Stereochemical Studies of *N,N'*-Diacetyl-*N,N'*-dimethyl-1,2-diamino-1,2-diphenylethanes and their Mono- and Di-thio Analogues by NMR and CD Spectroscopy and by Molecular Mechanics Calculations

José Luis Chiara,[a] Rumyana Petrova,[b] Mario Simeonov,[b] Stefan L. Spassov,[b]* Agha Zul-Quarnain Khan,[c‡] and Jan Sandström[c]*

[a]Instituto de Quimica Organica General, C.S.I.C., Juan de la Cierva 3, E-28006 Madrid, Spain, [b]Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences, 1113 Sofia, Bulgaria and [c]Division of Organic Chemistry 3, Chemical Center, University of Lund, P.O. Box 124, S-221 00 Lund, Sweden

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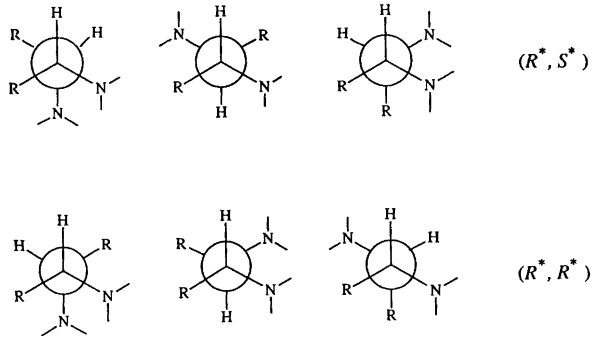
The *R*,R** and *R*,S** diastereomers of *N,N'*-diacetyl-*N,N'*-dimethyl-1,2-diamino-1,2-diphenylethane and their mono- and di-thio analogues (**1–6**) have been studied by ^{1}H and ^{13}C NMR spectroscopy and by empirical force-field calculations (MMP2-85). The NMR spectral data (chemical shifts, coupling constants and NOE) clearly show that all compounds exist in the *anti* conformation with the *Z,Z* configuration for the (thio)amide groups. The same result is obtained by the force-field calculations.

Four of the compounds (**2**, **3**, **4** and **6**) are chiral and have been resolved into enantiomers by chromatography on triacetylcellulose. The CD spectra of the first eluted enantiomers of **4** and **6** could be reasonably well reproduced by calculations based on minimum energy geometries for the *S,S* enantiomers, whereas no agreement could be reached for **2** and **3**. This agrees with the results of the force-field calculations, which predict one predominant conformer for each of **4** and **6**, but significant amounts of two rotamers (both *anti ZZ*) for each of **2** and **3**.

Two previous studies[1,2] of *N,N'*-diacyl-*N,N'*-dimethyl-1,2-diaminoethanes and their thio analogues have shown that the (thio)amide groups prefer the *ZZ* arrangement much in excess of the statistical average. Studies by NMR spectroscopy and empirical force-field calculations could in part explain this effect in terms of a preference for the *gauche* ethane conformation, which permits attractive dipole–dipole interactions between the (thio)amide groups in the *ZZ* orientation. However, the *ZZ* forms were shown to be favoured by other non-bonding interactions as well.

Introduction of substituents on the two ethane carbon atoms affects the *anti–gauche* equilibrium (referred to the remaining hydrogen atoms). In the *R*,S(meso)* diastereomer the conformer with *gauche* oriented (thio)amide groups is disfavoured, while it is favoured in the *R*R** analogue (Scheme 1). It was therefore considered of interest to extend the study to 1,2-disubstituted 1,2-bis-[(thio)acylamino]ethanes. With identical substituents, the *R*,R** and the monothio *R*,S** compounds are chiral, and



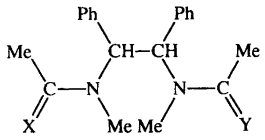
Scheme 1.

circular dichroism (CD) spectroscopy offers a further possibility for conformational study.

This study deals with *N,N'*-diacetyl-*N,N'*-dimethyl-1,2-diamino-1,2-diphenylethanes and their thio analogues **1–6** (Scheme 2). These compounds have been studied by ^{1}H and ^{13}C NMR spectroscopy, in particular the ^{1}H–^{1}H coupling constants and by 2D NOE spectra, by empirical force-field calculations, and after chromatographic enantiomer resolution (**2**, **3**, **4** and **6**), by CD spectroscopy.

[g] Present address: P.C.S.I.R. – F.R.C., Off University Road, Karachi-39, Pakistan.

* Authors to whom correspondence should be addressed.



	X = Y = O	X = O, Y = S	X = Y = S
R,S**	**1**	**3**	**5**
R,R**	**2**	**4**	**6**

Scheme 2.

Experimental

Preparations. meso-*1,2-Diamino-1,2-diphenylethane* was prepared according to Trippett,[3] an also, in better yield, by reduction of diphenylglyoxime with sodium in butanol. M.p. 119–120 °C (lit.[3] 120.5–121.5 °C). (1*R**,2*R**)-*1,2-Diamino-1,2-diphenylethane* was synthesized via (1*R**,2*R**)-isoamarine following the procedure described by Hawn *et al.*[4] *meso* and (1*R**,2*R**)-*N,N'-Diacetyl-1,2-diamino-1,2-diphenylethane* were prepared by heating the respective diamines with excess acetic anhdride. On being cooled, the acetic anhydride solution separated colourless crystals in 70–75 % yield, m.p. 320–323 °C after a crystal transformation at 230 °C (*meso*) and 260–261 °C (1*R**,2*R**). *meso* and (1*R**,2*R**)-*N,N'-diacetyl-N,N'-dimethyl-1,2-diamino-1,2-diphenylethane* (**1** and **2**) were prepared by reaction of the above acetylamino compounds with two equivalents of sodium hydride in dry DMF followed by addition of methyl iodide. Work-up by addition of water and extraction with dichloromethane gave colourless crystals in 75–80 % yield, m.p. 255–256 °C (*meso*, lit.[5] 258–259 °C and 135–136 °C (1*R**,2*R**) after recrystallization from ethanol. (1*R**,2*S**)- and (1*R**,2*R**)-*N-Acetyl-N,N'-dimethyl-N'-thioacetyl-1,2-diamino-1,2-diphenylethane* (**3** and **4**) were prepared by reaction of **1** and **2**, respectively, with one equivalent of 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane 2,4-disulfide ('Lawesson's reagent')[6,7] in 1.2-dimethoxyethane at ambient temperature. After evaporation and chromatography on silica (Merck 60) with toluene–ethyl acetate as the mobile phase, **3** and **4** were obtained in 57 and 63 % yield, m.p. 139–140 and 194–196 °C after recrystallization from ethanol.

The dithio analogues **5** (*meso*) and **6** (1*R**,2*R**) were prepared from **1** and **2** by reaction with the somewhat more efficient thionating reagent 2,4-bis(4-methylthiophenyl)-1,3,2,4-dithiadiphosphetane 2,4-disulfide[8] in dry boiling toluene for 4 and 7 h, respectively (until TLC showed complete consumption of the starting material). Chromatography as above gave **5** in 83 % and **6** in 85 % yield, m.p. 229–230 and 189–191 °C, respectively, after recrystallization from ethanol.

The structures of compounds **1–6** and their precursors follow from the structures of the starting diamines and from ^1H and ^{13}C NMR spectra of the products.

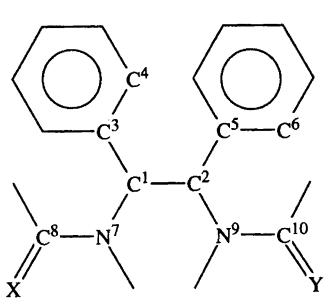
^1H and ^{13}C NMR spectra were recorded with a Varian Model XL-300 pulsed FT NMR spectrometer operating at 299.9 MHz for ^1H and at 75.4 MHz for ^{13}C and at ambient temperature (ca. 300 K). Proton-coupled ^{13}C spectra were obtained in the gated-decoupling mode. Difference NOE ^1H spectra were measured in the usual way, employing the 'interleaving' technique[9] to minimize subtraction artifacts. Irradiation times of 10 and 30 s were used, which gave practically the same NOE enhancements. The 2D ^1H–^{13}C NMR shift correlation was obtained by using the standard Varian HECTOR software. The digital resolution in the ^1H and ^{13}C spectra was 0.2 and 1.0 Hz respectively.

The chromatographic separations of **2**, **3**, **4** and **6** were performed with ethanol as the mobile phase, using the equipment already described,[10] with an UV (225 nm) and a polarimeter (365 nm) detector. The separations were not very good, with only one maximum on the UV detector trace, but the first fraction, taken to the first maximum/minimum on the polarimeter trace, was recycled twice in the same way to give a sample (E_1), which showed no sign of the second enantiomer (E_2) on rechromatography, indicating a high enantiomeric excess for E_1. The final solutions were evaporated to dryness and redissolved in acetonitrile (Merck Uvasol) and used directly for recording the CD spectra. Their concentrations were determined from their UV spectra. Less pure samples of the second enantiomer were studied in the same way to make certain that the two fractions really were enantiomers.

The CD spectra were recorded with a Jasco Model J-500A spectropolarimeter and *the UV spectra* with a Cary Model 2290 spectrophotometer.

The theoretical CD spectra were calculated by the matrix technique described by Schellman and coworkers,[11] and the input data were obtained as described before.[12] The directions of the transitions moments in the amide[13] and thioamide[14] groups were taken from published polarized spectra.

The empirical force-field calculations were performed with the Allinger MMP2-85 force field[15,16] in conjunction with the interactive computer graphics program MOLBUILD.[17] The non-standard force constants for the amide[1] and thioamide[18] groups have been reported earlier.



Scheme 3.

Results and discussion

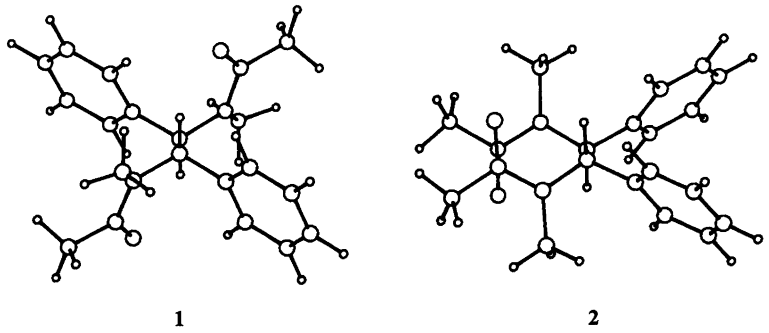
Molecular mechanics calculations. Calculations were performed on **1** and **2** with a large number of starting geometries, based on all combinations of *EE, EZ,* and *ZZ* configurations of the amide groups. The C–H groups were arranged *anti*, (+)-*gauche*, and (−)-*gauche* [(+) and (−) are equivalent for **1**] and with the amide and phenyl planes parallel or perpendicular to the ethane C–C bond. In this way, 22 energy minima were found for **1** and 33 for **2**. The calculated strain energies spanned a region of 62 kJ mol^{-1} for **1** and 69 kJ mol^{-1} for **2**. For both compounds, the *anti ZZ* forms were predicted to be the most stable ones (Fig. 1 and Table 1). For **2** a second *anti ZZ* form [**2**-(2)] was found only 0.9 kJ mol^{-1} higher in energy.

The lowest *EZ* and *EE* forms of **1** (both *anti*) were calculated to be 8.1 and 13.7 kJ mol^{-1}, and the lowest *gauche* form (*EZ*) 33.9 kJ mol^{-1} above the global energy minimum. The corresponding energies for **2** were 16.1, 23.5 and 23.5 kJ mol^{-1}.

Calculations were also performed for the mono- and di-thio analogues **3**–**6**, using, as starting geometries, the energy minima for the oxygen analogues but discarding those which were > 20 kJ mol^{-1} higher in energy than the global energy minima. Also in these cases *anti ZZ* forms were predicted to be lowest in energy. For **3** and **5**, the second most stable rotamers, only 3.7 and 4.3 kJ mol^{-1} higher in energy, were predicted.

A consequence of the *anti* conformation is that **1**, **3**, and **5** will also have *anti* orientation of the phenyl groups and of the amide/thioamide groups, while **2**, **4**, and **6** will have these groups *gauche* related (Fig. 1).

NMR results. The ^{1}H and ^{13}C NMR parameters for compounds **1**–**6** are presented in Table 2. The signal assignments were based on chemical shift comparisons with struc-



1 2

Fig. 1. Calculated minimum energy conformations of **1** and **2**.

Table 1. Calculated steric energies and dihedral angles for the most stable conformers of **1**–**6** [(*R,R*) configuration for **2**, **4** and **6**, *R*(S), *S*(O) for **3**]. For **3** and **4**, X = O, Y = S. Numbering according to Scheme 3.

Compound (conformer)	*E*/kJ mol^{-1}	Dihedral angle/°				
		C^3–C^1–C^2–C^5	C^2–C^1–C^3–C^4	C^1–C^2–C^5–C^6	C^1–C^2–N^9–C^{10}	C^2–C^1–N^7–C^8
1-(1)	−11.5	178.7	44.3	−48.5	52.0	−55.0
1-(2)	−4.2	179.3	41.3	−81.6	−157.7	141.3
1-(3)[a]	−3.4	178.9	71.4	−7.8	60.6	−40.0
2-(1)	−10.2	−46.4	−32.8	−33.4	−86.2	−86.1
2-(2)	−9.4	−60.5	−74.6	−74.4	37.4	37.4
3-(1)	−1.8	−179.7	−68.9	10.4	−71.1	39.4
3-(2)	+1.9	179.8	26.3	−58.0	−147.7	104.7
3-(3)[a]	+6.1	−179.4	74.7	−9.0	69.6	−36.7
4-(1)	−2.0	−47.5	−28.2	−29.3	−97.6	−88.1
4-(2)	+8.8	−57.9	−77.1	−79.1	34.3	36.5
5-(1)	+10.9	178.5	−77.2	58.7	−141.4	125.7
5-(2)	+14.8	179.2	11.0	−69.9	27.8	−71.6
5-(3)[a]	+15.1	−177.8	9.5	−78.7	−165.4	−71.8
6-(1)	+5.3	−47.7	−28.5	−28.3	−96.0	−95.8
6-(2)[a]	+19.0	−44.5	−30.5	−30.1	−95.9	−110.0
6-(3)	+25.2	−55.9	−79.9	−78.5	35.2	35.0

[a] *anti, EZ.* All other forms are *anti, ZZ.*

Table 2. ^1H and ^{13}C NMR chemical shifts (ppm) and coupling constants (Hz, in parentheses) for compounds **1–6** in $CDCl_3$.

Compd.	Rel. config.	Nucl.	CH_3C		CH_3N		CH		Ph		C=O	C=S
			O[a]	S[a]	O	S	O	S	O	S		
1	(*R*,S**)	^1H	1.79 s		2.62 s		6.69 s (11.6)[b]		7.2–7.4 m, 6 H[c] 7.53, dd, 4 H[d]			
		^{13}C	22.01 q (128.5)[e]		29.97 q (137.5)		53.12 d (138.5)		128.0–128.6 (CH) 136.61 (C)		170.74	
2	(*R*,R**)	^1H	2.09 s		2.72 s		6.71 s (10.2)[b]		7.15–7.23 m, 6 H 7.27 dd, 4 H			
		^{13}C	22.43 q (128.4)		31.44 q (138.0)		53.08 d (138.6)		127.6–129.2 (CH) 136.90 (C)		171.08	
3	(*R*,S**)	^1H	1.83 s	2.34 s	2.72 s	2.91 s	6.82 d (12.6)	7.93 d (12.6)	7.3–7.4 m, 6 H 7.71 dd, 2 H; 7.82 dd, 2 H			
		^{13}C	22.07 q (128.4)	33.28 q (129.6)	30.27 q (138.8)	33.99 q (139.6)	54.82 d (139.3)	60.30 d (138.4)	128.2–128.7 (CH) 135.63; 135.73 (C)		170.70	201.36
4	(*R*,R**)	^1H	2.10 s	2.64 s	2.83 s	3.01 s	6.82 d (12.0)	8.07 d (12.0)	7.15–7.25 m, 6 H 7.29 dd, 2 H; 7.45 dd, 2 H			
		^{13}C	22.54 q (128.3)	33.73 q (129.6)	33.14 q (138.6)	35.44 q (140.3)	53.77 d (138.1)	60.70 d (139.0)	127.8–129.2 (CH) 136.16; 136.46 (C)		171.48	201.55
5	(*R*,S**)	^1H		2.36 s		3.00 s		8.08 (12.1)[b]	7.35–7.45 m, 6 H 7.96 dd, 2 H			
		^{13}C		33.28 q (129.9)		34.25 q (139.5)		61.70 d (139.0)	128.4–129.0 (CH) 134.81 (C)			201.59
6	(*R*,R**)	^1H		2.64 s		3.12 s		8.22 (12.1)[b]	7.2–7.3 m, 6 H 7.50 dd, 4 H			
		^{13}C		33.80 q (130.2)		36.93 q (140.4)		60.84 d (140.4)	128.3–128.6 (CH) 135.67 (C)			201.99

[a]Denotes the amide and thioamide part of the molecule. [b]Vicinal ^1H–^1H coupling constant obtained from ^{13}C satellites in the ^1H spectrum. [c]*meta*- and *para*-H. [d]*ortho*-H. [e]One-bond ^{13}C–^1H coupling constant.

Table 3. Difference NOE enhancements (%) for compounds **1–6**.

Comp.	Rel. config.	CH_3N–C=O[a]					CH_3N–C=S					CH_3–C=O CH_3N(O)	CH_3–C=S CH_3N(S)
		CH_3(O)[b,c]	CH(O)	CH(S)	*o*-Ph(O)	*o*-Ph(S)	CH_3C(S)	CH(O)	CH(S)	*o*-Ph(S)	*o*-Ph(O)		
1	(*R*,S**)	4	12		3							4	
2	(*R*,R**)	4	9		2							3	
3	(*R*,S**)	4		10	3	1	3	11		3	2	5	4
4	(*R*,R**)	4		6	2	0	3	6		3	0	5	3
5	(*R*,S**)						3		9	4			6
6	(*R*,R**)						4		14	3			5

[a]Irradiated protons. [b]Protons for which NOE were observed. [c](O) and (S) denote the amide and thioamide part of the molecule for compounds **3** and **4**.

turally similar compounds,[2] difference NOE data (Table 2), and values of the one-bound ^{13}C–^1H coupling constants[19] (ca. 10 Hz larger for CH_3N than for CH_3C, Table 2), and they were ultimately confirmed by two-dimensional heteronuclear NMR shift correlation of compound **3** (Fig. 2). Unlike the non-phenylated analogues studied earlier,[1,2] the spectra of compounds **1–6** displayed signals for only one configurational isomer with respect to the (thio)amide C–N partial double bond within the limits of the NMR detection. The force-field calculations predict the *ZZ* form to be by far the most stable one, and this is unequivocally shown to be the case by the results of the ^1H NOE difference experiment. Clear NOE enhancements were obtained for the CH_3–C resonances upon irradiation of the CH_3N resonance frequency and *vice versa* (Table 3 and Fig. 3).

The high values of the vicinal proton–proton coupling

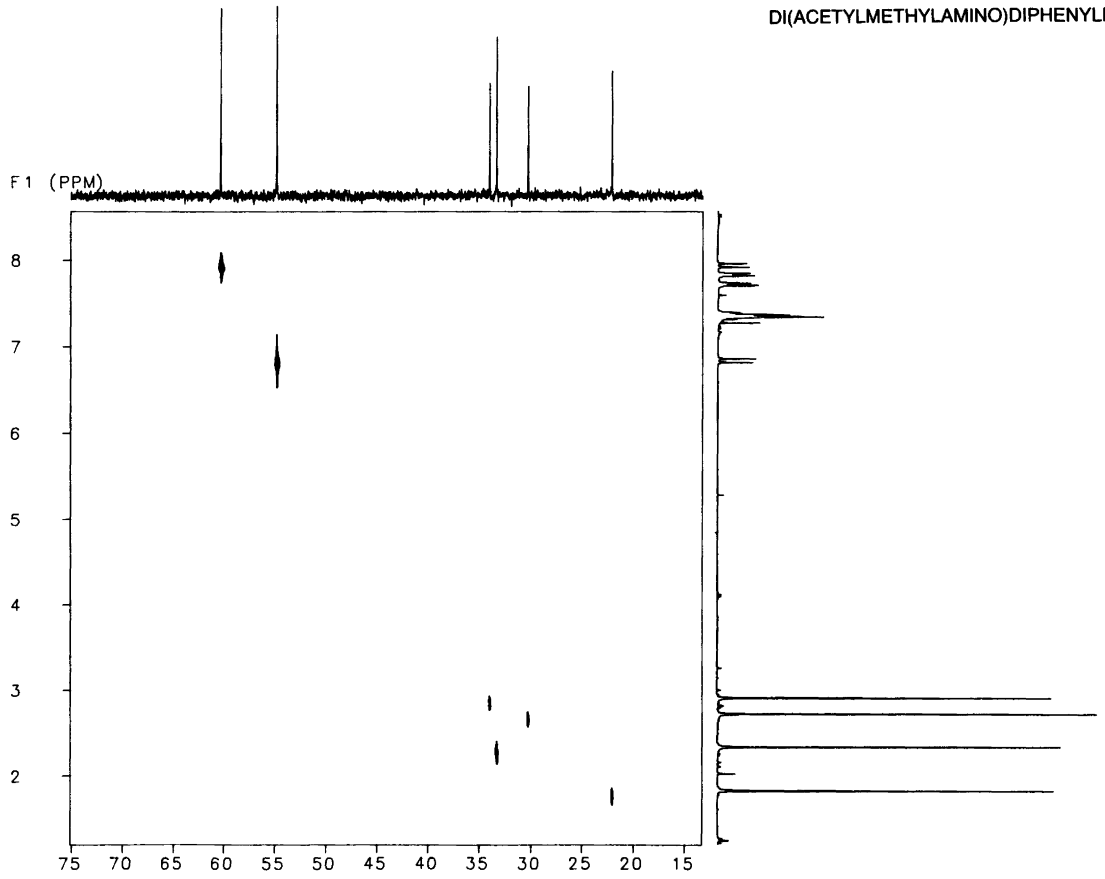


Fig. 2. 2D ^{1}H–^{13}C NMR shift correlation of **3** in $CDCl_3$ at 300/75 MHz, showing the ^{1}H and ^{13}C (aliphatic part) spectra in the vertical and horizontal directions, respectively, as well as the corresponding cross-peaks.

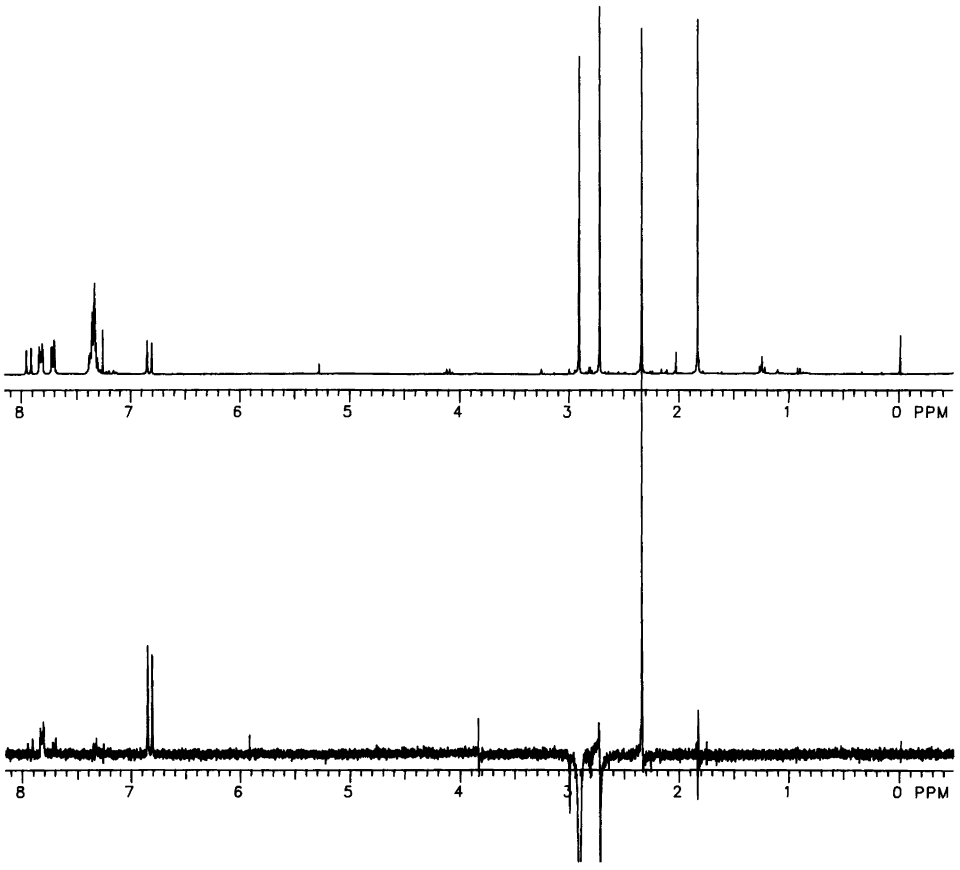


Fig. 3. Normal ^{1}H NMR spectrum of **3** at 300 MHz in $CDCl_3$ (top). Difference ^{1}H NOE spectrum of the same compound upon irradiation of the CH_3N–C=S proton resonance at 2.91 ppm. NOE enhancements are observed for the respective protons as shown in Table 3.

constants (10.2–12.6 Hz, Table 2) indicate favoured rotamers with *anti* hydrogen atoms for all compounds **1–6**. Calculations according to the expression due to Haasnoot *et al.*[20] predict a coupling constant of 10.5 Hz for the *anti* and ca. 1.7 Hz for the *gauche* forms, and evidently all compounds must be almost exclusively represented by their *anti* forms. This result is in agreement with literature data for other 1,2-diphenyl-substituted ethanes containing vicinal polar substituents.[21,22]

The NMR data, and in particular the NOE effects observed, may also be useful for gaining information concerning the rotational preference about the single C–N bonds and the phenyl group orientations. It follows from Table 3 that irradiation at the CH_3N proton frequency in the 'O-part' of **3** and **4** leads to NOE enhancements for the ethane CH proton resonance in the 'S-part' and for the *ortho* phenyl proton resonance in the 'O-part' and *vice versa*. This indicates spatial proximity between the respective irradiated and affected protons as shown in Fig. 1. The unusually strong deshielding of the ethane protons in all compounds (6.69–6.82 in the O part, 7.93–8.22 in the S part, Table 2) could be attributed to the combination of the anisotropy effects of the phenyl rings and the carbonyl and in particular the thiocarbonyl groups,[23] also in agreement with the proposed conformations. Furthermore, the considerable shielding ($\Delta\delta$ ca. 0.3 ppm) of the C–CH_3 protons in the '*meso*' compounds **1**, **3**, and **5**, as compared with the '*rac*' compounds **2**, **4** and **6**, is explained by a combination of shielding by the phenyl rings on the opposite carbon atom in the '*meso*' forms and deshielding by the C=O/C=S groups on the opposite carbon atom in the '*rac*' forms. The NMR spectra were recorded in $CDCl_3$ solution, but the NOE study was repeated with **3** in CD_3CN solution with practically identical results. Therefore, solvent effects on the conformations can probably be neglected.

With respect to the ^{13}C data, one should note the considerable shielding of the CH_3N carbons in compounds **1–6** as compared with the non-phenylated analogues studied before.[2] This effect amounts to ca. 7 and ca. 5 ppm for the '*meso*' and '*rac*' compounds, respectively. It can be attributed to increased steric hindrance (γ-*gauche* effect)[24] in compounds **1–6**. No similar effect is observed for the (thio) acetyl carbon atoms, which is in agreement with the conformations proposed (Fig. 1).

Table 4. UV and CD spectra of compounds **1–6**. Solvent acetonitrile, ε and $\Delta\varepsilon$ in units of $M^{-1}\ cm^{-1}$.

Compd.	UV λ_{max}/nm (ε)	CD λ_{max}/nm ($\Delta\varepsilon$)[a]
1	264 (320), 258 (430), 252 (380), 200 (32700)[b]	
2	268S[c] (530), 264S (410), 258 (510), 252 (510), 247 (530), 200 (20 000)[b]	268 (−0.42), 261 (−0.54), 254 (−0.43), 248 (−0.30), 220 (−60), 202 (−53)
3	279 (11 800), 200 (33 000)[b]	363 (+0.54), 271 (−3.63), 215 (+6.1)
4	350 (47), 281 (12 900), 200 (36 000)[b]	342 (−1.00), 281 (−33.2), 238 (+2.8), 220 (−37), 199 (−41)
5	355 (99), 280.5 (22 000), 200 (31 800)[b]	
6	340 (107), 280.5 (25 000), 200 (46 300)[b]	370 (+0.43), 286 (−43.6), 227 (+20), 193 (−34)

[a]First eluted enantiomer (E_1). [b]End absorption. [c]Shoulder.

UV and CD spectra. The UV spectra of **1** and **2** (Table 4) show a band with fine structure centred at 258 nm (^1A–^1L_b of the benzene chromophore)[25] but apart from that only strong end absorption ($\varepsilon \geq 20\,000$) at 200 nm. Not even shoulders due to ^1L_a transitions, expected at ca. 205 nm, are observed at $\lambda \geq 195$ nm. The thio analogues **3–6** show the typical thioamide bands,[26,27] a weak $n \rightarrow \pi^*$ band in the range 340–350 nm (for **3**, too broad to be observed) and a strong $\pi \rightarrow \pi^*$ band near 280 nm, and then only strong end absorption.

The CD spectrum of **2** (E_1) shows a weak negative ^1L_b band with fine structure, and two stronger negative bands at 220 and 202 nm. The latter are probably the long-wavelength part of a band system originating from interaction between the ^1L_a, ^1B_b and ^1B_a transitions in the two benzene rings and the $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions in the amide groups.[28] Calculations by the Schellman matrix method[11] with the geometries calculated for **2**-(1) and **2**-(2) (Table 1) reproduced the shapes and relative signs of the bands in the experimental spectrum quite well, although with too high an intensity ($|\Delta\varepsilon|$ up to 167). However, the calculated spectra of the two rotamers showed the opposite signs of all bands, which makes attempts to establish the absolute configuration futile.

Calculations without the amide groups led to large changes in the spectra, notably to reduction in the intensity of the ^1L_a band at 215–220 nm. The difference between **2**-(1) and **2**-(2) is in the rotation of the amide groups and phenyl rings with respect to the C^1–C^2 bond, and evidently the creation of rotational strength for all transitions is dominated by interactions involving the amide, ^1L_b and ^1B_b transitions, since the relative orientations of the ^1L_a and ^1B_a transitions are the same in the two rotamers.

The CD spectrum of **3** (E_1) shows a distinct negative $n \rightarrow \pi^*$ band at 361 nm, a negative thioamide $\pi \rightarrow \pi^*$ band at 271 nm, and a positive band at 215 nm. A calculation on the [*R*(O), *S*(S)] enantiomer with the **3**-(1) geometry gave negative bands at 360 and 270 nm ($\Delta\varepsilon = -2.8$ and -17.8) but also negative bands at 212 (−66.2) and 194 (−127.7) nm. A similar calculation with the **3**-(2) geometry gave a nearly inverted spectrum with negative bands at 360 and 184 nm ($\Delta\varepsilon = -0.62$ and 125.6), and positive bands at 271 (+6.1), 210 (+75.3), and 198 (+57.2) nm. The observed spectrum, which is rather weak, may well result from overlap of the

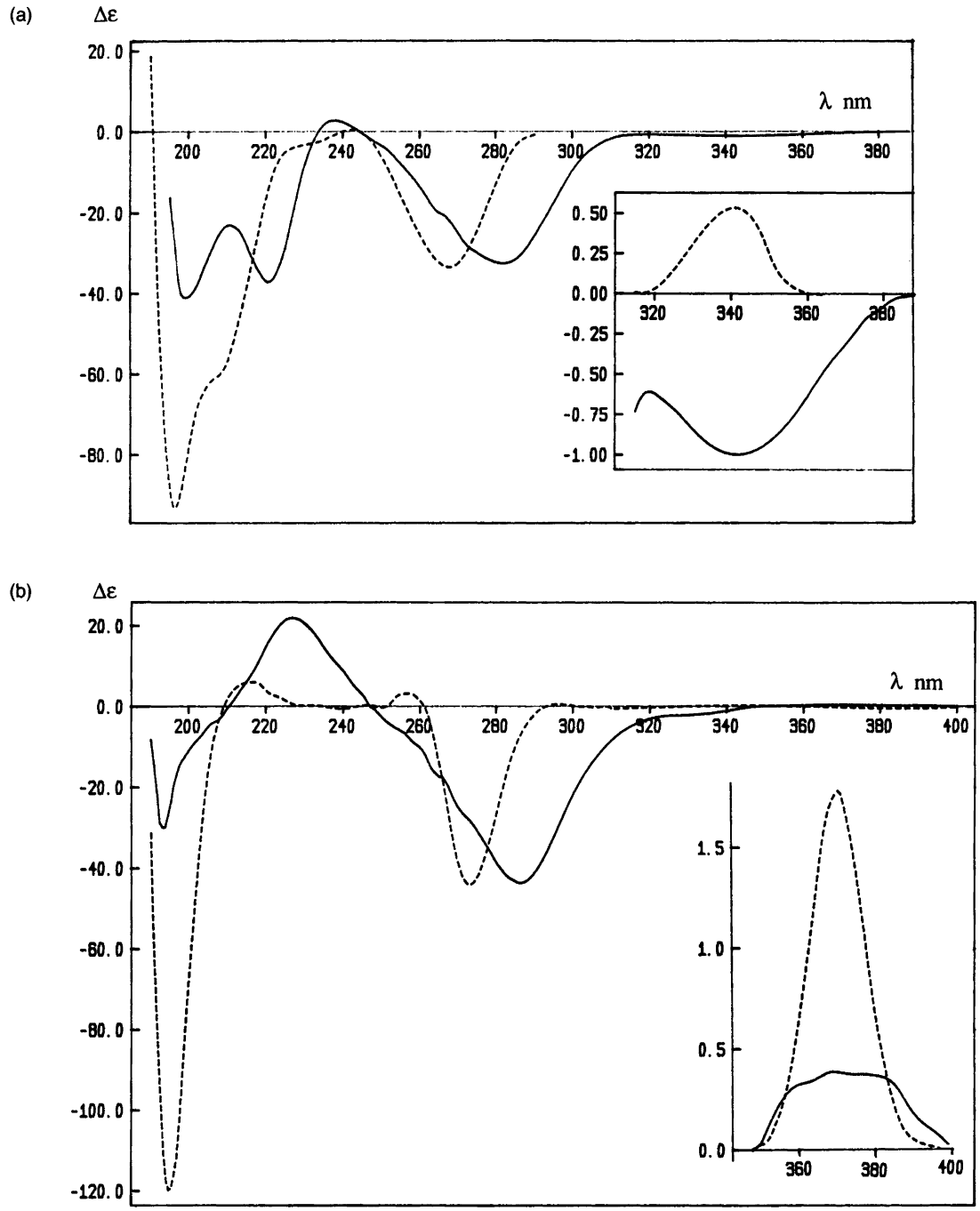


Fig. 4. (a) Experimental CD spectrum for **4** (E_1, ———) and calculated spectrum for (*S*, *S*)-**4**-(1) (-----). (b) The same for **6**.

spectra of two rotamers with mainly oppositely signed bands, but the uncertainty in the rotamer populations precludes any conclusion about the absolute configuration.

The CD spectrum of **4** (E_1) is considerably stronger than that of **3**. It shows negative bands at 342, 281, 220 and 199 nm, and a very weak positive band at 238 nm. The spectrum calculated for the (*RR*) enantiomer has positive bands at 270 (+31.6), 210s (+58), and 196 (+93.4) nm and negative bands at 340 (−0.63) and 184 (−155.6) nm. For this compound, the force-field calculations predict one major conformer, and the agreement between signs and intensities for the major bands in the experimental spectrum and that calculated for the *S*(O),*S*(S) enantiomer is reasonable [Fig. 4 (a)]. The deviation for the thioamide n → π* band may well be due to neglect of the one-electron mechanism. In view of the large number of atoms involved, the inclusion of static charges was not judged to be meaningful.

The CD spectrum of the bis-thioamide **6** (E_1) showed

positive bands at 370 and 227 nm and negative bands at 286 and 193 nm. Calculation for the *S,S* enantiomer with the **6**-(1) geometry gave negative bands at 274 (−44.6) and 195 (−120.0) nm and positive bands at 370 (+1.8) and 216 (+6.1) nm. Thus there is a reasonable agreement between the experimental spectrum for E_1 and that calculated for the *S,S* enantiomer [Fig. 4(b)].

Conclusions. The lack of agreement between experimental and theoretical CD spectra for **2** and **3** is ascribed to the existence of significant quantities of more than one rotamer. These systems will be studied by variable-temperature CD spectroscopy, which, if only two forms are involved, should reveal the free energy differences between them.[29,30] For **4** and **6**, which are predicted to have one dominant rotamer, comparison between experimental and calculated CD spectra allows conclusions about the absolute configurations. However, the agreement between the experimental and calculated spectra is not as good as for more rigid molecules,[31,32] which may be ascribed to significant population of higher torsional energy levels with respect to the chromophoric groups, which can lead to considerable deviations of the spectra from those valid for the minimum energy conformations.

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