Tetrahedron Letters No. 48, pp 4245 - 4248, 1977. Pergamon Press. Printed in Great Britain.

ON THE FORMATION OF A NEW HETEROCYCLIC RING SYSTEM: REACTIONS AND THE CRYSTAL STRUCTURE OF 3-BENZOYLIMINO-4-METHYL-PERHYDRO-1,2,4-OXATHIAZINE

Sándor Sólyom, Pál Sohár and Lajos Toldy
Research Institute for Pharmaceutical Chemistry
H-1325-Budapest, POB 82., Hungary

Alajos Kálmán* and László Párkányi
Central Research Institute for Chemistry, Hungarian
Academy of Sciences, H-1525-Budapest, POB 17., Hungary

(Received in UK 29 September 1977; accepted for publication 6 October 1977)

A synthesis of 1,2,4-oxathiazines as a new class of heterocyclic compounds - the cyclic analogues of the open chained sulfenic acid esters - has been developed by oxidizing N-acyl-N'-(β -hydroxyethyl)-thioureas with bromine. So e.g. oxidation of compound 1[1] (Figure 1) in pyridine with bromine produced the title compound[2] (hereinafter 2). The structure of 2 (mp: 173°) was inferred from chemical and spectroscopic[3] investigations.

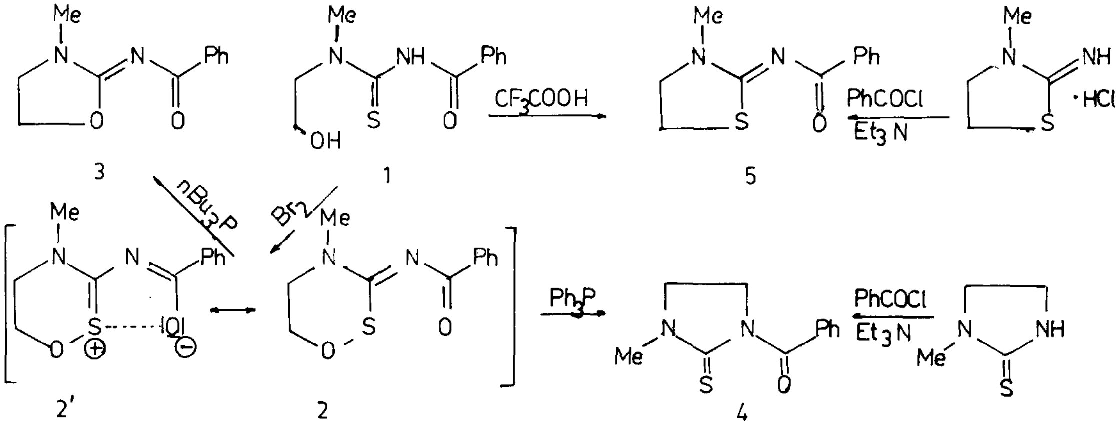

Figure 1.

Because of the presence of the monothioperoxide group, 2 liberates iodine from KI and can be titrated iodometrically. Reduction of 2 with $NaBH_4$ resulted in 1 (50% yield) and also produced some elemental sulphur. The reaction of 2 with nBu_3P yielded 3 (mp: 85°) quantitatively. Structure 3 was proved by the

νC=O and νC=N absorption (1635 and 1590 cm^{-1}), the AA'BXX' type multiplet of the benzoyl protons[4] and also by the absorption of the OCH$_2$ group in the ^{1}H- and ^{13}C-n.m.r. (4.50 and 65.6 ppm) spectra. The less nucleophilic Ph$_3$P transformed 2 in a slower reaction (5-6 days) into a homogeneous product 4 (mp:111°) with a yield of about 40%. 5 as a possible product of this reaction had to be rejected due the absence of the AA'BXX' multiplet of the ring protons in ^{1}H-n.m.r. which is characteristic of the analogous compound 3. This conclusion was corroborated by two independent syntheses of 5 (mp: 101-2°) as depicted in Figure 1. The structure 4 was finally established by an other synthesis by benzoylating the known 1-methyl-imidazolidin-2-thione[5].

Although a carbonyl-carbon signal at 177.3 ppm was found in the ^{13}C-n.m.r. of 2, the absence of the i.r. absorption in the region of 1600-1800 cm^{-1} and the novelty of the heterocyclic ring system claimed to corroborate the molecular structure by X-ray diffraction.

The structure was solved with XTL version of MULTAN supplied by Syntex and refined to R = 0.060 for 2257 reflexions with $I - 1.96\sigma(I) > 0$ out of the total 3220 intensities recorded on a Syntex P2$_1$ diffractometer using MoK$_{\bar{\alpha}}$ radiation. The lattice parameters are: $\underline{a}$ = 7.402(1), $\underline{b}$ = 10.916(2), $\underline{c}$ = 14.827(2) Å, β = 112.83(2)°, D_x = 1.42, D_m = 1.40 g.cm^{-3}, Z = 4, space group P2$_1$/c, F(000) = 496, μ(MoK$_{\bar{\alpha}}$, $\bar{\lambda}$ = 0.71069 Å) = 2.8 cm^{-1}. Fractional coordinates of the heavy atoms are given in Table 1, the hydrogen coordinates (the methyl hydrogens were located in a difference map, while the positions of the others were generated) are presented in Table 2. The structure obtained (Figure 2) confirmed formula 2 and revealed a rather short intramolecular S...O approach (2.255 Å) which is considerably less than the sum of the van der Waals radii (ca. 3.25 Å)[6]. This strong S...O interaction with a σ-bond order[7] of 0.64 and the accompanying increased C=O distance (1.247 Å) explain the anomalous i.r. spectra and suggest that the 2$\leftrightarrow$2' mesomerism may be taken also into account in the description of the molecular structure.

The oxathiazine ring is of a half-chair conformation with low asymmetry parameter (ΔC_2 = 1.25°)[8]. The C=O group forms a five-membered ring with the S(2)-C(3)-N(7) moiety which has a flat envelope conformation [Δ= 17.8° if

φ_o is[9] assigned to the rotation about S(2) - O(9)]. The plane of the phenyl ring [maximum deviation from the least-squares plane: 1.5860X + 8.6555Y + 8.0584Z + 0.4836 = 0 is 0.006 Å] is tilted to the best plane [3.1162X - 6.9723Y + 6.3792Z - 1.3606 = 0] of the five-membered ring by an angle of 12.6°. Due to the strong interaction between the thiourea group and the benzoyl moiety no localized exocyclic (with respect to the six-membered ring) C=N double bond could be formed, which is characteristic in the case of the rather similar 2-arylimino-1,3-thiazines[10] where the endocyclic oxygen is replaced by a CH_2 group. As can be seen a strong delocalized multiple bond system is formed on the five-membered ring extending also to the N(4) atom.

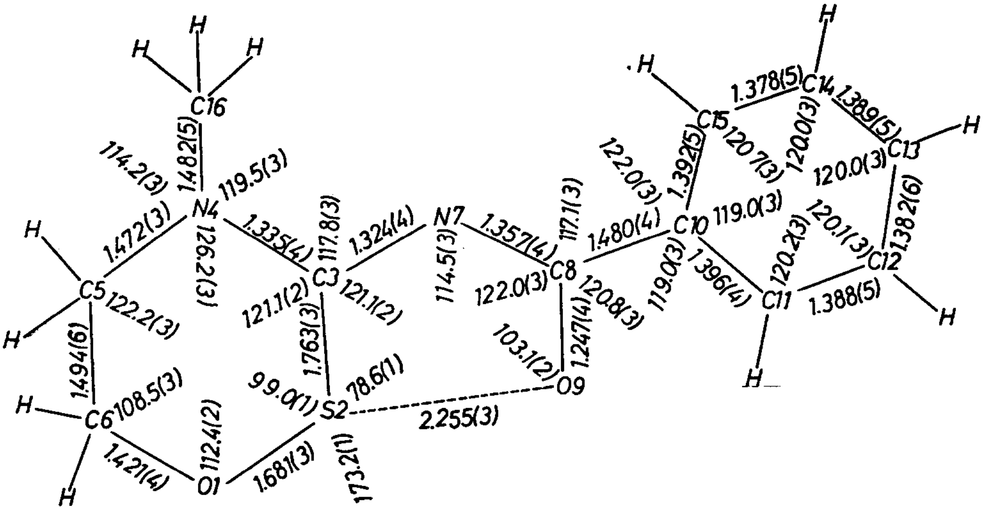

Figure 2. Atomic distances and bond angles with their e.s.d.'s

Table 1. Atomic coordinates (x10^4) and their e.s.d.'s for heavy atoms

	x	y	z		x	y	z
O(1)	7092(4)	1154(2)	0445(2)	O(9)	10126(3)	4123(2)	1575(2)
S(2)	8250(1)	2479(1)	0893(1)	C(10)	13056(4)	4958(3)	1336(2)
C(3)	9713(4)	2578(3)	0199(2)	C(11)	13251(5)	5779(3)	2290(2)
N(4)	9435(4)	1820(2)	-0550(2)	C(12)	14890(6)	6528(3)	2666(2)
C(5)	7811(5)	0944(3)	-0970(2)	C(13)	16353(5)	6448(3)	2308(2)
C(6)	6229(5)	1144(4)	-0595(3)	C(14)	16176(5)	5626(3)	1564(2)
N(7)	11164(4)	3380(2)	0422(2)	C(15)	15542(5)	4889(3)	1183(2)
C(8)	11332(4)	4137(3)	1177(2)	C(16)	10785(6)	1871(4)	-1071(3)

Table 2. Atomic coordinates (x10^3) and C-H distances for the hydrogen atoms

	x	y	z	C-H(Å)		x	y	z	C-H(Å)
H(5A)	726	100	-171	1.01	H(13)	1756	698	259	1.01
H(5B)	834	008	-079	1.02	H(14)	1724	556	130	1.01
H(6A)	554	196	-085	1.02	H(15)	1441	430	063	1.02
H(6B)	518	048	-084	1.02	H(16A)	1076	135	-154	1.02
H(11)	1218	583	256	1.02	H(16B)	1192	221	-077	1.02
H(12)	1502	713	321	1.01	H(16C)	1100	135	-173	1.09

Notes and References

1. Compound 1 (mp: 133°) was prepared by the reaction of 2-(methylamino)-ethanol with benzoylisothiocyanate.
2. An other 1,2,4-oxathiazine derivative [3-(3,4,5-trimethoxybenzoylimino)-4-methyl-perhydro-1,2,4-oxathiazine (mp: 165°)] was prepared analogously from 1-methyl-1-(β-hydroxyethyl)-3-(3,4,5-trimethoxybenzoyl)thiourea (mp: 158°).
3. All compounds have correct analytical data; mp.'s are not corrected. The i.r. spectra were obtained on a Perkin-Elmer 577, the ^{1}H-n.m.r. spectra etc. were recorded on a JEOL 60-HL and the ^{13}C-n.m.r. spectra on a Varian XL-100 FT instrument.
4. Peaks of the ortho-protons (480-500 Hz) separate well from those of the meta and para protons (430-455 Hz) giving AA'BXX' type multiples, characteristic for benzoyl compounds, as a result of the anisotropic effect of the carbonyl group; see P. Sohár: Nuclear Magnetic Resonance Spectroscopy (in Hungarian), Akadémiai Kiadó, Budapest, 1976, p. 477.
5. A.F. McKay, M.E. Kreling, J. Org. Chem., 22, 1581 (1957).
6. Several further examples of abnormally short (2.03-2.67 Å) approaches between formally nonbonded S and O atoms have been reported so far, cf. e.g. A. Atkinson, A.C. Brewster, S.V. Ley, R.S. Osborn, D. Rogers, D.J. Williams, and K.A. Woode, J.C.S. Chem. Comm., 325 (1977) and references herein.
7. A. Hordvik and H. Kjøge, Acta Chem. Scand., 20, 1923 (1966).
8. W.L. Duax, C.M. Weeks and D.S. Rohrer, In Topics in Stereochemistry, Vol. 9. ed. by N.L. Allinger and E.L. Eliel, pp. 271-383, J. Wiley & Sons, New York (1976).
9. C. Altona, H.J. Geise and C. Romers, Tetrahedron, 24, 13 (1968).
10. A. Kálmán, Gy. Argay, B. Ribár and L. Toldy, Tetrahedron Letters, (1977) and references herein.