# Molecular structure and conformation flexibility of 2-oxo- and 2-thioxo-1,2,3,4-tetrahydropyrimidines and their derivatives

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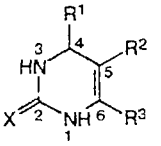
The conformational flexibility and effects of the substituents in 2-oxo- and 2-thioxo-1,2,3,4-tetrahydropyrimidines were studied by the semiempirical quantum-chemical AM1 method. The substituents at the double bond have no appreciable effect on the conformational characteristics of the heterocycle. The introduction of substituents to the saturated carbon atom results in the conversion of the tetrahydrocycle to a half-chair conformation and in a substantial decrease in the ring flexibility. The results of calculations are confirmed by the X-ray study of both compounds.

**Key words:** 2-oxo-1,2,3,4-tetrahydropyrimidine, 2-thioxo-1,2,3,4-tetrahydropyrimidine, conformational analysis, AM1, molecular structure, X-ray study.

Studies of the conformational flexibility of six-membered carbo- and heterocycles we had undertaken recently[1—3] showed that it is a property intrinsic in dihydrogenated rings of all types. The previously studied compounds contained two endocyclic double bonds. At the same time, the tetrahydropyrimidine cycle in the uracyl molecule was also shown to possess a high conformational flexibility.[4] In this connection it was of interest to study this property in other tetrahydro analogs of dihydroazines.

This work is dedicated to the investigation of the molecular structure and conformational flexibility of 2-oxo- and 2-thioxo-1,2,3,4-tetrahydropyrimidines as well as of their 4-phenyl-, 5-carbomethoxy-, and 6-methylsubstituted derivatives (**1—16**).



**1—16**

| Compound | X | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|---|
| **1** | O | H | H | H |
| **2** | O | H | H | Me |
| **3** | O | H | COOMe | H |
| **4** | O | Ph | H | H |
| **5** | O | H | COOMe | Me |
| **6** | O | Ph | H | Me |
| **7** | O | Ph | COOMe | H |
| **8** | O | Ph | COOMe | Me |
| **9** | S | H | H | H |
| **10** | S | H | H | Me |
| **11** | S | H | COOMe | H |
| **12** | S | Ph | H | H |
| **13** | S | H | COOMe | Me |
| **14** | S | Ph | H | Me |
| **15** | S | Ph | COOMe | H |
| **16** | S | Ph | COOMe | Me |

## Experimental

The structures of molecules **1—16** were calculated by the semiempirical quantum-chemical AM1 method[5] with full geometry optimization. The conformational flexibility of tetrahydro cycles was studied by scanning the C(=X)—N—C($sp^3$)—C= torsion angle in the ±30° interval for compounds **1—3**, **5**, **9—11**, **13** and in the +40° to −30° interval for molecules **4**, **6—8**, **12**, **14—16** with an increment of 10° and full optimization of the remaining geometric parameters of the molecules. The results of calculations are listed in Tables 1 and 2.

**X-ray study of compounds 20 and 21.** Crystals of compound **20** are triclinic. The parameters obtained at 20 °C are $a$ = 7.347(4), $b$ = 9.503(11), $c$ = 12.273(14) Å, α = 71.80(4)°, β = 88.38(4)°, γ = 70.31(4)°, $V$ = 777(1) Å$^3$, $d_{calc}$ = 1.519 g cm$^{-3}$, μ = 2.78 mm$^{-1}$, space group $P\bar{1}$, and $Z$ = 2. The intensities of 2755 independent reflections ($R_{int}$ = 0.08) were measured on an automatic four-circle Syntex $P2_1$ diffractometer (λ-Mo-Kα, β-filter, θ/2θ scan, $2\theta_{max}$ = 50°). The profile analysis of the totality of reflections obtained was performed using the PROFIT program.[6]

The structure was solved by direct methods using the SHELXTL PLUS 5.0 program package.[7] The absorption correction was introduced semiempirically using the ψ-scan data ($T_{min}$ = 0.603, $T_{max}$ = 0.891). The positions of hydrogen atoms were calculated geometrically and refined using the riding model with fixed $U_{iso}$ values for the C or N atom bonded to the corresponding H atoms ($U_{iso} = nU_{eq}$, $n$ = 1.5 for the H atoms

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of the methyl groups and 1.2 for the rest of the H atoms). The full-matrix LSM $F^2$-refinement in anisotropic approximation for nonhydrogen atoms using 2725 reflections was conducted to $R_1 = 0.084$ (for 896 reflections with $F > 4\sigma(F)$), $wR_2 = 0.222$, and S = 0.85. The final atomic coordinates are listed in Table 3, and the bond lengths and bond angles are given in Tables 4 and 5.

Crystals of compound **21** are triclinic. The parameters obtained at 20 °C are $a = 8.141(8)$, $b = 9.592(9)$, $c = 9.787(8)$ Å, $\alpha = 112.04.(7)°$, $\beta = 110.11(7)°$, $\gamma = 97.28(7)°$, $V = 682(3)$ Å$^3$, $d_{calc} = 1.478$ g cm$^{-3}$, $\mu = 0.23$ mm$^{-1}$, space group $P\bar{1}$, and $Z = 2$. The intensities of 4107 independent reflections ($R_{int} = 0.15$) were measured on an automatic four-circle Enraf-Nonius CAD-4 diffractometer ($\lambda$-Mo-K$\alpha$, graphite monochromator, $\theta/2\theta$ scan, $2\theta_{max} = 60°$).

The structure was solved by direct methods using the SHELXTL PLUS 4.2 program package.[8] The positions of hydrogen atoms were also calculated geometrically and refined using the riding model with a fixed $U_{iso} = 0.08$ Å$^2$. The full-matrix LSM $F$-refinement in anisotropic approximation for nonhydrogen atoms using 1660 reflections with $F > 6\sigma(F)$ was conducted to $R = 0.093$, $R_w = 0.099$, and S = 3.78. Atomic coordinates are listed in Table 3, and the bond lengths and bond angles are listed in Tables 4 and 5.

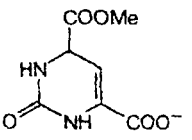
The conformation of the tetrahydropyrimidine cycle was described by the puckering parameters[9] (S is the degree of puckering, and $\theta$ and $\psi$ are polar angles defining the type of conformation).

## Results and Discussion

The equilibrium conformations of 2-oxotetrahydropyrimidine and 2-thioxotetrahydropyrimidine cycles are defined, on the one hand, by conjugation between the double bond, the lone electron pairs of the nitrogen atoms, and the exocyclic double bond and, on the other hand, by the 1,2-allylic strain in which hydrogen atoms of the methylene group are involved. Both these interactions favor a planar equilibrium conformation of the tetrahydro cycle. On the other hand, such a geometry of the ring causes an appreciable distortion of the endocyclic bond angle at the saturated carbon atom.

In accordance with the data of the calculations, the equilibrium conformation of the partly hydrogenated cycle in unsubstituted molecules **1** and **9** is planar, which is evidence of the prevailing effect of flattening factors. Introduction of substituents to the atoms of the double C=C bond, as well as in the case of related dihydro cycles,[10,11] does not result in violation of planar geometry of the tetrahydropyrimidine ring.

Replacement of one of the hydrogen atoms of the methylene group by a substituent leads to violation of the symmetry of the nonvalence interactions along the C($sp^2$) — C($sp^3$) and N—C($sp^3$) bonds and to conversion of the cycle to a conformation intermediate between a half-chair and a sofa (Table 1), analogously to 1,4-dihydro cycles.[10,12] Introduction of substituents to the double C=C bond results in adoption of a half-chair conformation by the tetrahydropyrimidine ring owing to nonvalence interactions with the hydrogen atoms of the adjacent methylene and imino groups. In this case, the conformation of the enone fragment (either *s-cis* or *s-trans*) has little effect on the geometry of the partly hydrogenated ring. The results of calculations are in agreement with the data of the X-ray study of compound **17**.[13]




**17**

In trisubstituted derivatives **8** and **16**, the equilibrium conformation of the heterocycle is less twisted (the $\psi$ angle, Table 1). In all cases, the introduction of substituents to the atoms of the double C=C bond results in a drastic increase in the degree of puckering of the tetrahydro cycle. A comparison of the geometry of compounds **18** and **19** [14,15] shows that increasing the size of

**Table 1.** Some torsion angles ($\alpha$), puckering parameters of the tetrahydropyrimidine cycle, and relative energies of the *s-cis* — *s-trans*-conversion ($\Delta E$/kcal mol$^{-1}$) of the conformers in compounds **4**, **6**—**8**, **12**, and **14**—**16**

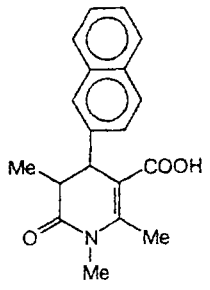
| Compound | Conformation | Puckering parameters | | | α/deg | | $\Delta E$** |
|---|---|---|---|---|---|---|---|
| | | S | θ | Ψ | $\alpha_1$ | $\alpha_2$ | |
| **4** | | 0.10 | 49.7 | 7.0 | — | −124.8 | |
| **6** | | 0.09 | 52.3 | 15.1 | — | −125.9 | |
| **7** | *s-cis* | 0.31 | 50.1 | 25.9 | 12.3 | −108.7 | 0.46 |
| | *s-trans* | 0.29 | 50.0 | 26.1 | −165.9 | −110.2 | 0 |
| **8** | *s-cis* | 0.35 | 52.3 | 21.6 | 12.1 | −105.6 | 0 |
| | *s-trans* | 0.33 | 53.1 | 22.8 | −162.5 | −107.5 | 0.47 |
| **12** | | 0.07 | 62.0 | 1.6 | — | −128.8 | |
| **14** | | 0.09 | 52.7 | 27.3 | — | −126.6 | |
| **15** | *s-cis* | 0.29 | 53.3 | 24.0 | 14.1 | 109.0 | 0.70 |
| | *s-trans* | 0.26 | 52.3 | 24.4 | −164.7 | 111.7 | 0 |
| **16** | *s-cis* | 0.29 | 55.9 | 20.3 | 14.5 | −108.1 | 0 |
| | *s-trans* | 0.26 | 55.6 | 25.1 | −165.7 | −106.3 | 2.40 |

* Torsion angles are: C=C—C=O ($\alpha_1$), and C=C—C—$C_{Ar}$ ($\alpha_2$).
** $\Delta E$/kcal mol$^{-1}$: 0 (*s-cis*-**3**), 0.13 (*s-trans*-**3**); 0 (*s-cis*-**5**), 0.92 (*s-trans*-**5**); 0 (*s-cis*-**11**), 0.10 (*s-trans*-**11**); and 0 (*s-cis*-**13**), 1.16 (*s-trans*-**13**).

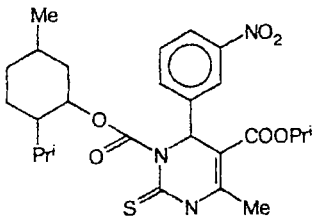
**Table 2.** The energy changes (kcal mol$^{-1}$) at different torsion angles in compounds **1**—**3**, **5**, **9**—**11**, and **13**

| Compound | Conformer | Torsion angle/deg | | | |
|---|---|---|---|---|---|
| | | 0 | 10 | 20 | 30 |
| **1** | | 0 | 0.1 | 0.4 | 1.1 |
| **2** | | 0 | 0.1 | 0.4 | 1.1 |
| **3** | *s-cis* | 0 | 0.1 | 0.4 | 1.1 |
| | *s-trans* | 0 | 0.1 | 0.4 | 1.0 |
| **5** | *s-cis* | 0 | 0.1 | 0.4 | 1.0 |
| | *s-trans* | 0 | 0.1 | 0.3 | 0.8 |
| **9** | | 0 | 0.1 | 0.4 | 1.1 |
| **10** | | 0 | 0.1 | 0.4 | 1.0 |
| **11** | *s-cis* | 0 | 0.1 | 0.4 | 1.0 |
| | *s-trans* | 0 | 0.1 | 0.4 | 0.9 |
| **13** | *s-cis* | 0 | 0.1 | 0.4 | 0.9 |
| | *s-trans* | 0 | 0.1 | 0.3 | 0.8 |

the substituents at the atoms adjacent to the saturated carbon atom strongly affects the degree of puckering of the heterocycle.



**18**

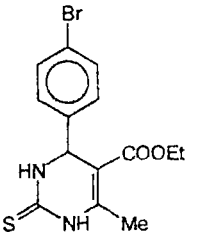


**19**

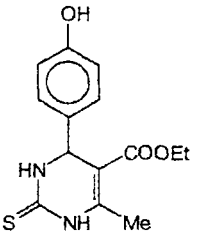
| Compound | S | θ | ψ |
|---|---|---|---|
| **17** | 0.22 | 38.4° | 29.3° |
| **18** | 0.39 | 42.1° | 11.8° |
| **19** | 0.68 | 29.3° | 26.1° |

Unlike **17**, the phenyl substituent at the saturated carbon atom in compounds **4**, **6**, **12**, and **14** has a pseudoequatorial orientation. The introduction of an ester group to position 5 of the tetrahydro cycle gives rise to unfavorable nonvalence interactions between the substituents and, hence, in destabilization of the pseudoequatorial orientation (molecules **7**, **8**, **15**, and **19**).

An X-ray study of compounds **20** and **21** (Fig. 1, *a*, *b*; Tables 4 and 5) showed that the tetrahydropyrimidine ring has a half-chair conformation in both substances.



**20**



**21**

| Compound | S | θ | ψ |
|---|---|---|---|
| **20** | 0.38 | 33.0 | 13.5 |
| **21** | 0.30 | 24.0 | 15.9 |

The aryl substituents at the saturated carbon atom have a pseudoaxial orientation (the C(4)-C(3)-C(2)-C(5) torsion angle is equal to 100(1)° and −107.5(7)° for **20** and **21**, respectively). The enone fragment has the *s-trans*-conformation in structure **20** and the *s-cis*-conformation in **21** (the C(4)—C(3)—C(11)—O(1) torsion angle is equal to 165(1)° and 5(2)°, respectively). The carbonyl group of the ester substituent has the sp-conformation relative to the O(2)—C(12) bond (the O(1)—C(11)—O(2)—C(12) torsion angle is equal to 1(1)° and 15(2)° for **20** and **21**, respectively). The molecules considered differ in the conformation of the terminal methyl group of the substituent in question relative to the O(2)—C(11) bond: ap (**20**) and +sc (**21**) (the C(11)—O(2)—C(12)—C(13) torsion angle is equal to 168(1)° and 76(1)°, respectively).

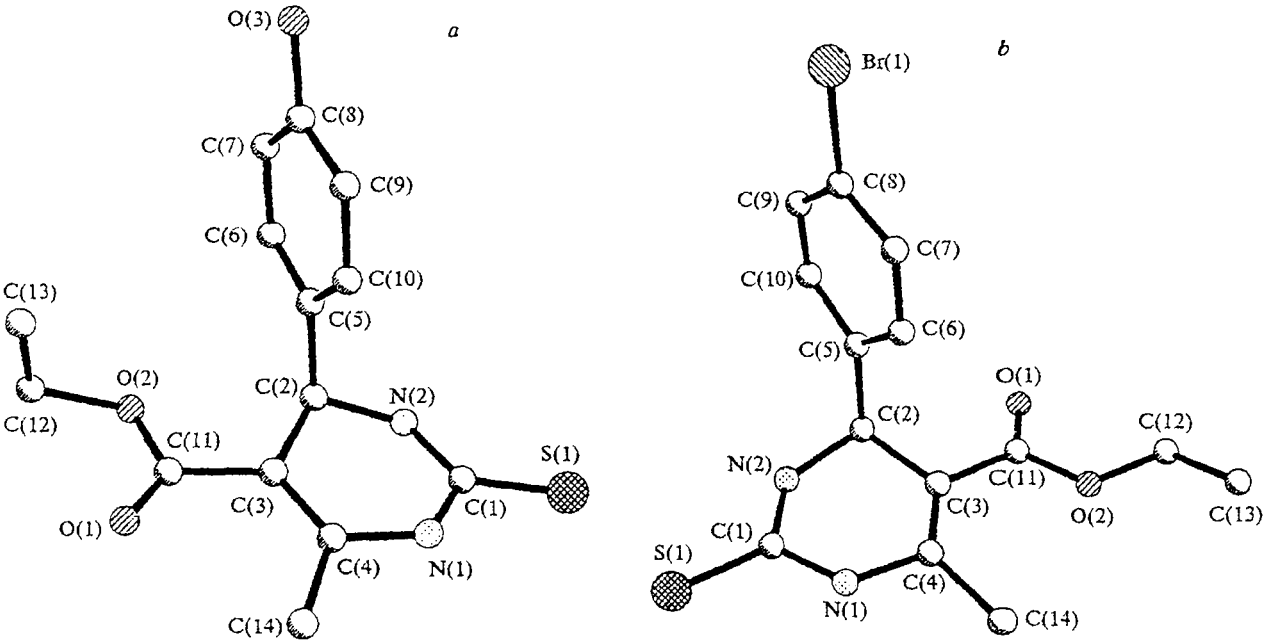



**Fig. 1.** The structure of molecules **20** (*a*) and **21** (*b*) (hydrogen atoms are not shown).

Unfavorable nonvalence interactions between the O(2)...C(14) [2.77 Å] (the sum of the van der Vaals radii is equal to 3.00 Å [16]) and O(2)...H(14A) [2.32 Å] (2.45 Å) atoms in the structure of **20** lead to an essential distortion of the exocyclic bond angles at the C(3) and C(4) atoms (see Table 5). An analogous but a much less pronounced effect is also observed in molecule **21** (see Table 5, the shortened intermolecular C(14)....O(1) and H(14C)....O(1) contacts of length 2.78 Å and 2.37 Å, respectively). Thus, one can conclude that the *s-cis*-orientation of the enone fragment in the compounds in question is less sterically strained.

**Table 3.** Coordinates ($\times 10^4$) and equivalent isotropic thermal parameters ($\times 10^3$/Å$^2$) of non-hydrogen atoms in structures **20** and **21**

| Atom | *x* | *y* | *z* | *U*(eq) |
|---|---|---|---|---|
| | | Molecule **20** | | |
| Br(1) | 223(2) | 7727(2) | 9090(1) | 94(1) |
| S(1) | 8043(4) | 4007(3) | 14602(2) | 54(1) |
| N(1) | 7750(11) | 1796(8) | 13753(6) | 41(2) |
| N(2) | 4915(12) | 3366(9) | 14204(6) | 43(2) |
| O(1) | 2126(11) | 532(8) | 13484(6) | 67(2) |
| O(2) | 4810(10) | −851(8) | 12814(6) | 63(2) |
| C(1) | 6806(14) | 3043(11) | 14165(7) | 35(2) |
| C(2) | 3734(12) | 2806(9) | 13619(7) | 34(2) |
| C(3) | 4945(15) | 1209(10) | 13487(7) | 37(2) |
| C(4) | 6836(16) | 805(11) | 13501(8) | 44(3) |
| C(5) | 2806(14) | 4004(11) | 12485(7) | 42(3) |
| C(6) | 3545(14) | 3801(11) | 11459(8) | 45(3) |
| C(7) | 2755(16) | 4900(12) | 10453(8) | 57(3) |
| C(8) | 1260(14) | 6240(12) | 10456(8) | 53(3) |
| C(9) | 461(11) | 6416(9) | 11528(7) | 20(2) |
| C(10) | 1231(14) | 5388(12) | 12391(10) | 56(3) |
| C(11) | 3781(17) | 302(11) | 13296(8) | 45(3) |
| C(12) | 3743(15) | −1780(11) | 12528(9) | 59(3) |
| C(13) | 5005(19) | −2674(16) | 11829(13) | 115(6) |
| C(14) | 8349(14) | −670(11) | 13354(9) | 62(3) |
| | | Molecule **21** | | |
| S(1) | 401(2) | 1799(2) | 2470(2) | 46(1) |
| N(1) | −2425(6) | 2730(5) | 2186(5) | 36(2) |
| N(2) | −1999(8) | 1017(6) | −21(5) | 47(2) |
| O(1) | −7252(9) | 2619(8) | −235(8) | 99(4) |
| O(2) | −6641(7) | 1045(8) | −2274(6) | 88(3) |
| O(3) | −1568(6) | 4439(5) | −4430(4) | 48(2) |
| C(1) | −1423(8) | 1854(6) | 1478(6) | 34(2) |
| C(2) | −3429(9) | 1177(6) | −981(6) | 44(3) |
| C(3) | −4589(8) | 1904(6) | −34(6) | 40(2) |
| C(4) | −4038(7) | 2669(6) | 1505(6) | 34(2) |
| C(5) | −2899(8) | 2075(6) | −1883(6) | 37(2) |
| C(6) | −3084(8) | 1331(6) | −3435(6) | 41(2) |
| C(7) | −2641(9) | 2124(8) | −4279(7) | 53(3) |
| C(8) | −1988(7) | 3681(6) | −3561(6) | 36(2) |
| C(9) | −1756(9) | 4449(7) | −2001(6) | 43(2) |
| C(10) | −2234(9) | 3628(7) | −1195(6) | 47(3) |
| C(11) | −6311(11) | 1917(11) | −809(9) | 68(4) |
| C(12) | −8150(11) | 1434(11) | −3095(11) | 86(5) |
| C(13) | −7747(12) | 2861(11) | −3279(11) | 91(5) |
| C(14) | −5013(8) | 3448(8) | 2571(7) | 48(3) |

**Table 4.** Bond lengths (*d*) in structures **20** and **21**

| Molecule **20** | | Molecule **21** | |
|---|---|---|---|
| Bond | *d*/Å | Bond | *d*/Å |
| Br(1)—C(8) | 1.87(1) | S(1)—C(1) | 1.644(6) |
| S(1)—C(1) | 1.673(9) | N(1)—C(1) | 1.337(8) |
| N(1)—C(1) | 1.37(1) | N(1)—C(4) | 1.348(8) |
| N(1)—C(4) | 1.42(1) | N(2)—C(1) | 1.339(7) |
| N(2)—C(1) | 1.32(1) | N(2)—C(2) | 1.425(9) |
| N(2)—C(2) | 1.45(1) | O(1)—C(11) | 1.16(1) |
| O(1)—C(11) | 1.19(1) | O(2)—C(11) | 1.317(9) |
| O(2)—C(11) | 1.37(1) | O(2)—C(12) | 1.51(1) |
| O(2)—C(12) | 1.47(1) | O(3)—C(8) | 1.368(9) |
| C(2)—C(3) | 1.53(1) | C(2)—C(3) | 1.49(1) |
| C(2)—C(5) | 1.55(1) | C(2)—C(5) | 1.52(1) |
| C(3)—C(4) | 1.31(1) | C(3)—C(4) | 1.363(7) |
| C(3)—C(11) | 1.46(1) | C(3)—C(11) | 1.48(1) |
| C(4)—C(14) | 1.52(1) | C(4)—C(14) | 1.461(9) |
| C(5)—C(6) | 1.39(1) | C(5)—C(6) | 1.385(7) |
| C(5)—C(10) | 1.41(1) | C(5)—C(10) | 1.371(8) |
| C(6)—C(7) | 1.38(1) | C(6)—C(7) | 1.38(1) |
| C(7)—C(8) | 1.37(1) | C(7)—C(8) | 1.374(8) |
| C(8)—C(9) | 1.45(1) | C(8)—C(9) | 1.388(8) |
| C(9)—C(10) | 1.23(1) | C(9)—C(10) | 1.37(1) |
| C(12)—C(13) | 1.46(1) | C(12)—C(13) | 1.45(2) |

**Table 5.** Bond angles (φ) in structures **20** and **21**

| Molecule **20** | | Molecule **21** | |
|---|---|---|---|
| Angle | φ/deg | Angle | φ/deg |
| C(1)—N(1)—C(4) | 123.6(8) | C(1)—N(1)—C(4) | 123.1(4) |
| C(1)—N(2)—C(2) | 126.2(7) | C(1)—N(2)—C(2) | 125.8(6) |
| C(11)—O(2)—C(12) | 116.2(8) | C(11)—O(2)—C(12) | 109.2(7) |
| N(2)—C(1)—N(1) | 114.8(8) | S(1)—C(1)—N(1) | 119.4(4) |
| N(2)—C(1)—S(1) | 124.6(7) | S(1)—C(1)—N(2) | 123.2(5) |
| N(1)—C(1)—S(1) | 120.6(7) | N(1)—C(1)—N(2) | 117.4(5) |
| N(2)—C(2)—C(3) | 109.3(7) | N(2)—C(2)—C(3) | 108.7(5) |
| N(2)—C(2)—C(5) | 111.0(7) | N(2)—C(2)—C(5) | 112.3(6) |
| C(3)—C(2)—C(5) | 113.5(7) | C(3)—C(2)—C(5) | 111.9(6) |
| C(4)—C(3)—C(11) | 126.6(9) | C(2)—C(3)—C(4) | 121.4(6) |
| C(4)—C(3)—C(2) | 119.8(9) | C(2)—C(3)—C(11) | 118.5(5) |
| C(11)—C(3)—C(2) | 113.5(9) | C(4)—C(3)—C(11) | 119.8(6) |
| C(3)—C(4)—N(1) | 119.4(9) | N(1)—C(4)—C(3) | 119.2(6) |
| C(3)—C(4)—C(14) | 130.2(9) | N(1)—C(4)—C(14) | 113.3(5) |
| N(1)—C(4)—C(14) | 110.2(9) | C(3)—C(4)—C(14) | 127.5(6) |
| C(6)—C(5)—C(10) | 114.4(9) | C(2)—C(5)—C(6) | 120.3(5) |
| C(6)—C(5)—C(2) | 121.1(8) | C(2)—C(5)—C(10) | 121.5(5) |
| C(10)—C(5)—C(2) | 124.4(8) | C(6)—C(5)—C(10) | 118.2(6) |
| C(7)—C(6)—C(5) | 120.9(9) | C(5)—C(6)—C(7) | 121.3(5) |
| C(8)—C(7)—C(6) | 120.2(9) | C(6)—C(7)—C(8) | 119.2(5) |
| C(7)—C(8)—C(9) | 118.3(8) | O(3)—C(8)—C(7) | 117.9(5) |
| C(7)—C(8)—Br(1) | 119.7(8) | O(3)—C(8)—C(9) | 121.5(5) |
| C(9)—C(8)—Br(1) | 121.9(7) | C(7)—C(8)—C(9) | 120.6(7) |
| C(10)—C(9)—C(8) | 117.9(8) | C(8)—C(9)—C(10) | 118.8(5) |
| C(9)—C(10)—C(5) | 128.1(9) | C(5)—C(10)—C(9) | 121.9(5) |
| O(1)—C(11)—O(2) | 122(1) | O(1)—C(11)—O(2) | 123.6(8) |
| O(1)—C(11)—C(3) | 126.1(9) | O(1)—C(11)—C(3) | 125.7(7) |
| O(2)—C(11)—C(3) | 111.7(9) | O(2)—C(11)—C(3) | 110.6(7) |
| C(13)—C(12)—O(2) | 105.2(9) | O(2)—C(12)—C(13) | 114.1(7) |

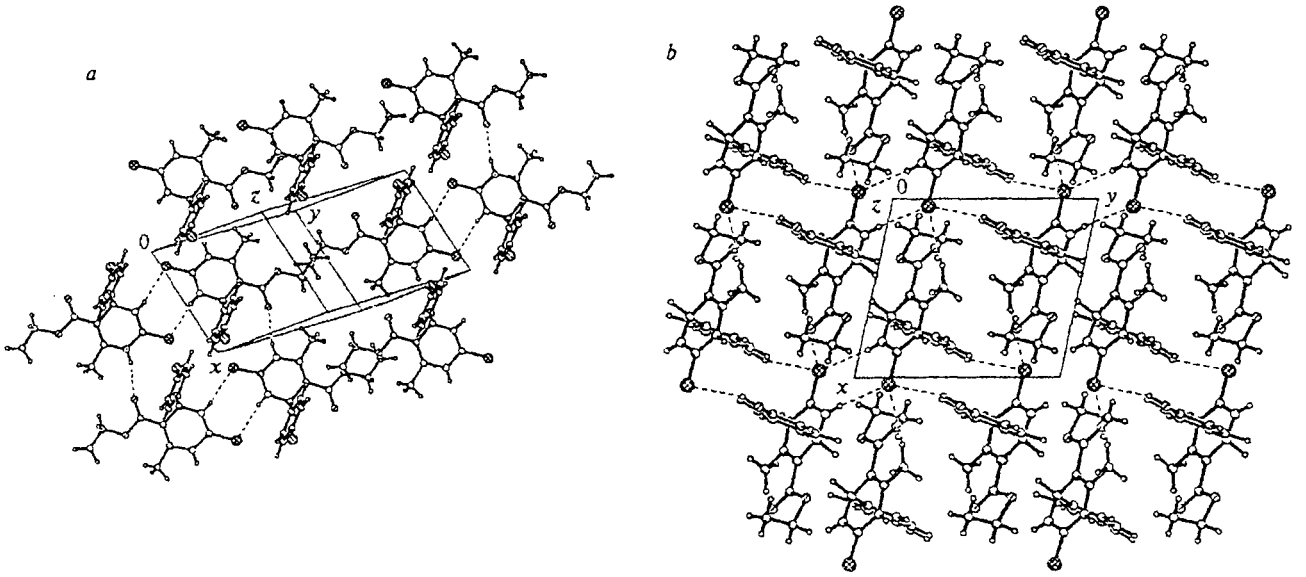



**Fig. 2.** General view of the layer in the crystals of compounds **20** (*a*) and **21** (*b*).

The crystal structures of compounds **20** and **21** differ significantly. The molecules of **20** are bound by weak hydrogen H(1N)...O(1)′ (1 + *x*, *y*, *z*) (O...H 2.23 Å, O...H—N 167°) and S(1)...H(2N)′ (1 − *x*, 1 − *y*, 3 − *z*) (S...H 2.51 Å, S...H—N 165°) bonds to form layers (Fig. 2, *a*). Molecules of **21** are bound by a three-dimensional network (Fig. 2, *b*) due to the intermolecular hydrogen O(3)....H(1N)′ bonds (*x*, *y*, 1 − *z*) (O...H 2.14 Å, O....H—N 167°) and the shortened intermolecular H(14C)....S(1)′ (−1 + *x*, *y*, *z*) [2.89 Å] (the sum of the van der Vaals radii is equal to 3.00 Å [16]), H(2N)...S(1)′ (−*x*, −*y*, −*z*) [2.66 Å], H(30).... S(1)′ (−*x*, 1 − *y*, −*z*) [2.49 Å], and H(12B)... C(7)′ (−1 − *x*, −*y*, −1 − *z*) [2.83 Å] contacts.

As a whole, the results of calculations of molecule **16** coincide with the experimental data for structures **20** and **21**, which is evidence in favor of the possibility to use the AM1 method for conformational analysis of such compounds.

Previously,[1–4] we have established that the presence of two groups of factors acting in opposite directions, which define the conformation of the molecule, results in a high conformational flexibility of the dihydro cycle. The AM1 calculations showed that the tetrahydropyrimidinone and tetrahydropyrimidinethione rings are conformationally nonrigid. Conversion from a planar equilibrium conformation to a half-chair with a C—N—C($sp^3$)—C= torsion angle of ±30° results in a 1.1 kcal $mol^{-1}$ increase in the energy of molecule (Table 2). The introduction of substituents to the atoms of the double C=C bond has no considerable effect on this property of the partly hydrogenated ring. Among compounds **3**, **5**, **11**, and **13**, the molecules with the *s-trans*-configuration of the enone fragment are somewhat more flexible than those with the *s-cis*-conformation, which is in agreement with the conclusion of their different steric crowding. Introduction of a phenyl substituent to the saturated carbon atom results in an increase in conformational rigidity of the tetrahydrocycle due to the substantial increase in the allylic strain (Fig. 3).

The substituents at the double bonds in phenyl-substituted compounds **6**, **7**, **14**, and **15** also have little effect on the cycle flexibility. However, in the case of trisubstituted **8** and **16**, the partly hydrogenated ring becomes much more rigid (Fig. 3). This is due likely to the close proximity of the ester group and the substituents at the saturated carbon atom (the $C_{Ar}$ and H atoms)

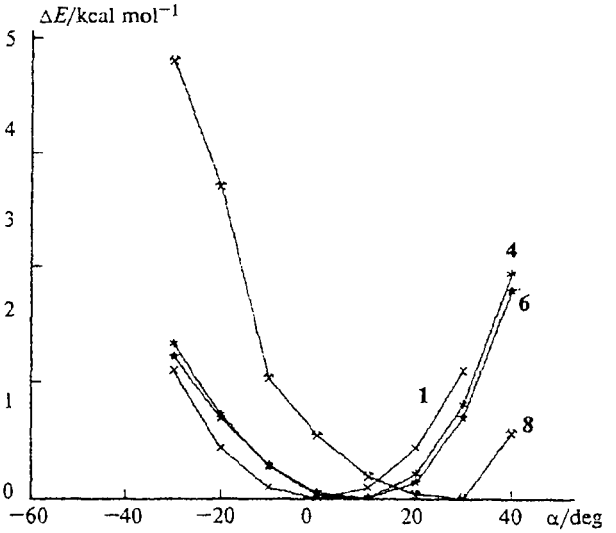



**Fig. 3.** Dependence of the energy change on the C—N—C($sp^3$)—C= torsion angle in molecules **1**, **4**, **6**, and **8**.

due to the mutual repulsion between the substituent and the vicinal methyl group.

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