3) |

**Table S5.** Torsion angles [°] in **II**.

| | |
|---|---|
| O(1)-C(1)-C(2)-C(3) | 179.4(3) |
| C(6)-C(1)-C(2)-C(3) | -0.5(5) |
| C(1)-C(2)-C(3)-C(4) | 0.9(6) |
| C(2)-C(3)-C(4)-C(5) | -0.4(5) |
| C(2)-C(3)-C(4)-C(8) | -179.6(3) |
| C(3)-C(4)-C(5)-C(6) | -0.7(4) |
| C(8)-C(4)-C(5)-C(6) | 178.4(3) |
| C(4)-C(5)-C(6)-C(1) | 1.2(5) |
| O(1)-C(1)-C(6)-C(5) | 179.6(3) |
| C(2)-C(1)-C(6)-C(5) | -0.6(5) |
| C(5)-C(4)-C(8)-O(2) | -159.4(3) |
| C(3)-C(4)-C(8)-O(2) | 19.8(4) |
| C(5)-C(4)-C(8)-N(1) | 20.4(4) |
| C(3)-C(4)-C(8)-N(1) | -160.5(3) |
| N(2)-C(10)-C(11)-C(12) | 167.8(8) |
| C(10)-C(11)-C(12)-C(13) | -173.9(8) |
| O(2)-C(8)-N(1)-C(9) | -4.3(5) |
| C(4)-C(8)-N(1)-C(9) | 176.0(3) |
| O(3)-C(9)-N(1)-C(8) | -173.9(3) |
| N(2)-C(9)-N(1)-C(8) | 5.2(4) |
| O(3)-C(9)-N(2)-C(10) | 2.7(5) |
| N(1)-C(9)-N(2)-C(10) | -176.3(3) |
| C(11)-C(10)-N(2)-C(9) | -85.9(5) |
| C(2)-C(1)-O(1)-C(7) | 177.1(3) |
| C(6)-C(1)-O(1)-C(7) | -3.1(5) |

**Table S6.** Atomic coordinates (x $10^4$) and equivalent isotropic displacement parameters ($Å^2$ x $10^3$) for (**I**). U(eq) is defined as one third of the trace of the orthogonalized $U^{ij}$ tensor.

| Atom | x | y | z | U(eq) |
|---|---|---|---|---|
| C(1) | -2264(3) | 3351(1) | 5560(2) | 46(1) |
| C(2) | -1679(3) | 3906(1) | 5446(3) | 45(1) |
| C(3) | 2(3) | 4047(1) | 4742(2) | 42(1) |
| C(4) | 1141(3) | 3632(1) | 4136(2) | 39(1) |
| C(5) | 524(3) | 3079(1) | 4251(3) | 50(1) |
| C(6) | -1155(4) | 2934(1) | 4959(3) | 54(1) |
| C(7) | -4602(5) | 2697(1) | 6465(5) | 73(1) |
| C(8) | 2922(3) | 3750(1) | 3314(2) | 42(1) |
| C(9) | 5283(3) | 4518(1) | 2670(2) | 41(1) |
| C(10) | 7650(4) | 4366(1) | 842(3) | 53(1) |
| C(11) | 8586(4) | 3863(1) | 176(3) | 48(1) |
| C(12) | 10431(4) | 4033(1) | -612(3) | 54(1) |
| C(13) | 11563(5) | 3534(1) | -1155(4) | 63(1) |
| N(1) | 3773(3) | 4280(1) | 3434(2) | 44(1) |
| N(2) | 6034(3) | 4191(1) | 1714(2) | 48(1) |
| O(1) | -3943(2) | 3259(1) | 6288(2) | 64(1) |
| O(2) | 3581(2) | 3392(1) | 2543(2) | 58(1) |
| S | 6003(1) | 5186(1) | 2994(1) | 55(1) |

**Table S7.** Atomic coordinates (x $10^4$) and equivalent isotropic displacement parameters ($Å^2$ x $10^3$) for (**II**). U(eq) is defined as one third of the trace of the orthogonalized $U^{ij}$ tensor.

| Atom | x | y | z | U(eq) |
|---|---|---|---|---|
| C(1) | 8807(6) | 3606(2) | 7308(2) | 61(1) |
| C(2) | 7581(8) | 4112(3) | 7798(2) | 82(1) |
| C(3) | 5698(7) | 4749(3) | 7562(2) | 77(1) |
| C(4) | 4957(6) | 4889(2) | 6828(1) | 54(1) |
| C(5) | 6179(6) | 4374(2) | 6347(2) | 59(1) |
| C(6) | 8111(6) | 3741(2) | 6579(2) | 60(1) |
| C(7) | 11887(8) | 2433(3) | 7118(2) | 87(1) |
| C(8) | 2925(6) | 5594(2) | 6620(2) | 57(1) |
| C(9) | -538(6) | 6115(2) | 5624(2) | 55(1) |
| C(10) | -3496(7) | 7369(2) | 5742(2) | 75(1) |
| C(11) | -2631(13) | 8081(4) | 5267(4) | 173(3) |
| C(12) | -4600(30) | 8571(7) | 4873(6) | 299(7) |
| C(13) | -3330(40) | 9189(6) | 4369(5) | 439(14) |
| N(1) | 1562(5) | 5563(2) | 5931(1) | 56(1) |
| N(2) | -1238(5) | 6795(2) | 6003(1) | 64(1) |
| O(1) | 10668(5) | 2998(2) | 7599(1) | 78(1) |
| O(2) | 2498(5) | 6178(2) | 7044(1) | 79(1) |
| O(3) | -1671(5) | 5936(2) | 5014(1) | 77(1) |

**Table S8.** Anisotropic displacement parameters ($Å^2$ x $10^3$) for **I**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + ... + 2\ hka^*b^*\ U^{12}]$.

| Atom | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{23}$ | $U^{13}$ | $U^{12}$ |
|---|---|---|---|---|---|---|
| C(1) | 38(1) | 49(2) | 51(1) | 3(1) | 4(1) | -4(1) |
| C(2) | 39(1) | 42(1) | 56(1) | -4(1) | 9(1) | 2(1) |
| C(3) | 39(1) | 35(1) | 53(1) | -2(1) | 7(1) | -2(1) |
| C(4) | 36(1) | 38(1) | 42(1) | -4(1) | 4(1) | 0(1) |
| C(5) | 50(1) | 38(1) | 65(2) | -5(1) | 14(1) | 0(1) |
| C(6) | 57(1) | 36(1) | 70(2) | 2(1) | 10(1) | -9(1) |
| C(7) | 63(2) | 64(2) | 97(3) | 17(2) | 26(2) | -11(2) |
| C(8) | 41(1) | 38(1) | 47(1) | -6(1) | 6(1) | -1(1) |
| C(9) | 38(1) | 43(1) | 41(1) | -3(1) | 8(1) | 0(1) |
| C(10) | 62(2) | 49(2) | 51(2) | -1(1) | 24(1) | 0(1) |
| C(11) | 54(1) | 47(2) | 45(1) | -4(1) | 15(1) | -2(1) |
| C(12) | 62(2) | 51(2) | 53(2) | 2(1) | 23(1) | 4(1) |
| C(13) | 68(2) | 64(2) | 62(2) | -2(2) | 23(2) | 11(2) |
| N(1) | 45(1) | 40(1) | 50(1) | -14(1) | 17(1) | -4(1) |
| N(2) | 51(1) | 46(1) | 51(1) | -10(1) | 20(1) | -7(1) |
| O(1) | 56(1) | 59(1) | 81(1) | 6(1) | 28(1) | -10(1) |
| O(2) | 63(1) | 44(1) | 72(1) | -19(1) | 29(1) | -7(1) |
| S | 71(1) | 40(1) | 61(1) | -7(1) | 28(1) | -8(1) |

**Table S9.** Anisotropic displacement parameters ($Å^2$ x $10^3$) for **II**.

| Atom | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{23}$ | $U^{13}$ | $U^{12}$ |
|---|---|---|---|---|---|---|
| C(1) | 61(2) | 61(2) | 59(2) | 14(1) | -5(1) | -5(1) |
| C(2) | 100(3) | 96(3) | 48(2) | 6(2) | -5(2) | 20(2) |
| C(3) | 93(2) | 84(2) | 51(2) | -6(2) | -5(2) | 18(2) |
| C(4) | 56(2) | 57(2) | 47(2) | 0(1) | -4(1) | -8(1) |
| C(5) | 61(2) | 69(2) | 44(2) | 4(1) | -2(1) | -4(2) |
| C(6) | 60(2) | 65(2) | 55(2) | 0(1) | 2(1) | 2(1) |
| C(7) | 84(2) | 87(3) | 88(3) | 21(2) | 10(2) | 19(2) |
| C(8) | 59(2) | 60(2) | 51(2) | -7(1) | -3(1) | -8(1) |
| C(9) | 63(2) | 52(2) | 49(2) | -1(1) | -2(1) | -4(1) |
| C(10) | 84(2) | 63(2) | 74(2) | -1(2) | -5(2) | 11(2) |
| C(11) | 158(5) | 95(4) | 243(8) | 60(4) | -71(5) | 2(3) |
| C(12) | 500(20) | 170(9) | 206(9) | 83(8) | -40(11) | -3(12) |
| C(13) | 1070(40) | 131(7) | 154(7) | 62(6) | 223(15) | 62(14) |
| N(1) | 61(1) | 55(1) | 48(1) | -7(1) | -3(1) | 2(1) |
| N(2) | 70(2) | 61(2) | 56(2) | -9(1) | -7(1) | 7(1) |
| O(1) | 85(2) | 79(2) | 68(1) | 18(1) | -4(1) | 14(1) |
| O(2) | 93(2) | 78(2) | 62(1) | -23(1) | -16(1) | 15(1) |
| O(3) | 98(2) | 71(2) | 56(1) | -12(1) | -22(1) | 16(1) |

**Table S10.** Hydrogen coordinates (x $10^4$) and isotropic displacement parameters (Å$^2$ x $10^3$) for **I**.

| Atom | x | y | z | U(eq) |
|---|---|---|---|---|
| H(1N) | 3470(30) | 4487(10) | 4040(20) | 41(7) |
| H(2) | -2430(30) | 4178(11) | 5850(20) | 63(7) |
| H(2N) | 5550(40) | 3866(11) | 1670(30) | 56(8) |
| H(3) | 320(30) | 4431(10) | 4680(20) | 40(6) |
| H(5) | 1220(30) | 2793(11) | 3800(30) | 63(7) |
| H(6) | -1500(30) | 2570(10) | 5050(20) | 51(6) |
| H(7A) | -4990(40) | 2523(13) | 5530(30) | 89(11) |
| H(7B) | -5840(40) | 2737(13) | 6960(30) | 89(9) |
| H(7C) | -3440(40) | 2475(13) | 6990(30) | 91(10) |
| H(10A) | 8780(40) | 4582(13) | 1500(30) | 88(9) |
| H(10B) | 7070(30) | 4616(11) | 180(30) | 59(8) |
| H(11A) | 9060(30) | 3594(10) | 880(30) | 53(7) |
| H(11B) | 7560(30) | 3653(10) | -530(30) | 58(7) |
| H(12A) | 9920(30) | 4294(11) | -1370(30) | 56(7) |
| H(12B) | 11430(40) | 4274(12) | 30(30) | 71(8) |
| H(13A) | 12200(40) | 3301(12) | -400(30) | 65(8) |
| H(13B) | 10670(40) | 3311(13) | -1810(30) | 81(10) |
| H(13C) | 12720(50) | 3641(13) | -1640(30) | 97(10) |

**Table S11.** Hydrogen coordinates (x $10^4$) and isotropic displacement parameters (Å$^2$ x $10^3$) for **II**.

| Atom | x | y | z | U(eq) |
|---|---|---|---|---|
| H(2) | 80364021 | 829299 | | |
| H(3) | 49095091 | 789993 | | |
| H(5) | 56924455 | 585270 | | |
| H(6) | 89353408 | 624373 | | |
| H(7A) | 104702088 | 6849130 | | |
| H(7B) | 131922053 | 7391130 | | |
| H(7C) | 128222778 | 6788130 | | |
| H(10A) | -42527629 | 615490 | | |
| H(10B) | -49487025 | 547390 | | |
| H(11A) | -14528480 | 5571207 | | |
| H(11B) | -14937817 | 4930207 | | |
| H(12A) | -56178907 | 5199359 | | |
| H(12B) | -59028186 | 4591359 | | |
| H(13A) | -14469022 | 4339658 | | |
| H(13B) | -33849777 | 4552658 | | |
| H(13C) | -43579161 | 3896658 | | |
| H(1) | 20635154 | 565667 | | |
| H(2A) | -3206900 | 641976 | | |

**Table S12.** Main bond lengths [Å], angles [°] and torsion angles [°] for **I** and **II**.

| Bond/angles | **I** | | **II** | |
|---|---|---|---|---|
| | Exp. | Calc. | Exp | Calc. |
| C(8)-O(2) | 1.224(2) | 1.2288 | 1.222(3) | 1.2277 |
| C(8)-N(1) | 1.369(3) | 1.3828 | 1.371(3) | 1.3794 |
| C(9)-N(2) | 1.319(3) | 1.3349 | 1.320(4) | 1.3484 |
| C(9)-N(1) | 1.394(3) | 1.4064 | 1.393(4) | 1.4264 |
| C(9)-S | 1.665(2) | 1.6772 | --- | --- |
| C(9)-O(3) | --- | --- | 1.232(3) | 1.2209 |
| C(10)-N(2) | 1.458(3) | 1.4594 | 1.443(4) | 1.4581 |
| C(10)-C(11) | 1.506(3) | 1.5277 | 1.490(7) | 1.5337 |
| C(11)-C(12) | 1.525(3) | 1.5326 | 1.361(10) | 1.5323 |
| C(12)-C(13) | 1.510(4) | 1.5312 | 1.509(12) | 1.5314 |
| O(2)-C(8)-N(1) | 121.5(2) | 122.24 | 121.8(3) | 122.37 |
| N(2)-C(9)-N(1) | 116.4(2) | 115.08 | 118.5(2) | 115.76 |
| O(3)-C(9)-N(2) | --- | --- | 123.3(3) | 126.14 |
| N(2)-C(9)-S | 124.4(2) | 125.73 | --- | --- |
| O(3)-C(9)-N(1) | --- | --- | 118.1(3) | 118.10 |
| N(1)-C(9)-S | 119.1(2) | 118.18 | --- | --- |
| N(2)-C(10)-C(11)-C(12 | -174.2(2) | 179.91 | 167.8(8) | 179.50 |
| C(10)-C(11)-C(12)-C(1 | 173.8(3) | 170.92 | -173.9(8) | -179.86 |
| O(2)-C(8)-N(1)-C(9) | 6.3(3) | -3.38 | -4.3(5) | -178.81 |
| C(4)-C(8)-N(1)-C(9) | -172.52(19 | 177.21 | 176.0(3) | -178.15 |
| N(2)-C(9)-N(1)-C(8) | -1.2(3) | -0.08 | 5.2(4) | 1.83 |
| O(3)-C(9)-N(1)-C(8) | --- | --- | -173.9(3) | -178.81 |
| S-C(9)-N(1)-C(8) | 178.18(18 | -179.92 | --- | --- |
| C(11)-C(10)-N(2)-C(9 | 164.5(2) | 177.70 | -85.9(5) | 91.01 |
| O(3)-C(9)-N(2)-C(10) | --- | --- | 2.7(5) | 2.19 |
| S-C(9)-N(2)-C(10) | 2.0(3) | 0.18 | --- | --- |
| N(1)-C(9)-N(2)-C(10) | -178.7(2) | -179.64 | -176.3(3) | -178.51 |

**Table S13.** Stabilization energies for the **I** and **II** dimers, calculated by NBO (B3LYP/6-31g(d,p).

| Dim. | Donor | | Acceptor | $E^{(2)}$ | |
|---|---|---|---|---|---|
| | NBO (i) | | NBO (j) | kJ mol$^{-1}$ | |
| | | | | I | II |
| A | Lp (S) | → | σ*N1-H | 5.65 | |
| B | Lp (S) | → | σ*C2-H | 5.44 | |
| C | Lp (O) | → | σ*C7-H | 0.25 | |
| A | Lp (O3) | → | σ*N1-H | | 25.9 |
| | Lp (O3) | → | σ*C5-H | | 2.85 |
| B | Lp (O2) | → | σ*C7-H | | 2.72 |
| C | Lp (O1) | → | σ*N2-H | | 4.60 |

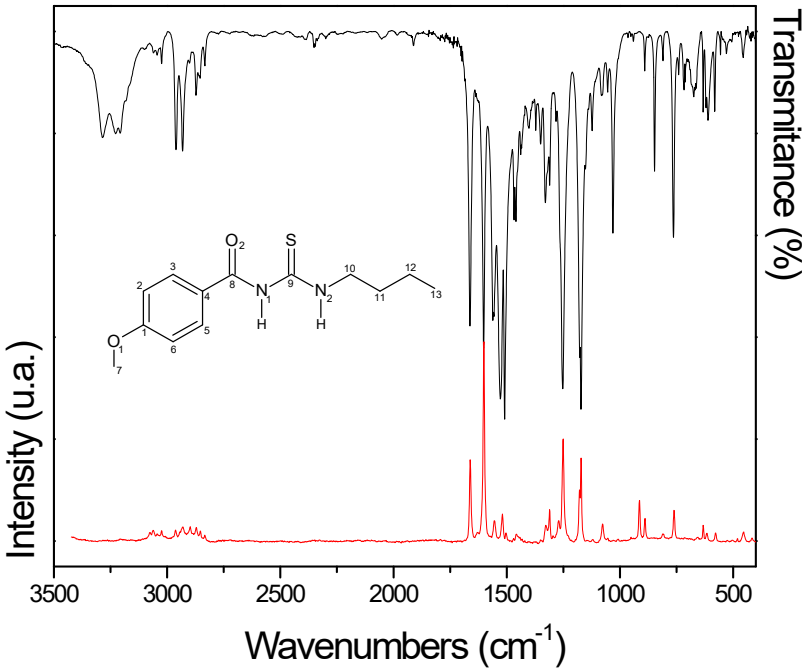



**Figure S1.** Infrared spectrum (upper trace, KBr pellets) and Raman spectrum (solid, lower trace) of **I**.

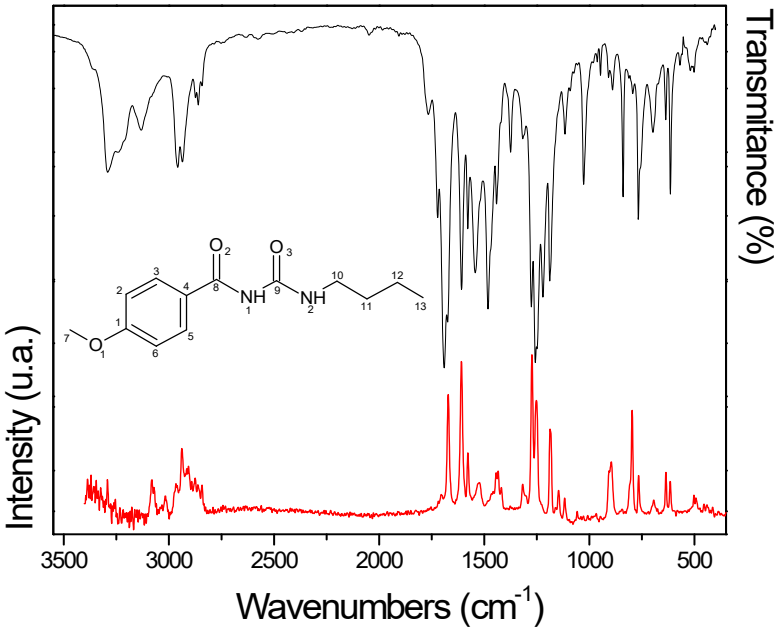



**Figure S2.** Infrared spectrum (upper trace, KBr pellets) and Raman spectrum (solid, lower trace) of **II**.

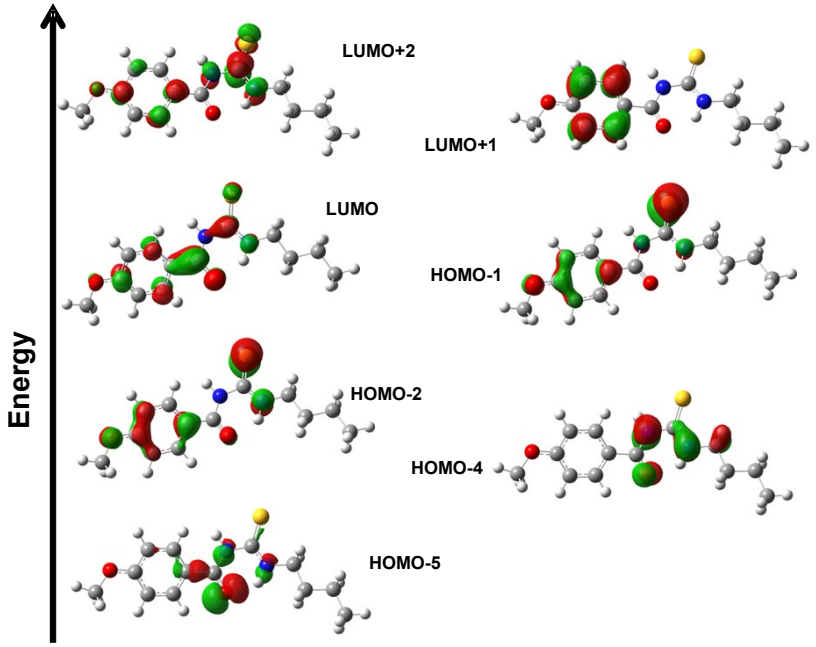



**Figure S3.** Calculated molecular orbitals for **I**.

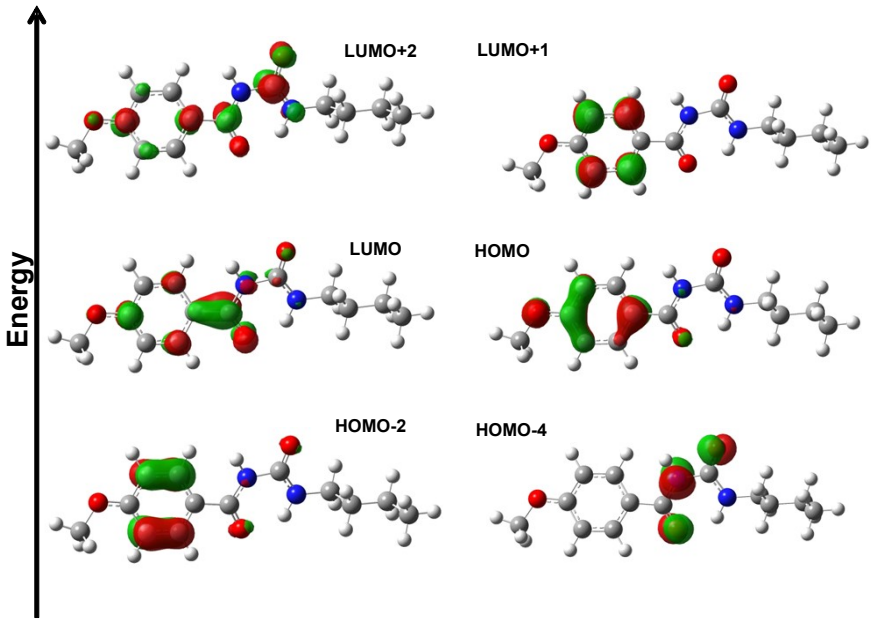



**Figure S4.** Calculated molecular orbitals for **II**.

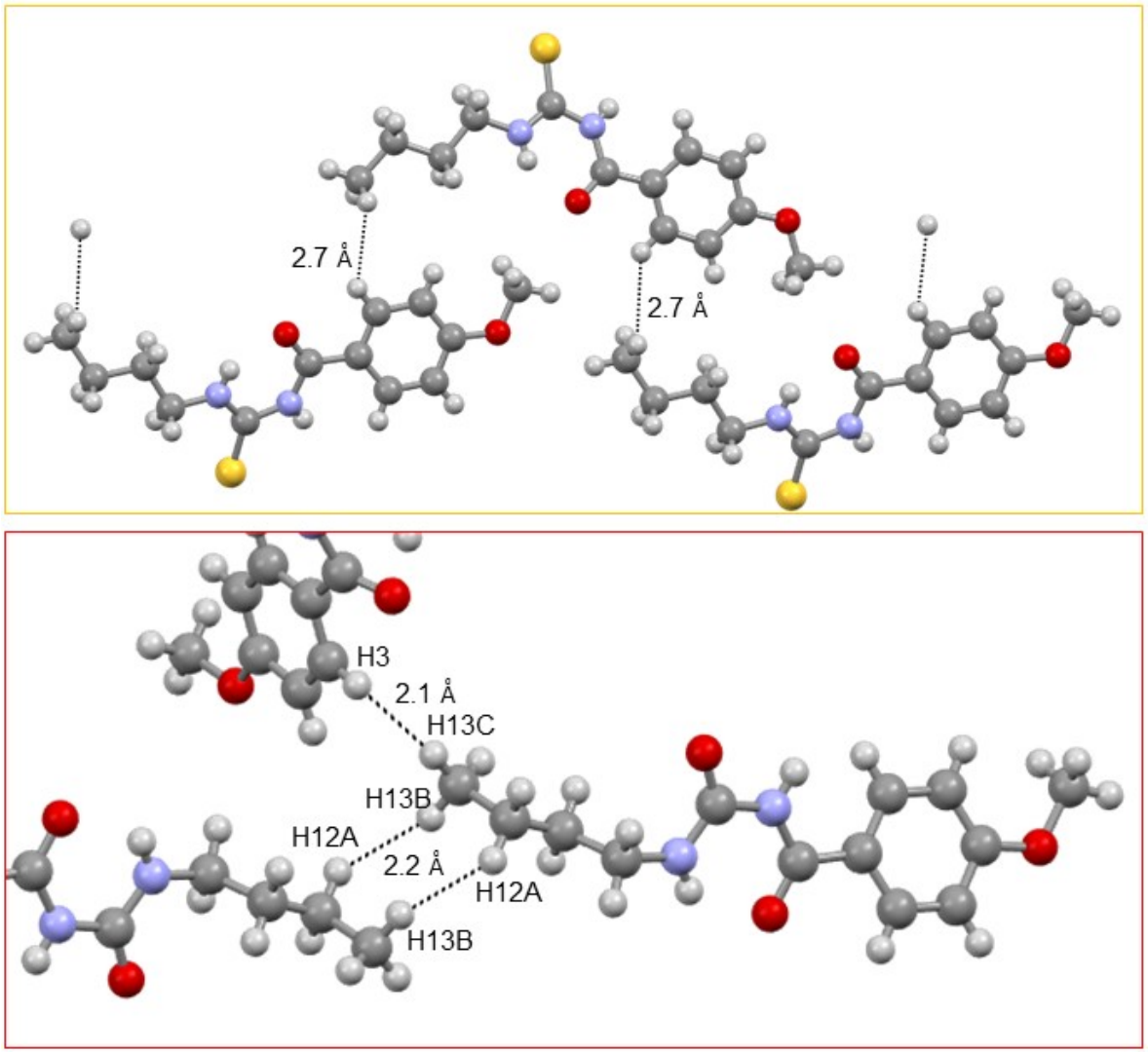



**Figure S5.** H···H contacts in **I** (top) and **II** (bottom).

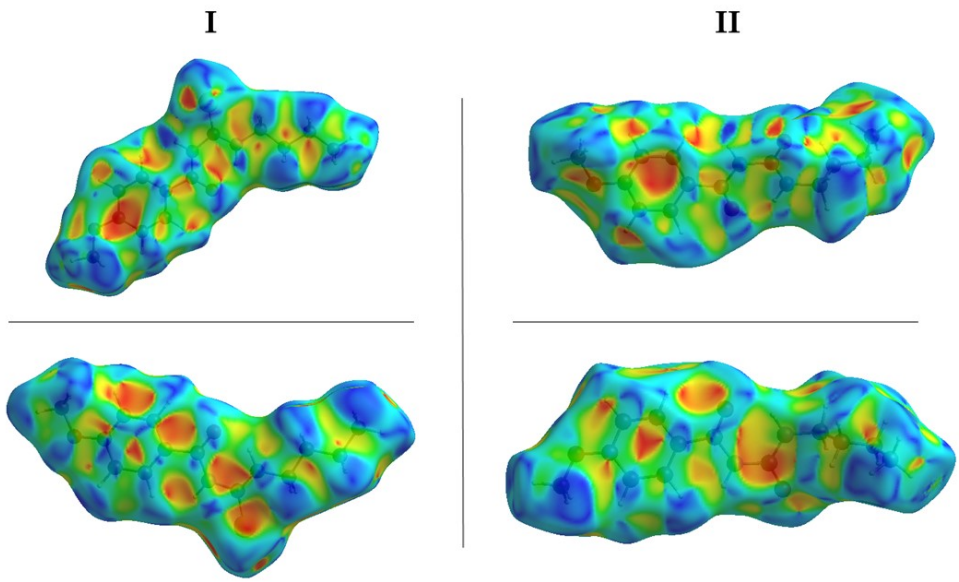



**Figure S6.** Anterior (top) and posterior (bottom) views of the Hirshfeld surface of **I** (left) and **II** (right) evaluated with the Shape Index descriptor.

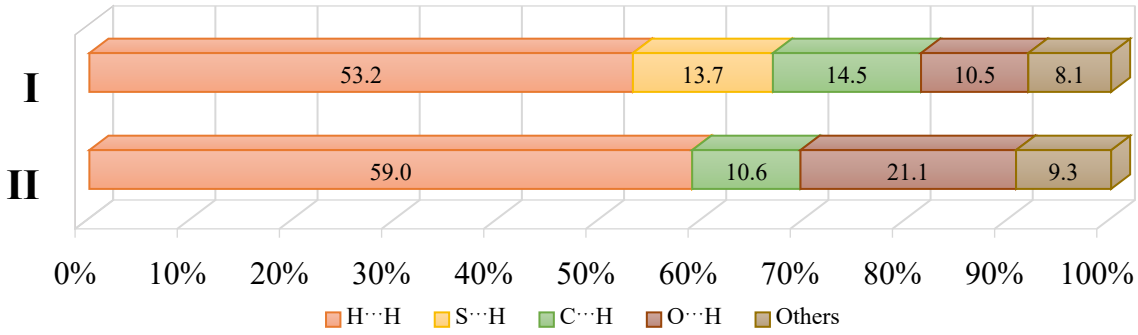



**Figure S7.** Contribution (%) of the intermolecular contacts of **I** and **II**.

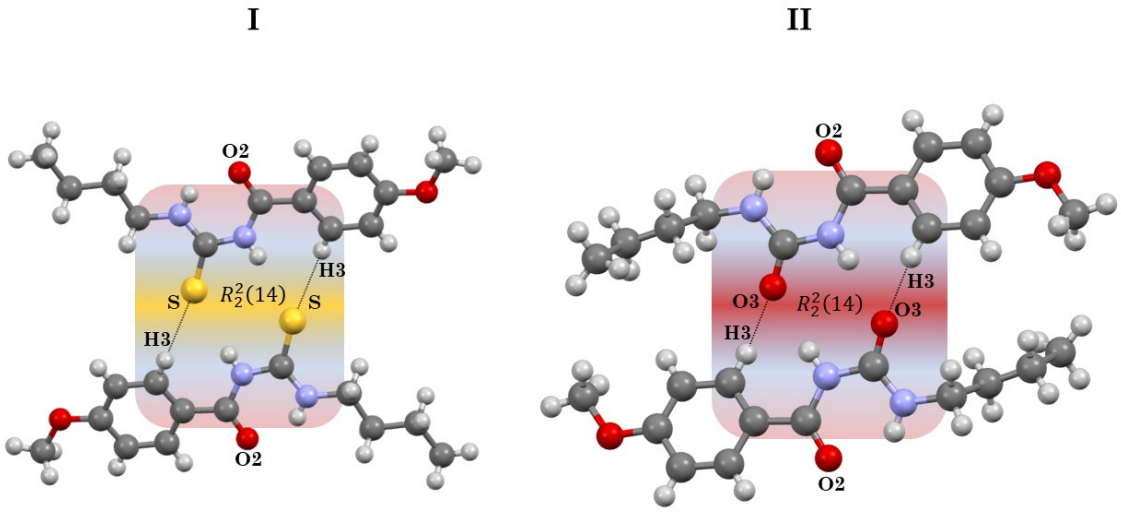



**Figure S8.** Dimers formed by the interaction C3-H3···S in **I** and C3-H3···O3 **II**.

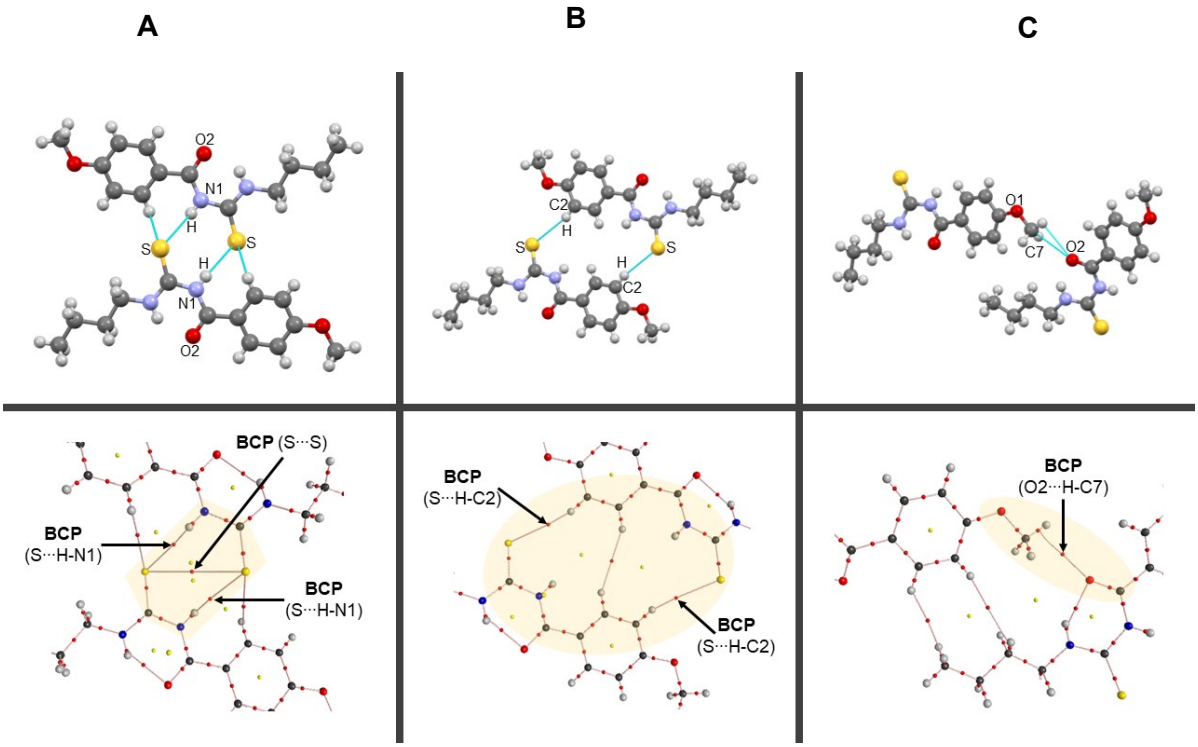



**Figure S9.** Dimers formed by the interaction N1-H···S (A), C2-H2···S (B) and $C7H_3$···O2 (C) in **I**.

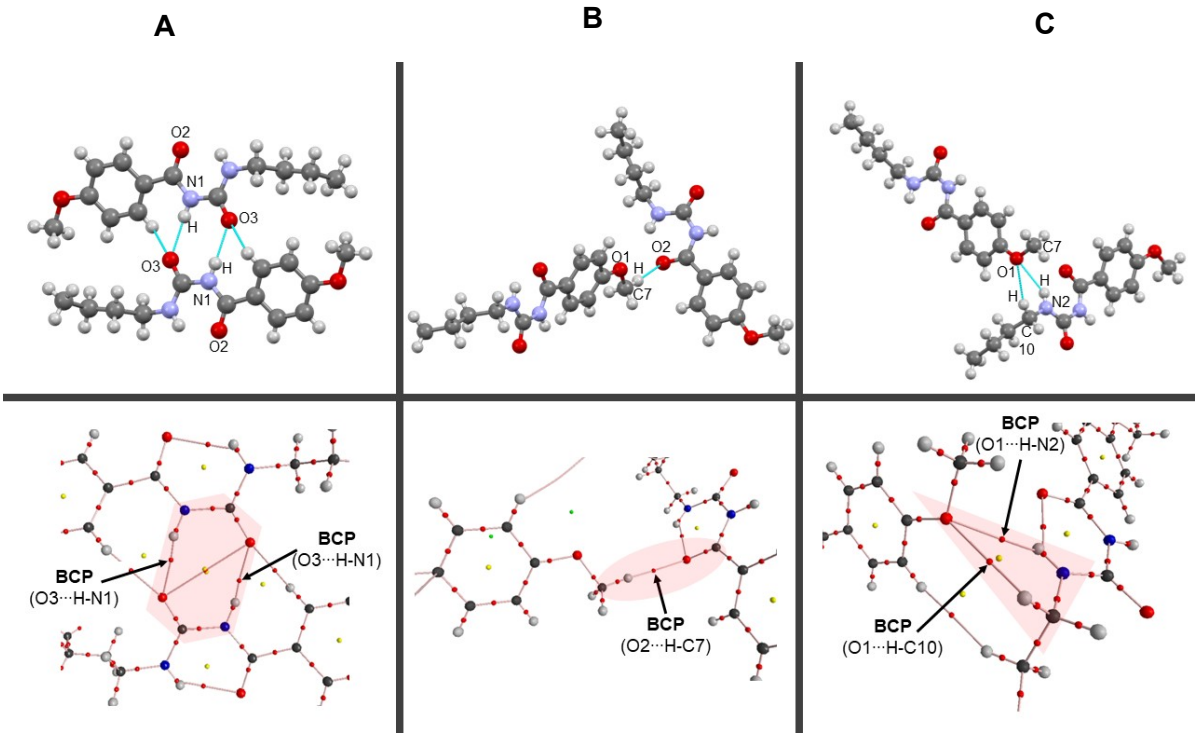



**Figure S10.** Dimers formed by the interaction N1-H···O3 (A), $C7H_3$···O2 (B) and N2-H2···O1 (C) in **II**.

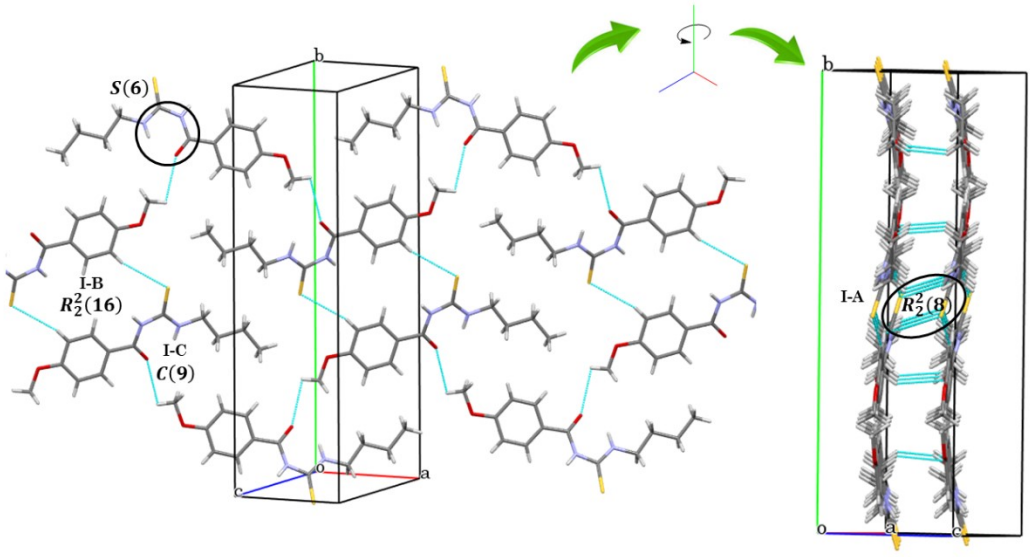



**Figure S11.** Motifs that form sheets in the crystalline packing of **I**.

In addition to the $R_2^2(8)$ motif associated with the I-A dimer, whose energy contributes to the stabilization of the layers in the packing (see Figure 7), $S(6)$, $R_2^2(16)$ y $C(9)$ motifs that form the sheets were identified in the crystalline packing of **I** (see Figure S11). These motifs correspond to the O2C8N1C9N2H pseudo ring, the ring found in the **I**-B dimer, and the chain established by the C7-H···O2 interaction displayed in the I-C dimer, respectively. These interactions are depicted in Figure S11. The sheets have a small curvature, as shown on the left side of Figure S11.

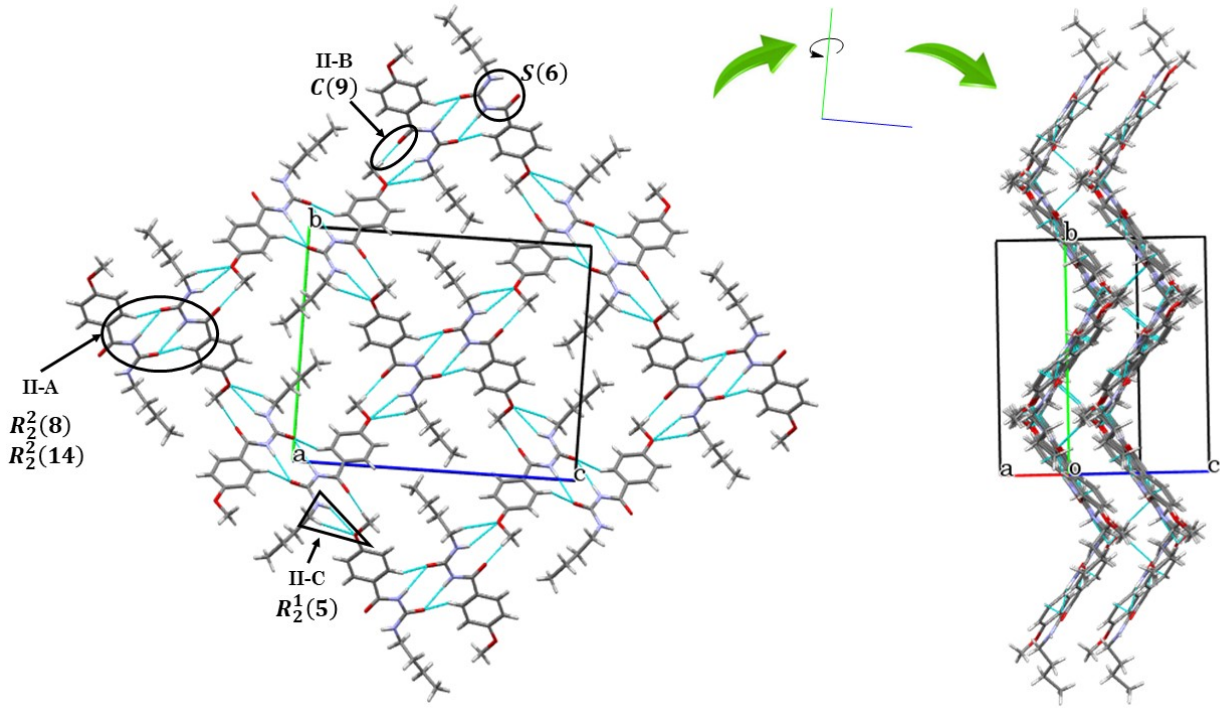
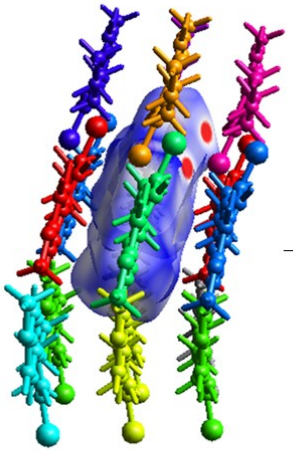



**Figure S12.** Motifs that form sheets in the crystal packing of **II**.

Likewise, motifs S(6) (of the intramolecular hydrogen bond N2H···O2), C(9) (**II**-B dimer) and $R_2^1(5)$ (**II**-C dimer) were identified in **II**. In addition, $R_2^2(8)$ is observed in dimer **II**-A, in which the $R_2^2(14)$motif is also formed, as shown in Figure S12. In this case, the indicated motifs are oriented in such a way that favor the formation of sheets, now in the zig-zag form, as represented on the right side of figure S12. The lattice energies (calculated as energy Frameworks) are studied later, as well as the interactions that stabilize the formation of layers in the crystal packing of **II**.

Comp. I



| Comp. | N | Symmetry | R | E_ele | E_pol | E_dis | E_rep | E_tot |
|---|---|---|---|---|---|---|---|---|
| I | 2 | x, y, z | 6.38 | -20,3 | -2,8 | **-103,6** | 38,6 | -88,2 |
| | 1 | -x, -y, -z | 7.87 | -7,6 | -3,6 | **-13,4** | 12,9 | -11,7 |
| | 2 | x, -y+1/2, z+1/2 | 10.62 | -11,2 | -3,3 | **-31,9** | 12,9 | -33,5 |
| | 2 | x, -y+1/2, z+1/2 | 7.98 | -1,7 | -1,2 | -17,4 | 4,1 | -16,2 |
| | 1 | x, y, z | 16.80 | -1,1 | -0,1 | -3,9 | 0,0 | -5,1 |
| | 1 | x, -y+1/2, z+1/2 | 15.59 | -0,2 | -0,2 | -3,0 | 0,0 | -3,4 |
| | 2 | x, y, z | 11.98 | -4,9 | -0,3 | -32,2 | 13,8 | -23,5 |
| | 1 | -x, -y, -z | 8.48 | -7,2 | -2,3 | -13,8 | 5,6 | -17,8 |
| | 1 | -x, -y, -z | 12.31 | -0,1 | -2,7 | **-17,4** | 0,0 | -20,3 |
| | 1 | -x, -y, -z | 6.59 | **-44,1** | -6,7 | -20,0 | 31,8 | -39,1 |
| | | **Total energy** | | **-98,3** | **-23,2** | **-256,8** | **119,5** | **-258,8** |
| II | 2 | x, y, z | 4,86 | -12,0 | -2,7 | **-100,0** | 31,4 | **-83,3** |
| | 2 | -x, y+1/2, -z+1/2 | 9,44 | -0,6 | -0,1 | -10,1 | 1,2 | -9,6 |
| | 2 | x, -y+1/2, z+1/2 | 11,5 | -4,9 | -0,6 | -14,6 | 16,2 | -3,9 |
| | 1 | -x, -y, -z | 5,57 | **-86,7** | -18,1 | -27,2 | 53,0 | **-79,0** |
| | 1 | -x, -y, -z | 5,72 | -7,8 | -3,9 | -23,3 | 5,5 | -29,6 |
| | 2 | -x, y+1/2, -z+1/2 | 8,97 | -20,9 | -2,7 | **-35,5** | 15,5 | **-43,7** |
| | 1 | -x, -y, -z | 15,9 | -0,2 | -0,1 | -11,2 | 0,0 | -11,5 |
| | 2 | -x, y+1/2, -z+1/2 | 10,9 | **-13,7** | -1,9 | -12,2 | 6,9 | **-20,9** |
| | 1 | -x, -y, -z | 14,4 | -1,0 | 0,0 | -3,7 | 0,0 | -4,6 |
| | | **Total energy** | | **-147,9** | **-30,1** | **-237,9** | **129,7** | **-286,2** |

Comp. II

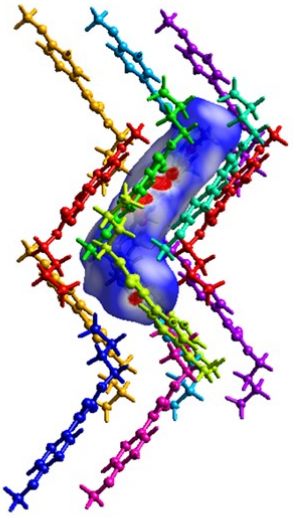


**Figure S13.** Interaction Energies (kJ/mol). Total energies, only reported for two benchmarked energy models, are the sum of the four energy components, scaled appropriately (CE-B3LYP ... B3LYP/6-31G(d,p) electron densities: k_ele, 1.057; k_pol, 0.740; k_disp, 0.871 and k_rep, 0.618).[1]

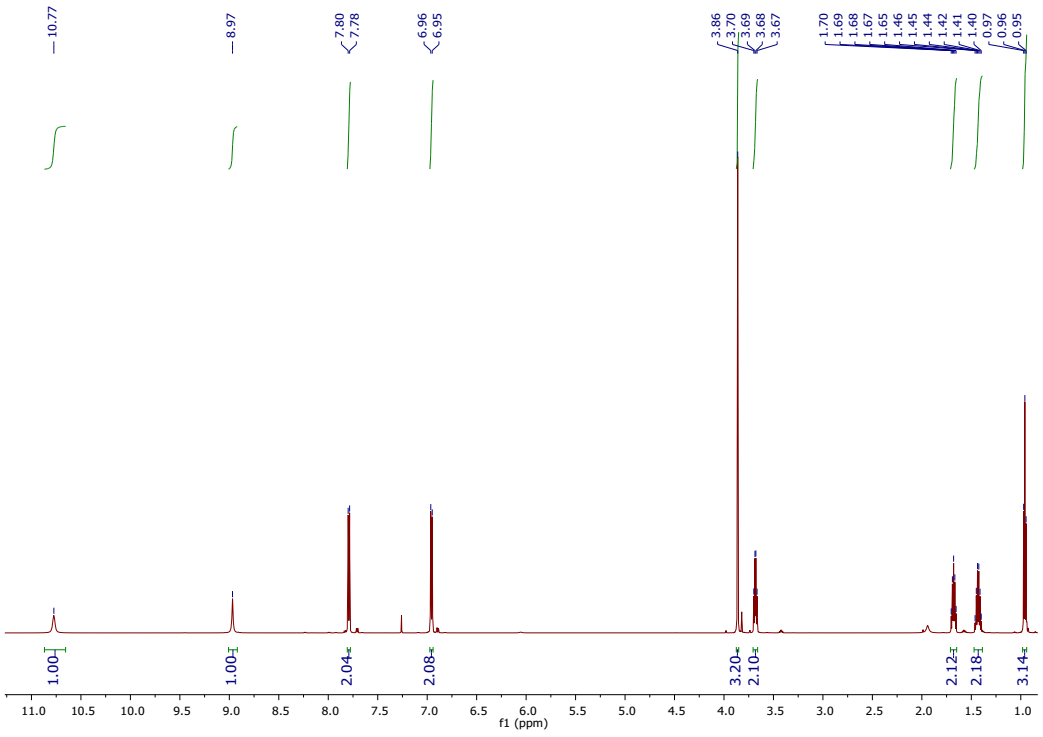



**Figure S14.** [1]H NMR of *N*-(butylcarbamothioyl)-4-methoxybenzamide (**I**).

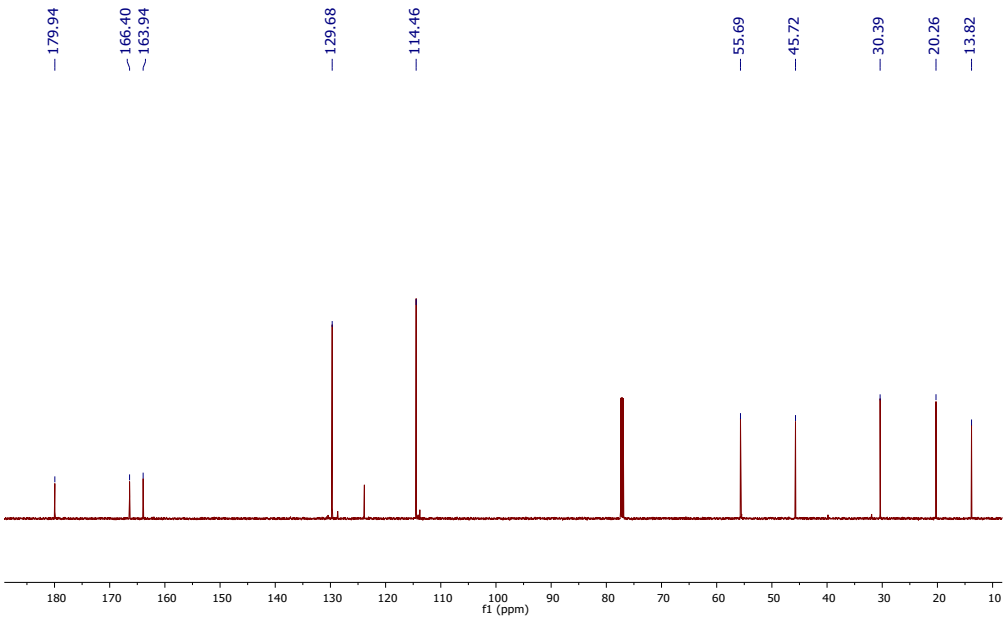



**Figure S15.** $^{13}$C NMR of *N*-(butylcarbamothioyl)-4-methoxybenzamide (**I**).

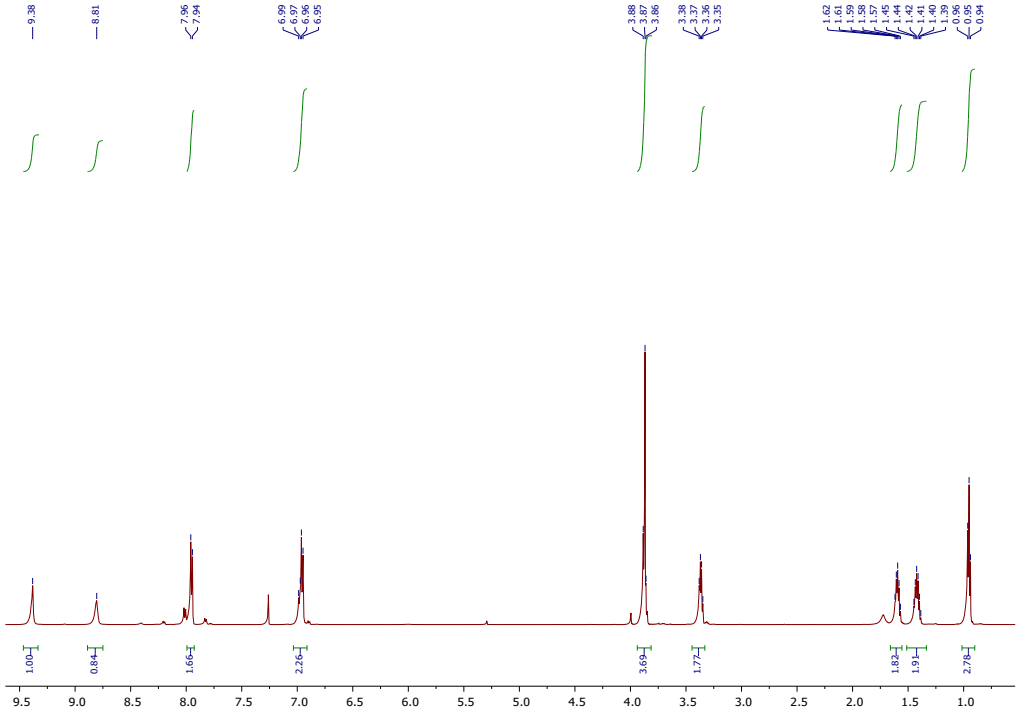



**Figure S16.** $^{1}$H NMR of *N*-(butylcarbamoyl)-4-methoxybenzamide (**II**).

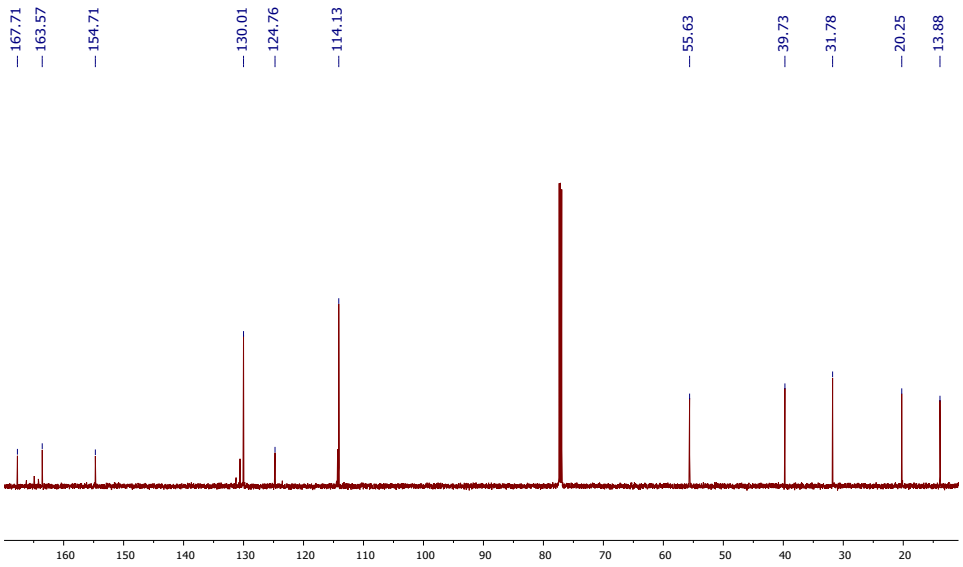



**Figure S17.** $^{13}C$ NMR of *N*-(butylcarbamoyl)-4-methoxybenzamide (**II**).

## Reference

1 M. A. Spackman, P. R. Spackman and S. P. Thomas, in *Complementary Bonding Analysis*, De Gruyter, 2021, pp. 329–352.