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# 1,3-THIAZEPINES.

# 4.* REACTIONS OF 2-IMINOTHIAZEPINES WITH METHYL ACRYLATE. CRYSTAL AND MOLECULAR STRUCTURE OF 2-PHENYLIMINO-3-(β-METHOXYCARBONYLETHYL)- AND 2-BENZYLIMINOHEXAHYDRO-1,3-THIADIAZEPINES

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*Addition of 2-aryliminohexahydro-1,3-thiazepines to methyl acrylate occurs with participation of the endocyclic nitrogen atom. Structures of the products have been established by IR and mass spectroscopy and x-ray diffraction. The previously described 2-benzylaminotetrahydro-1,3-thiazepine is in fact 2-benzyliminohexahydro-1,3-thiazepine.*

In a continuation of our investigation of the synthesis [2] and chemical properties [3, 4] of nitrogen containing derivatives of 1,3-thiazepines, we have investigated the interaction of the heterocyclic amines (Ia-e) with methyl acrylate. There is no information in the literature on the addition of amino(imino)-1,3-thiazepines to activated ethylenic or acetylenic bonds. Moreover there is only a single report of alkylation of 2,6-dichlorophenyliminohexahydro-1,3-thiazepine with methyl iodide. Initially the authors [5] described the alkylation product as an amine, but later, as a result of study of the $^1$H NMR spectra of its 5- and 6-membered analogs they concluded that the product was an imine [6].

The 2-aryliminohexahydrothiazepines Ia-d added to methyl acrylate to give 2-arylimino-3-(β-methoxycarbonylethyl)-hexahydro-1,3-thiazepines (IIa-d), i.e., adducts at the endocyclic nitrogen atom.

Ia-e IIa-d

a R = Ph, b R = 2,6-Me$_2$C$_6$H$_3$, c R = 2,4,6-Me$_3$C$_6$H$_2$, d R = C$_{10}$H$_7$, e R = PhCH$_2$

The reaction occurs both at room temperature and on heating. Products IIa-d are quite thermally stable and do not isomerize over 10 h at 110°C into their amino analogs. Characteristics of compounds IIa-d are given in Table 1. However, as the result of the reaction of methyl acrylate with compound Ie, described as 2-benzylaminotetrahydro-1,3-thiazepine [7], a mixture of compounds was obtained from which it was not possible to isolate the expected product IIe. This encouraged us to study more closely the structure of the initial thiazepine Ie, particularly since its IR spectrum contained a band at 1630 cm$^{-1}$ which is not characteristic of an endocyclic C=N bond [2]. An x-ray diffraction study showed that this compound, in contrast to the data published previously [7], is 2-benzyliminohexahydro-1,3-thiazepine (Fig. 1a). It follows that the Canadian authors [8] were in error in ascribing the $^1$H NMR signal at 3.5-3.6 ppm to a CH$_2$ group next to the cyclic nitrogen atom in the amino structure of the thiazepine molecule, whereas the signal of the N-CH$_2$ group in the $^1$H NMR spectrum of compound Ie occurs at 3.52 ppm [2].

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*For Communication 3 see [1].

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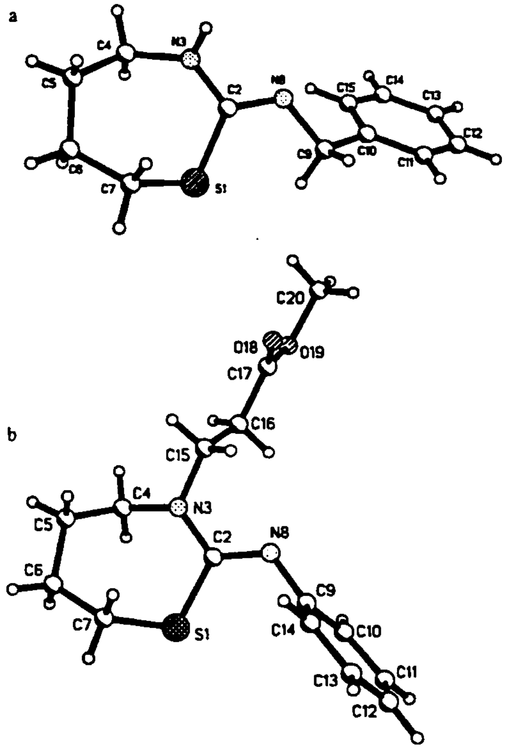

Fig. 1. Structures of the molecules of compounds Ie (a) and IIa (b).

The structures of alkylation products IIa-d were confirmed by their spectroscopic characteristics (Table 1). The IR spectra of these compounds include intense absorption bands in the 1740-1748 $\mathrm{cm}^{-1}$ region, corresponding to vibrations of ester groups, and there are no bands corresponding to NH groups (Table 1). The most intense peaks in the mass spectra correspond to the ions $[M\text{-}CH_2CH_2COOCH_3]^+$ in contrast to the ions $[M\text{-}CH_2COOCH_3]^+$ which are used as an analytical sign of the imino structure in five membered heterocycles [9]. On the other hand there are no obvious bands for the exocyclic C−N bonds so an unambiguous decision as to whether the compounds synthesized had the amino or imino structure required x-ray diffraction analysis of compound IIa. Solution of the structure showed that addition of the thiazepine to methyl acrylate involved the endocyclic nitrogen atom (Fig. 1b).

The geometric parameters of molecules Ie and IIa (bond lengths and bond angles) are given in Table 2. Both molecules are present in the imino form in the crystals, since the exocyclic $C_{(2)}-N_{(8)}$ bond is noticeably shorter than the endocyclic $C_{(2)}-N_{(3)}$ bond and close to the formal C=N bond (1.265 Å [10]).

The stereochemistry of the seven membered rings in compounds Ie and IIa is considerably different from the canonical symmetric form of cyclopentane which is associated with the presence of atoms $S_{(1)}$ and $N_{(3)}$ in the ring. However, the cyclic nitrogen atom has planar $sp^2$ hybridization geometry because of conjugation of its unshared pair with the $\pi$-system of the $C_{(2)}=N_{(3)}$ bond (sum of valence bonds equals 359.7°) with an endocyclic bond angle which is markedly different from the 104° angle at $S_{(1)}$.

According to the x-ray diffraction data, the conformation of the seven membered ring in both structures can be described as a strongly distorted chair, the back of which may be the $S_{(1)}-C_{(2)}$ or $C_{(2)}-N_{(3)}$ bonds. From analysis of the torsion angles (see Fig. 1, Table 3) it is seen that the configurational fragments with torsion angles $C_{(7)}-S_{(1)}-C_{(2)}-N_{(3)}$ (28.1° for Ie and 43.6° for IIa) and $S_{(1)}-C_{(2)}-N_{(3)}-C_{(4)}$ (43.1° and 23.2° respectively) are approximately planar. However, calculations of the asymmetry parameter $\Delta C$ [11] show that the heterocycles in molecules Ie and IIa prefer a third conformational state, the twist-chair with symmetry $C_2$, passing through atom $C_{(2)}$ and bisecting the $C_{(5)}$-$C_{(6)}$ bond as indicated by the values of $\Delta C_2$ of 13.1° (Ie) and 10.2° (IIa).

In the literature the only discussion of the conformational state of a 1,3-thiazepine has been for 2,3,4,5-tetrahydro-7,7-diphenylimidazo(2,1-β)thiazepin-8(7H)-one [12] in which the seven membered ring is fused with the five membered ring at the $C_{(2)}-N_{(3)}$ bond [3] and has a chair form with $C_{(2)}-N_{(3)}$ as the back. In this structure the formally single and double

TABLE 1. Characteristics of Compounds IIa-d

| Compound | Molecular formula | (Found, %)/ (Calculated; %) | | | mp, °C | IR spectrum, $\nu$, cm$^{-1}$ | Mass spectrum, $m/z$ ($I_{rel}$, %) | | Yield, % |
|---|---|---|---|---|---|---|---|---|---|
| | | C | H | N | | | M$^+$ | principal fragments | |
| IIa | $C_{15}H_{20}N_2O_2S$ | 61.4<br>61,6 | 6.7<br>6,8 | 9.5<br>9.5 | 68...69 | 1740,<br>1585 | 292 (100) | 291 (24), 261 (19), 233 (53), 205 (62), 145 (26), 130 (28), 118 (26), 77 (36) | 94 |
| IIb | $C_{17}H_{24}N_2O_2S$ | 63.5<br>63,7 | 7.7<br>7,5 | 8.6<br>8,7 | 67...68 | 1748,<br>1608 | 320 (37) | 305 (100), 219 (27), 159 (10), 146 (14), 142 (23), 130 (26), 116 (10), 105 (10) | 97 |
| IIc | $C_{18}H_{26}N_2O_2S$ | 64.9<br>64,6 | 7.6<br>7,8 | 8.3<br>8,4 | 28...29 | 1747,<br>1615 | 334 (19) | 319 (49), 248 (14), 233 (27), 160 (27), 145 (24), 130 (17), 119 (13), 57 (100) | 92 |
| IId | $C_{19}H_{22}N_2O_2S$ | 64.5<br>64,6 | 6.6<br>6,5 | 8.1<br>8,2 | Oil | 1740,<br>1580 | 342 (100) | 311 (10), 283 (27), 255 (44), 185 (20), 168 (49), 153 (41), 143 (31), 127 (35) | 95 |

bonds of $C_{(2)}$ with other atoms are "smeared out" because of strong conjugation. For example the $S_{(1)}-C_{(2)}$ bond (1.740 Å) is similar to the bond in thiophene (1.723 Å [13]), and the $C_{(2)}-N_{(3)}$ (1.337 Å) and $C_{(2)}-N_{(8)}$ (1.328 Å) bonds are analogous to the carbon–nitrogen bonds in piperidine (1.336 Å) [10]. In contrast to the tetrahydrothiazepines, the formally single and double bonds are retained in compound Ie and IIa and the conformation of the seven membered rings has the twist-chair form.

It should also be noted that the calculated values for the conformational states of amino and imino derivatives of 1,3-thiazepine [1] differ somewhat from the actual values revealed by x-ray diffraction analysis.

In the structures of compounds Ie and IIa the $N_{(8)}-C_{(9)}$ bond is in the Z configuration relative to atom $S_{(1)}$ which indicates that this direction is sterically favorable. While the aromatic fragment in compound Ie is placed on the side away from atom $S_{(1)}$, in compound IIa it screens that atom. The benzene ring is practically perpendicular (95.9°) to the plane containing atoms $S_{(1)}$, $C_{(2)}$, $N_{(3)}$, and $N_{(8)}$ which shows that there is no conjugation between the $\pi$ electron systems of the $C_{(2)}-N_{(8)}$ double bond and the aromatic ring. The substituent on atom $N_{(3)}$ — the methoxycarbonylethyl group — is practically planar and is perpendicular to the mean plane of the seven-membered ring.

## EXPERIMENTAL

Fourier IR spectra were recorded in KBr discs using a Perkin-Elmer System 2000 FT-IR instrument and mass spectra were obtained with an MX-1303 machine with an ionizing voltage of 40 eV.

Elemental analyses for C, H, and N for all compounds corresponded to calculated values (Table 1). The amine starting materials Ia-e were made by a published method [2].

**2-Arylimino-3-(β-methoxycarbonylethyl)hexahydro-1,3-thiazepines (IIa-d). General Method.** The amines Ia-d (10 mmol) were heated for 10 h with freshly distilled methyl acrylate (5 ml), stabilized with hydroquinone or sodium thiocyanate. The reaction mixture was evaporated to dryness under reduced pressure and the residue was extracted with boiling hexane. The residue after evaporation of the solvent was recrystallized or reprecipitated from hexane.

**X-Ray Diffraction Investigation of Compounds Ie and IIa.** Crystals of Ie and IIa, grown from aqueous ethanol, were chosen by photographic methods. Unit cell parameters and space groups were determined and refined with a Syntex $P2_1$ diffractometer.

TABLE 2. Bond Lengths and Bond Angles

| Bond | Length, Å | Angle | ω, deg |
|---|---|---|---|
| | | **Molecule Ie** | |
| S(1)—C(2) | 1,783(5) | C(2)—S(1)—C(7) | 105,0(3) |
| S(1)—C(7) | 1,815(6) | S(1)—C(2)—N(3) | 117,8(4) |
| C(2)—N(3) | 1,373(6) | S(1)—C(2)—N(8) | 122,6(4) |
| C(2)—N(8) | 1,279(6) | N(3)—C(2)—N(8) | 119,6(4) |
| N(3)—C(4) | 1,478(6) | C(2)—N(3)—C(4) | 122,4(4) |
| C(4)—C(5) | 1,501(7) | N(3)—C(4)—C(5) | 114,9(4) |
| C(5)—C(6) | 1,512(8) | C(4)—C(5)—C(6) | 114,5(5) |
| C(6)—C(7) | 1,509(8) | C(5)—C(6)—C(7) | 114,8(5) |
| N(8)—C(9) | 1,472(6) | S(1)—C(7)—C(6) | 116,1(3) |
| C(9)—C(10) | 1,506(6) | C(2)—N(8)—C(9) | 119,9(4) |
| C(10)—C(11) | 1,384(7) | N(8)—C(9)—C(10) | 111,1(3) |
| C(10)—C(15) | 1,396(6) | C(9)—C(10)—C(11) | 120,8(4) |
| C(11)—C(12) | 1,374(8) | C(9)—C(10)—C(15) | 122,3(4) |
| C(12)—C(13) | 1,380(7) | C(11)—C(10)—C(15) | 116,8(4) |
| C(13)—C(14) | 1,383(9) | C(10)—C(11)—C(12) | 122,0(4) |
| C(14)—C(15) | 1,352(7) | C(11)—C(12)—C(13) | 120,1(5) |
| | | C(12)—C(13)—C(14) | 118,2(5) |
| | | C(13)—C(14)—C(15) | 121,5(5) |
| | | C(10)—C(15)—C(14) | 121,3(5) |
| | | **Molecule IIa** | |
| S(1)—C(2) | 1,779(6) | C(2)—S(1)—C(7) | 103,6(4) |
| S(1)—C(7) | 1,82(1) | S(1)—C(2)—N(3) | 116,9(5) |
| C(2)—N(3) | 1,362(9) | S(1)—C(2)—N(8) | 122,9(5) |
| C(2)—N(8) | 1,27(1) | N(3)—C(2)—N(8) | 120,2(6) |
| N(3)—C(4) | 1,47(1) | C(2)—N(3)—C(4) | 123,2(6) |
| N(3)—C(15) | 1,453(8) | C(2)—N(3)—C(15) | 118,2(6) |
| C(4)—C(5) | 1,48(1) | C(4)—N(3)—C(15) | 117,5(5) |
| C(5)—C(6) | 1,52(1) | N(3)—C(4)—C(5) | 114,3(8) |
| C(6)—C(7) | 1,50(1) | C(4)—C(5)—C(6) | 113,4(8) |
| N(8)—C(9) | 1,402(8) | C(5)—C(6)—C(7) | 113,8(7) |
| C(9)—C(10) | 1,38(1) | S(1)—C(7)—C(6) | 116,7(8) |
| C(9)—C(14) | 1,38(1) | C(2)—N(8)—C(9) | 120,3(5) |
| C(10)—C(11) | 1,39(1) | N(8)—C(9)—C(10) | 121,3(7) |
| C(11)—C(12) | 1,35(2) | N(8)—C(9)—C(14) | 121,0(7) |
| C(12)—C(13) | 1,34(2) | C(10)—C(9)—C(14) | 117,4(7) |
| C(13)—C(14) | 1,36(1) | C(9)—C(10)—C(11) | 120,3(9) |
| C(15)—C(16) | 1,50(1) | C(10)—C(11)—C(12) | 120,0(11) |
| C(16)—C(17) | 1,48(1) | C(11)—C(12)—C(13) | 120,2(10) |
| C(17)—O(18) | 1,19(1) | C(12)—C(13)—C(14) | 120,8(11) |
| C(17)—O(19) | 1,33(1) | C(9)—C(14)—C(13) | 121,2(9) |
| O(19)—C(20) | 1,446(9) | N(3)—C(15)—C(16) | 113,1(7) |
| | | C(15)—C(16)—C(17) | 112,8(8) |
| | | C(16)—C(17)—O(18) | 125,7(8) |
| | | C(16)—C(17)—O(19) | 112,4(8) |
| | | O(18)—C(17)—O(19) | 121,9(7) |
| | | C(17)—O(19)—C(20) | 116,5(7) |

**Crystal Ie** : $a$ = 5.470(1) Å, $\alpha$ = 102.4(1)°, $b$ = 9.892(2) Å, $\beta$ = 97.9(1)°, $c$ = 11.594(3) Å, $\gamma$ = 101.5(1)°, $V$ = 589.6 Å$^3$, $d_{calc}$ = 1.270 g/cm$^3$, space group P-1, $Z$ = 2.

**Crystal IIa**: $a$ = 10.289(2) Å, $\alpha$ = 90.0°, $b$ = 14.727(3) Å, $\beta$ = 114.2(1)°, $c$ = 11.126(2) Å, $\gamma$ = 90.0°, $V$ = 1455.6 Å$^3$, $d_{calc}$ = 1.263 g/cm$^3$, space group P2$_1$/c, $Z$ = 4.

Intensities were measured on the same diffractometer, using $\theta/2\theta$ scanning with CuK$\alpha$ radiation (graphite monochromator), $\sin\theta/\lambda < 0.29$, number of independent non-zero reflections with $I > 2\sigma(I)$ equal to 1179 (Ie) and 1222 (IIa).

TABLE 3. Coordinates ($\times 10^4$) and Temperature Factors $U_{eq}$ (Å$^2$ $\times$ $10^3$) for Nonhydrogen Atoms

| Atom | $x$ | $y$ | $z$ | $U_{eq}$ |
|---|---|---|---|---|
| Molecule Ie | | | | |
| $S_{(1)}$ | 793(3) | 1171(1) | 8482(1) | 56(1) |
| $C_{(2)}$ | 416(9) | 2893(4) | 9168(4) | 41(2) |
| $N_{(3)}$ | 1397(7) | 4009(4) | 8708(3) | 45(1) |
| $C_{(4)}$ | 3931(9) | 4208(5) | 8372(4) | 51(2) |
| $C_{(5)}$ | 3928(11) | 3585(6) | 7071(5) | 64(2) |
| $C_{(6)}$ | 3449(11) | 1979(6) | 6719(5) | 68(2) |
| $C_{(7)}$ | 954(10) | 1199(6) | 6933(4) | 65(2) |
| $N_{(8)}$ | -756(7) | 3113(4) | 10046(3) | 44(1) |
| $C_{(9)}$ | -2161(10) | 1896(5) | 10417(4) | 55(2) |
| $C_{(10)}$ | -2140(8) | 2270(4) | 11749(4) | 43(2) |
| $C_{(11)}$ | -4222(10) | 1717(5) | 12205(5) | 58(2) |
| $C_{(12)}$ | -4203(11) | 1975(6) | 13419(5) | 69(3) |
| $C_{(13)}$ | -2075(12) | 2818(6) | 14227(5) | 70(3) |
| $C_{(14)}$ | 25(11) | 3361(6) | 13780(5) | 66(2) |
| $C_{(15)}$ | 0(9) | 3105(5) | 12585(4) | 54(2) |
| Molecule IIa | | | | |
| $S_{(1)}$ | 1998(2) | 7334(1) | 304(2) | 65(1) |
| $C_{(2)}$ | 3701(7) | 6930(5) | 1403(7) | 54(3) |
| $N_{(3)}$ | 4715(6) | 7567(4) | 2025(6) | 59(3) |
| $C_{(4)}$ | 4376(8) | 8498(5) | 2267(8) | 64(4) |
| $C_{(5)}$ | 4260(9) | 9152(6) | 1214(9) | 79(5) |
| $C_{(6)}$ | 2812(10) | 9139(6) | 52(10) | 85(5) |
| $C_{(7)}$ | 2415(10) | 8228(6) | -611(9) | 87(5) |
| $N_{(8)}$ | 3993(6) | 6089(4) | 1615(6) | 61(3) |
| $C_{(9)}$ | 3081(7) | 5433(5) | 779(7) | 49(3) |
| $C_{(10)}$ | 2231(8) | 4899(6) | 1178(8) | 68(4) |
| $C_{(11)}$ | 1421(9) | 4200(7) | 374(12) | 90(5) |
| $C_{(12)}$ | 1452(12) | 4051(7) | -812(12) | 95(5) |
| $C_{(13)}$ | 2287(11) | 4559(8) | -1206(10) | 90(5) |
| $C_{(14)}$ | 3114(8) | 5232(6) | -422(8) | 67(4) |
| $C_{(15)}$ | 6183(7) | 7268(5) | 2705(8) | 62(3) |
| $C_{(16)}$ | 6543(7) | 6961(6) | 4093(7) | 58(3) |
| $C_{(17)}$ | 8023(8) | 6620(5) | 4762(9) | 64(4) |
| $C_{(18)}$ | 8814(6) | 6477(5) | 4249(6) | 96(3) |
| $O_{(19)}$ | 8397(5) | 6468(4) | 6042(6) | 75(3) |
| $C_{(20)}$ | 9810(8) | 6106(8) | 6774(9) | 93(5) |

Structures were solved by direct methods using the SHELXS-86 program [14] (PC DOS version). The models of the molecules were successfully found under the automatic regime. All nonhydrogen atoms were found by successive Fourier syntheses and the structures were refined by the least squares method with successive isotropic and anisotropic approximations using the SHELX-76 program [15]. Coordinates of H atoms bonded to carbon atoms were calculated geometrically but the OH groups were found by electron density difference syntheses and refined isotropically. The final residual factors were $R = 0.064$ (Ie) and 0.072 (IIa). The coordinates of the nonhydrogen atoms from the last least squares refinement are given in Table 3.

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