

# **Oxazepines and Thiazepines, XX [1]: CD-Spectra of Optically Active 2-Phenyl-2,3-dihydro-1,5-benzothiazepin-4(5*H*)-ones and Related 3-Phenylthio-3-phenyl-propionic Acid Derivatives, and X-Ray Diffraction of One Phenylethylamide**

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**Summary.** The absolute configuration of (–)-(1'*R*,3*S*)-**4** has been determined by X-ray diffraction. The UV- and CD-spectra of the title compound **8** and the intermediates for its synthesis are discussed. The stronger Cotton effects can be explained by application of the exciton theory to the observed CD-couplets. The CD of the lower homologue **9** of known absolute configuration is in full agreement with that of homochirally analogue **8**.

**Keywords.** Chiroptical properties; Exciton couplets; X-Ray diffraction.

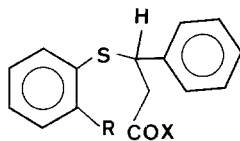
**Oxazepine und Thiazepine, 20. Mitt.: CD-Spektren optisch aktiver 2-Phenyl-2,3-dihydro-1,5-benzothiazepin-4(5*H*)-one und verwandter 3-Phenylthio-3-phenyl-propionsäure-Derivate und Röntgenstrukturanalyse eines Phenylethylamids**

**Zusammenfassung.** Die absolute Konfiguration von (–)-(1'*R*,3*S*)-**4** wurde durch Röntgenbeugung bestimmt. UV- und CD-Spektren der Titelverbindung **8** und der Zwischenprodukte für ihre Synthese werden diskutiert. Die stärkeren Cottoneffekte können durch Anwendung der Excitontheorie auf die erhaltenen CD-Couplets erklärt werden. Der CD des niederen Homologen **9** bekannter absoluter Konfiguration steht in voller Übereinstimmung mit dem des homochiral analogen **8**.

## **Introduction**

Recently optically active 2,3-dihydro-1,5-benzothiazepin-4(5*H*)-one derivatives have been introduced onto the market as antihypertensive drugs [2]. Since we had investigated the chiroptical properties of analogous benzodiazepines in detail [3, 4] and since no similar comprehensive studies are known for these aforementioned S-analogues we have synthesized four related series of such compounds [1]. In this paper we discuss the CD-spectra of 2-phenyl-2,3-dihydro-1,5-benzothiazepin-

4(5*H*)-one and of related intermediates. The resolution of these compounds was performed via diastereomeric salts **1** of the acid **2**, and both enantiomers have been prepared in each case [1].



	R	X
1	NO <sub>2</sub>	OH. Brucin
2	NO <sub>2</sub>	OH
3	NO <sub>2</sub>	OMe
4	NO <sub>2</sub>	NH.C(H,Me).C <sub>6</sub> H <sub>5</sub>
5	NH <sub>2</sub>	OH
6	NH <sub>2</sub>	OMe
7	NHAc	OMe

## Results and Discussion

### *X-Ray Analysis and Absolute Configuration of (-)-(1'R,3-S)-4*

The absolute configuration was determined by X-ray diffraction studies; since the sense of helicity of the phenyl ethyl amine moiety is known one could have used ordinary X-ray diffraction patterns, we have, however, also collected carefully the Bijvoet-pairs for independent proof.

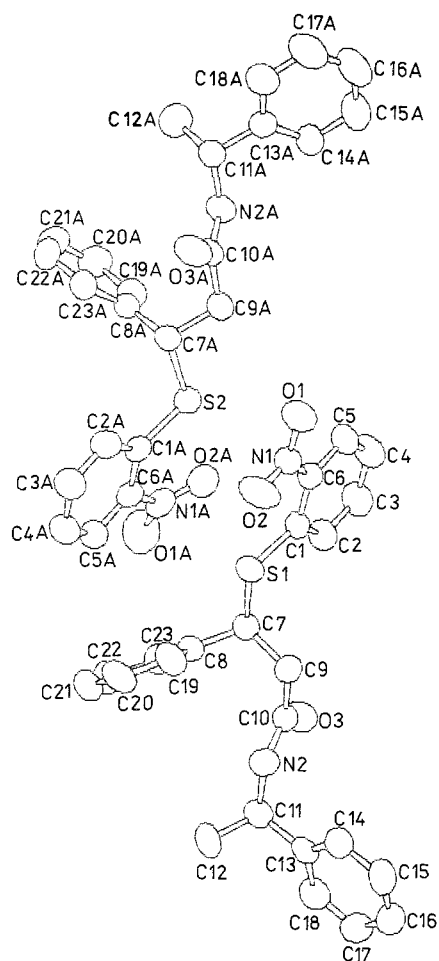
A suitable crystal of (-)-**4** was selected after examination in polarized light on the optical microscope, ground to a sphere of radius 0.15 mm and mounted for measurements on an ENRAF-NONIUS CAD-4 diffractometer. The setting angles of 25 reflections ( $10^\circ < \theta < 25^\circ$ ) were used to determine by least-squares fit accurate cell parameters and their standard deviations.

*Crystal Data:*  $M = 406.504$ , monoclinic,  $P2_1$ ,  $a = 841.3(1)$ ,  $b = 2472.8(2)$ ,  $c = 1008.2(1)$  pm,  $\alpha = 89.98(1)$ ,  $\beta = 98.60(1)$ ,  $\gamma = 90.00(1)^\circ$ ,  $V = 207.384$  pm<sup>3</sup>,  $Z = 4$ ,  $D_c = 1.302$ ,  $D_m = 1.276$  g cm<sup>-3</sup> (floatation), CuK $\alpha$  radiation,  $\lambda = 154.178$  pm,  $\mu = 1.56$  mm<sup>-1</sup>,  $F(000) = 852$ .

Intensity data were collected with graphite-monochromated CuK $\alpha$  radiation using  $\theta/2\theta$  scan in the range  $1.1 < \theta < 74^\circ$ ,  $0 < h < 10$ ,  $-30 < k < 0$ ,  $-12 < l < 12$ . The intensity fluctuation ( $< 3\%$ ) was monitored every hour with two reflections. Orientation control reflections (max. dev.  $0.08^\circ$ ) were measured after every 100 reflections. A total of 8371 reflections (7641 unique) were collected; each one was measured consecutively with its Friedel equivalent. Lp correction and absorption correction for spherical crystal with correction factors taken from the International Tables [5] were applied.

The structure was solved by the direct method in  $P2_1$  space group using the SHELXS86 program [6]. The  $E$ -map revealed all but hydrogen atoms. At the early stages of the refinement 22 hydrogen atoms were localized on the difference Fourier map, the remaining 20 H-atoms were geometrically positioned using the XANADU program [7]. The difference Fourier map calculated after this step did not show any other atoms apart from those predicted by the chemical formula. There are two molecules in the asymmetric unit cell.

The molecular structure of (1'*R*,3*S*)-**4** is shown in Fig. 1. The atomic parameters of non-hydrogen atoms are listed in Table 1. The bond lengths and angles are given in Table 2. Tables with H-atom parameters and bond lengths and with anisotropic temperature factors as well as the list of structure factors are to be deposited.



**Fig. 1.** ORTEP projection [15] of (-)-4 (H-atoms omitted for clarity) with thermal ellipsoids at 50% probability level

With two molecules in the asymmetric unit cell, each having two chiral centers, 16 combinations of *R/S* configurations are possible in solid state. X-ray analysis determined the one pair of isometric enantiomers present in the crystal; further analysis of anomalous dispersion allowed to eliminate the wrong enantiomer. In order to determine the absolute configuration by the Bijvoet method the primary molecular model was reversed after few cycles of refinement by changing the sign of the imaginary part of the anomalous scattering factors  $f''$ . The parallel refinement of both models was carried out with SHELX76 [8]; the atomic scattering factors and  $f'$  and  $f''$  values were taken from the International Tables [9]. The wrong enantiomer was rejected by the Hamilton test [10] calculated three times during the course of refinement for both models. The refinement was carried out for 7248 observations with  $|F_0| < 3\sigma(F)$  and 361 parameters; the final ratio of  $R_G$ -factors is then  $\mathfrak{R} = R_G^0(-)/R_G(+)$  = 1.1869 ( $R_G$  denotes generalized weighted discrepancy factor).

Its comparison with the tabulated value  $\mathfrak{R}_{1.7281, 0.005} = 1.00056$  allows to reject the wrong enantiomer at a significance level of  $\alpha = 0.005$ . The weighting scheme used during refinement is given by  $w = k[\sigma^2(F_0) + g(F_0)^2]^{-1}$ . Refinement was terminated at  $R = 0.069$ ,  $R_w = 0.082$ ,  $R_G = 0.105$  for  $k = 1$  and  $g = -0.0109$ ,  $\Delta/\sigma = 0.03$  (av.) and 0.1 (max) for non-hydrogen atom parameters, and  $\Delta/\sigma = 0.05$  (av.) and 0.1 (max.) for H-atom parameters; final electron density  $\Delta\rho$  (max.) = 0.17,  $\Delta\rho$  (min.) =  $-0.40$  e/pm<sup>3</sup>. Presence of minima, although without chemical meaning, might be caused by lower experimental density as compared to calculated one, what is usually associated with vacancies in the crystal.

**Table 1.** Fractional atomic coordinates and equivalent thermal parameters  $U_{\text{eq}}(\text{\AA}^2) \cdot 10^4$  with e.s.d.'s in parentheses.  $U_{\text{eq}} = 1/3 (U_{11} + U_{22} + U_{33} + 2U_{13} \cos \beta)$

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{eq}}$
N1	−8 599 (3)	416 (1)	−6 241 (2)	496 (6)
O1	−8 300 (3)	895 (1)	−5 993 (3)	716 (6)
O2	−9 069 (4)	118 (1)	−5 422 (3)	858 (6)
C6	−8 373 (3)	201 (1)	−7 533 (2)	438 (6)
C5	−7 741 (4)	553 (1)	−8 378 (3)	432 (6)
C4	−7 455 (4)	379 (2)	−9 621 (3)	383 (6)
C3	−7 821 (4)	−146 (2)	−10 000 (3)	635 (6)
C2	−8 452 (4)	−496 (1)	−9 165 (3)	546 (6)
C1	−8 771 (3)	−340 (1)	−7 903 (2)	440 (6)
S1	−9 687 (1)	−770 (0)	−6 840 (1)	506 (3)
C7	−9 994 (3)	−1 422 (1)	−7 729 (3)	469 (6)
C8	−11 404 (3)	−1 678 (1)	−7 189 (3)	469 (6)
C19	−11 444 (4)	−1 711 (2)	−5 819 (3)	635 (6)
C20	−12 774 (4)	−1 922 (2)	−5 329 (4)	757 (6)
C21	−14 045 (4)	−2 119 (2)	−6 199 (4)	765 (6)
C22	−14 004 (4)	−2 108 (2)	−7 549 (4)	888 (6)
C23	−12 691 (3)	−1 889 (2)	−8 050 (3)	569 (6)
C9	−8 447 (3)	−1 767 (1)	−7 462 (3)	526 (6)
C10	−8 656 (3)	−2 313 (1)	−8 148 (3)	458 (6)
O3	−8 660 (3)	−2 367 (1)	−9 358 (2)	657 (6)
N2	−8 857 (3)	−2 732 (1)	−7 334 (2)	504 (6)
C11	−9 051 (3)	−3 286 (1)	−7 782 (3)	510 (6)
C12	−10 194 (4)	−3 569 (2)	−6 962 (4)	803 (6)
C13	−7 467 (3)	−3 587 (1)	−7 672 (2)	448 (6)
C14	−6 106 (3)	−3 403 (1)	−6 837 (3)	539 (6)
C15	−4 652 (3)	−3 680 (2)	−6 717 (3)	633 (6)
C16	−4 538 (4)	−4 146 (2)	−7 452 (3)	636 (6)
C17	−5 881 (4)	−4 334 (2)	−8 277 (3)	646 (6)
C18	−7 312 (4)	−4 063 (1)	−8 388 (3)	586 (6)
N1A	−13 406 (3)	−373 (1)	−8 855 (3)	549 (6)
O1A	−14 158 (4)	−734 (2)	−9 496 (3)	969 (6)
O2A	−12 316 (3)	−121 (1)	−9 241 (2)	667 (6)
C6A	−13 860 (3)	−234 (1)	−7 553 (3)	464 (6)
C5A	−14 605 (4)	−640 (1)	−6 922 (3)	606 (6)
C4A	−15 058 (4)	−541 (2)	−5 702 (3)	659 (6)
C3A	−14 799 (4)	−32 (2)	−5 129 (3)	634 (6)
C2A	−14 048 (4)	369 (1)	−5 760 (3)	552 (6)
C1A	−13 521 (3)	278 (1)	−6 995 (3)	450 (6)
S2	−12 481 (1)	769 (0)	−7 802 (1)	529 (3)
C7A	−12 974 (3)	1 416 (1)	−7 092 (3)	460 (6)
C8A	−14 586 (3)	1 641 (1)	−7 733 (3)	437 (6)
C19A	−14 996 (3)	1 670 (1)	−9 123 (3)	648 (6)
C20A	−16 439 (4)	1 899 (2)	−9 693 (3)	666 (6)
C21A	−17 485 (4)	2 097 (2)	−8 896 (4)	682 (6)
C22A	−17 097 (3)	2 069 (2)	−7 529 (4)	640 (6)
C23A	−15 666 (3)	1 848 (1)	−6 949 (3)	512 (6)
C9A	−11 574 (3)	1 787 (1)	−7 349 (3)	587 (6)

**Table 1** (continued)

	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> <sub>eq</sub>
C10A	-11 817 (3)	2 353 (1)	-6 817 (3)	471 (6)
O3A	-11 881 (3)	2 430 (1)	-5 623 (2)	671 (6)
N2A	-11 985 (3)	2 745 (1)	-7 729 (2)	511 (6)
C11A	-12 285 (3)	3 305 (1)	-7 420 (3)	532 (3)
C12A	-13 769 (4)	3 496 (2)	-8 372 (5)	1 008 (6)
C13A	-10 841 (3)	3 662 (1)	-7 490 (2)	474 (6)
C14A	-9 619 (3)	3 515 (1)	-8 201 (3)	535 (6)
C15A	-8 321 (4)	3 861 (2)	-8 263 (3)	703 (6)
C16A	-8 244 (4)	4 349 (2)	-7 606 (4)	792 (6)
C17A	-9 433 (5)	4 498 (2)	-6 889 (4)	813 (6)
C18A	-10 725 (4)	4 157 (2)	-6 827 (3)	629 (6)

It should be mentioned that although the mean of  $|E^2 - 1|$  indicates unambiguously an acentric space group and the measured values of angles  $\alpha$  and  $\gamma$  confirm the choice of monoclinic system, there are few very weak reflections ( $0k0$  odd); suggesting rather a pseudo than an exact  $2_1$  axis. The structure was, however, successfully solved and refined in  $P2_1$  space group.

Further refinement would require much more extensive calculations (in  $P_1$  space group the model is described by 760 parameters instead of 361 in  $P2_1$ ) and seems from point of view of stereochemistry not necessary. Both molecules in the asymmetric unit have (*R*)-configuration at C(1'), [C(11) and C(11A) of Fig. 1], and (*S*)-configuration at C(3) [C(7) and C(7A) of Fig. 1], they differ, however, in their conformation. The torsional angle C(1)–S(1)–C(7)–C(8) (numbering according to Fig. 1) is equal to  $-154^\circ$  in the first molecule, thus the phenyl C(8)–C(19)–C(20)–C(21)–C(22)–C(23) and the *o*-nitrophenylthio substituent have anticlinical conformation. For the second molecule the corresponding torsional angle C(1A)–S(2)–C(7A)–C(8A) is  $-82^\circ$  and the conformation is synclinal. The remaining fragments of the two molecules are approximately congruent and related by a generally oriented pseudo twofold axis. The packing in the crystal lattice is shown in Fig. 2. Molecules are linked through a hydrogen bond formed between the amido nitrogen and carbonyl oxygen of the neighbouring molecule. The following scheme shows the relevant intermolecular distances: N2<sup>94.3 pm</sup>HN<sup>204.1 pm</sup>03A' with N2...03A' distance of 298.0 pm and N2A<sup>93.2 pm</sup>HN<sup>215.5 pm</sup>03' with N2A...03' distance of 307.7 pm; atoms 03A' and 03' are generated by the  $2_1$ -axis from atoms 03A and 03, respectively. The oxygen atoms of the nitro groups have no intermolecular close contacts, which is reflected in their relatively big temperature factors (see thermal ellipsoids in Fig. 2).

The absolute configuration of the phenyl ethyl amine moiety as derived here from application of Bijvoet's method is actually the correct one. The sense of helicity at the center of chirality of (–)-**2** has thus unequivocally been determined as (*S*).

The structure of **4** can be compared with that of  $C_{18}H_{20}N_2O_3S$  determined by van Bolhuis [11]. His compound crystallizes also in monoclinic system, space group

**Table 2.** Bond lengths (Å) and bond angles (°) between non-hydrogen atoms with e.s.d.'s in parentheses

N1–O1	1.230 (4)	N1A–O1A	1.224 (5)
N1–O2	1.216 (4)	N1A–O2A	1.219 (4)
N1–C6	1.445 (4)	N1A–C6A	1.461 (4)
C6–C1	1.416 (4)	C6A–C1A	1.398 (4)
C1–C2	1.394 (4)	C1A–C2A	1.400 (4)
C2–C3	1.368 (5)	C2A–C3A	1.381 (5)
C3–C4	1.375 (6)	C3A–C4A	1.387 (6)
C4–C5	1.380 (5)	C4A–C5A	1.364 (5)
C5–C6	1.380 (4)	C5A–C6A	1.388 (5)
C1–S1	1.765 (3)	C1A–S2	1.765 (3)
S1–C7	1.844 (3)	S2–C7A	1.826 (3)
C7–C8	1.515 (4)	C7A–C8A	1.517 (4)
C8–C19	1.389 (4)	C8A–C19A	1.394 (4)
C19–C20	1.391 (5)	C19A–C20A	1.384 (5)
C20–C21	1.367 (5)	C20A–C21A	1.367 (5)
C21–C22	1.367 (6)	C21A–C22A	1.370 (5)
C22–C23	1.392 (5)	C22A–C23A	1.372 (4)
C23–C8	1.385 (4)	C23A–C8A	1.389 (4)
C7–C9	1.545 (4)	C7A–C9A	1.546 (4)
C9–C10	1.516 (4)	C9A–C10A	1.522 (5)
C10–O3	1.227 (3)	C10A–O3A	1.228 (4)
C10–N2	1.346 (4)	C10A–N2A	1.330 (4)
N2–C11	1.443 (4)	N2A–C11A	1.450 (4)
C11–C12	1.529 (5)	C11A–C12A	1.531 (5)
C11–C13	1.517 (4)	C11A–C13A	1.512 (4)
C13–C14	1.392 (4)	C13A–C14A	1.387 (4)
C14–C15	1.390 (5)	C14A–C15A	1.394 (5)
C15–C16	1.382 (6)	C15A–C16A	1.376 (7)
C16–C17	1.380 (4)	C16A–C17A	1.368 (6)
C17–C18	1.368 (5)	C17A–C18A	1.385 (6)
C18–C13	1.396 (5)	C18A–C13A	1.391 (5)
O1–N1–O2	121.6 (4)	O1A–N1A–O2A	123.9 (3)
O1–N1–C6	119.2 (3)	O1A–N1A–C6A	117.6 (3)
O2–N1–C6	119.2 (3)	O2A–N1A–C6A	118.5 (3)
N1–C6–C5	116.1 (3)	N1A–C6A–C5A	116.0 (3)
N1–C6–C1	121.8 (2)	N1A–C6A–C1A	120.6 (3)
C1–C6–C5	122.1 (3)	C1A–C6A–C5A	123.4 (3)
C6–C5–C4	120.0 (3)	C6A–C5A–C4A	119.3 (3)
C5–C4–C3	119.0 (3)	C5A–C4A–C3A	119.4 (3)
C4–C3–C2	121.2 (3)	C4A–C3A–C2A	120.9 (3)
C3–C2–C1	92.7 (2)	C3A–C2A–C1A	121.5 (3)
C6–C1–S1	121.1 (2)	C6A–C1A–S2	121.5 (2)
C2–C1–C6	115.5 (3)	C6A–C1A–C2A	115.4 (3)
C2–C1–S1	123.3 (2)	C2A–C1A–S2	123.0 (2)
C1–S1–C7	105.9 (1)	C1A–S2–C7A	105.3 (1)
S1–C7–C9	110.2 (2)	S2–C7A–C9A	103.3 (2)
S1–C7–C8	104.5 (2)	S2–C7A–C8A	113.2 (2)
C7–C8–C19	121.2 (2)	C7A–C8A–C19A	121.2 (3)
C8–C19–C20	121.1 (3)	C8A–C19A–C20A	120.6 (3)

Table 2 (continued)

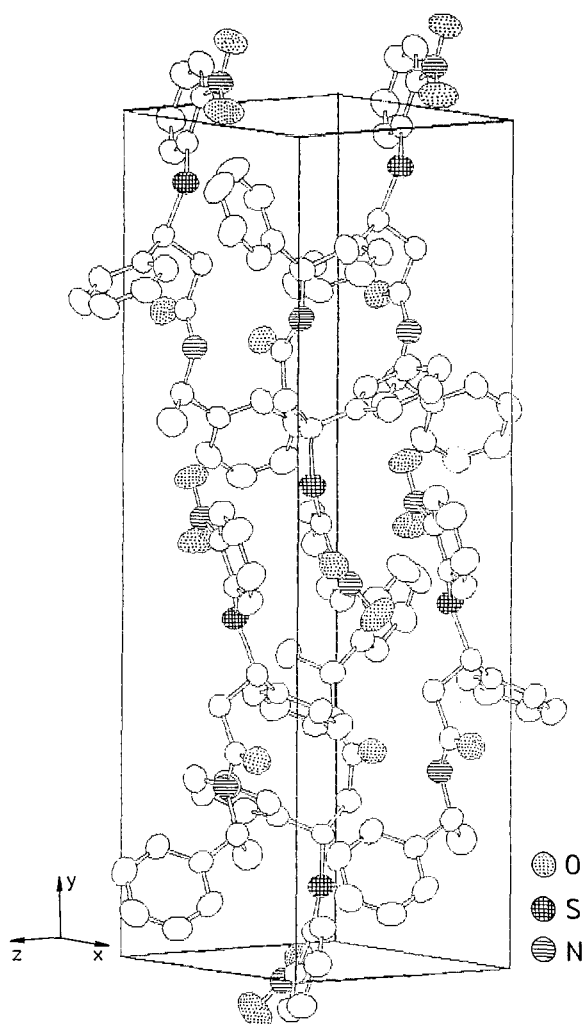
C19–C20–C21	119.9 (3)	C19A–C20A–C21A	120.2 (3)
C20–C21–C22	119.9 (3)	C20A–C21A–C22A	119.7 (3)
C21–C22–C23	120.6 (3)	C21A–C22A–C23A	120.8 (3)
C22–C23–C8	120.5 (3)	C22A–C23A–C8A	120.7 (3)
C23–C8–C7	120.8 (3)	C23A–C8A–C7A	120.7 (2)
C23–C8–C19	118.0 (3)	C23A–C8A–C19A	118.0 (2)
C8–C7–C9	113.1 (2)	C8A–C7A–C9A	111.5 (2)
C7–C9–C10	112.0 (2)	C7A–C9A–C10A	109.9 (2)
C9–C10–O3	122.2 (3)	C9A–C10A–O3A	121.0 (3)
C9–C10–N2	115.1 (2)	C9A–C10A–N2A	115.6 (3)
O3–C10–N2	122.7 (3)	O3A–C10A–N2A	123.3 (3)
C10–N2–C11	123.9 (2)	C10A–N2A–C11A	123.5 (2)
N2–C11–C12	108.5 (2)	N2A–C11A–C12A	108.1 (3)
N2–C11–C13	112.7 (2)	N2A–C11A–C13A	112.4 (3)
C12–C11–C13	110.6 (3)	C12A–C11A–C13A	112.1 (3)
C11–C13–C14	121.2 (3)	C11A–C13A–C14A	122.3 (3)
C11–C13–C18	121.7 (2)	C11A–C13A–C18A	119.4 (3)
C14–C13–C18	117.1 (3)	C14A–C13A–C18A	118.3 (3)

P2<sub>1</sub>, but the two molecules of the asymmetric unit have virtually identical anti-periplanar conformation (corresponding torsional angles are 177° and 173°). The compound has also (*R*)-configuration at C(11) and (*S*)-configuration at the centre of chirality C(7) (in both structures the same numbering scheme was used).

### CD-Spectra

Compounds **2** and **3** contain the *o*-nitro-phenylthio chromophore, and as the X-ray spectrum of **4** shows, in such a molecule the NO<sub>2</sub>-group is nearly coplanar with the benzene ring. Since both the nitro as well as the alkylmercapto group are very strong perturbers of the benzene  $\pi$ -system [12] it seems difficult to associate the individual CD-bands to localized transitions, and we merely discuss these spectra in a qualitative way. Independent of the nature of the substituent in position 3 (phenyl: this paper; methyl: [13]) such a compound shows two distinct Cotton effects around 370 and 300 nm of same sign [positive for (*S*)-configuration in case of 3-phenyl compounds], a third, very strong one of opposite sign is found around 250 nm, then follow two others ( $\approx 230$  and  $\approx 218$  nm) of same sign as the first two, and below 210 nm the CD sign changes again, revealing another Cotton effect around 205 nm as a shoulder in the CD-curve.

The bands below 230 nm cannot be distinctly seen for the amide **4** because of the additional phenyl chromophore, for which only a very small *g*-number can be expected. Of course, for the (*R*)-isomers the CD-curves are mirror images of the just mentioned (*S*)-compounds. From a comparison with the other CD-spectra follows that the Cotton effects at 370 and 250 nm are typical for the nitro derivatives only.



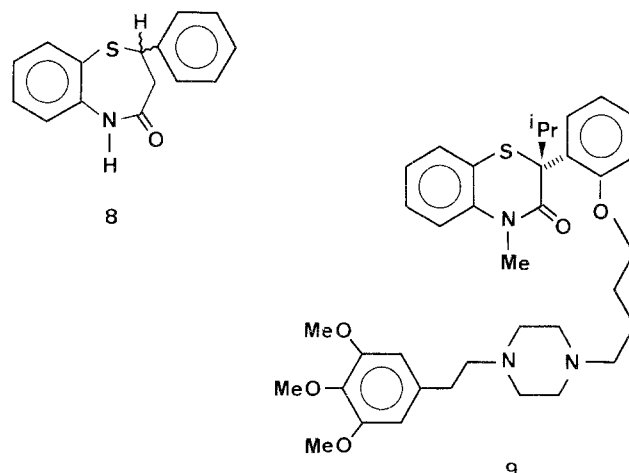
**Fig. 2.** View of the content of the unit cell, drawn by ORTEP [15]

The amino acids **5** and their methyl esters **6** give almost identical CD-spectra in acetonitrile solution, zwitterion formation seems therefore to be of no importance for these amino acids. Although the amino group is also a very strong  $\pi$ -system perturber one can approximately predict the position of the  $\alpha$ -band, obtaining thus 319 nm [12]. Actually the first Cotton effect is found around 307 nm, and it corresponds to the strongly enhanced  $\alpha$ -band with an  $\epsilon \approx 5000$ . Its CD is expected, therefore, to be also relatively strong, and indeed e.g. for (*R*)-**6**  $\Delta\epsilon_{\max}$  is + 5.71. Additional Cotton effects of same sign appear at 262, 228, and around 200 nm, at 218 and below 190 nm the CD has opposite sign. In all these CD-spectra there appears a distinct shoulder at appr. 205 nm, so we observe altogether 7 Cotton effects. The first two are at least five times stronger than for the corresponding butyric acids [13]. Since for both series of compounds the S-C(3) bond is strongly twisted out of the plane of the benzene ring we have to ascribe this enhancement of  $\Delta\epsilon$ -values to an interaction between the two aromatic systems present in these molecules **5** and **6**.



N-Acetylation of **6** to **7** should hypsochromically shift the  $\alpha$ -band, and this is nicely born out by the CD-spectra: the magnitude of the first Cotton effect remains unusually strong, but its maximum detectable only as a shoulder at appr. 290 to 285 nm on the second, also enhanced Cotton effect. This latter is, however, not shifted at all as compared with the analogous Cotton effect for the amines **5** and **6**. The third Cotton effect shows also up only as a shoulder around 230 nm, whereas below 220 nm the CD-spectra of the amines and their acetamide derivatives are quite similar.

After ring closure to **8** the chromophores are still the same as in **7**, but their steric arrangement is completely different in these two molecules. The hetero-ring is rather rigid and adopts according to the NMR-spectrum [14] mainly the conformation with an antiperiplanar arrangement  $Ph-C(2)-C(3)-C(4)$  (benzothiazepine numbering). Both moieties, the  $S-C-R$ -unit and the amide, are strongly twisted out of the benzene plane, and therefore all absorption bands of **8** are hypsochromically shifted with respect to those of **7**.



Whereas the rotational strength of the Cotton effect of **8** around 243 nm is of similar magnitude as in the methyl analogue [13], the first Cotton effect around 275 nm is appr. 10 times larger. Since there does not exist any conjugation or homoconjugation between the two chromophoric systems of **8** this drastic enhancement must be due to some exciton interaction. Usually such is not found with simple benzene chromophores above 215 nm, but that of the benzothiazepine system is substituted by two strong perturbing moieties and its  $\epsilon$  (and therefore also the associated electric transition moment) is quite strong even for the  $\alpha$ -band. The interacting transition moment vector of the 2-phenyl chromophore must be the one associated with the  $\beta'$ -transition, which is polarized along the benzylic bond, because the phenyl ring is not fixed and (partial) compensation is expected for the interaction with the  $\beta$ -transition moment vector. The second wing of this CD-couplet is most probably below 200 nm. That the conformations of the two groups on the *o*-substituted benzene ring (**1** through **7**) are quite different from those in the heterocyclic system is clearly born out by the sign of corresponding CD-bands of **7** and **8**: for the same absolute configuration the CD-spectra are enantiomorphous to each other, as are the rotations at the NaD-line.

For (*R*)-**8** this CD-couplet is negative; taking into account that the phenyl substituent is in a quasiaxial conformation [14] it becomes obvious from molecular models that the transition moment is not aligned with the (formal)  $C_2$ -axis of the *o*-disubstituted benzene chromophore, but inclined more towards the *Ar*-S-bond. It might even be oriented outside the sector defined by the *Ar*-S- and *Ar*-N-bonds as long the angle with the *Ar*-S-bond is smaller than that with the *Ar*-N-bond. A more precise prediction is impossible because no increments are tabulated for the substituents in question, furthermore it is known that these are not additive for such strong perturbers.

In **9** the condensed hetero-ring is six-membered and much flatter than the seven-membered one of **8**. Conjugation is thus barely disturbed, and the positions of the CD-bands are closer to those of **7**. Although the benzene ring in position 2 contains an *o*-R0-substituent this does not too strongly enhance its dipole strength, changes, however, the direction of its transition moments. We do, therefore, not dare to apply the exciton theory to this compound, but just note that the two strong Cotton effects at 260 and 238 nm have the same signs as the corresponding CD-bands of (*S*)-**8**, having analogous spacial arrangement around the centre of chirality, although according to the Cahn-Ingold-Prelog rules **9** has to be named as (*R*)-isomer.

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