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Conformational Preferences of α -Functionalised Keten-S,N-acetals: Potential role of S..O and S..S Interactions in Solution

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Abstract: PMR spectra of carbonyl compounds 2a-k reveal significant variations in the population of E and Z isomers on changing the solvent from CDCl₃ to DMSO-d₆. In non-polar media, the intramolecular N-H...O hydrogen bonded form is exclusively observed. In DMSO-d₆, the alternative Z form is also populated. A similar conformational switch is also noted in the corresponding thiones. Different interpretations are critically analysed. The most consistent explanation is suggested to involvean interplay of N-H....Xhydrogen bonding and S...X attractive interaction (X=O,S) in these systems. Ab initio calculations support this interpretation.

In earlier papers 1.2 we had reported an intriguing solvent-dependent conformational equilibrium in the nitro derivative 1. In non-polar solvents, 1 was shown to exist exclusively in the intramolecular H-bonded *E*-conformation. However, on increasing the solvent polarity, the *Z*-form was also populated, with two sets of peaks being seen simultaneously in ¹H, ¹³C and ¹⁵N NMR spectra. The *Z*:*E* ratio in DMSO-d6, the solvent of maximum polarity studied, was 4:1. The solid state structure of 1 as determined by X-ray diffraction corresponds to 1-*Z*. Interestingly, the structure revealed a short S..O contact of 2.68Å (sum of the van der Waals radii: 3.2 Å), suggesting a possible role for an attractive interaction between the atoms in determining the conformational equilibrium changes. In a preliminary study, we had shown that a similar solvent-dependent *E*/*Z* change occurs in the carbonyl derivative **2b** as well².

In the present article we establish the generality of the conformational behaviour for a number of carbonyl derivatives, **2a-k**. Various explanations for the observed population differences are discussed and evaluated using data obtained for the related models **9-12**. The conformational study has also been extended to the thione derivatives **7**. A consistent interpretation for all the observed results is provided with supportive ab initio calculations on model systems.

Synthesis

The enaminoketones 2 were prepared by using either one of the two known routes :(a) Condensation of an α -haloketone with a cyclic dithiocarbamate, followed by sulfur extrusion³ or (b) condensation of an acylketen dithioacetal with the appropriate amimoalcohol or aminothiol⁴. The methyl ketone 2h was prepared by the second method, using acetylacetone as the starting material; final mono deacetylation yielded 2h⁴. Lawesson thionation of the enaminoketones led to the thioacylketen S,N-acetals²³.



E/Z equilibria in carbonyl compounds 2.

The IR spectrum of 2a in CHCl₃ exhibits concentration-independent bands at 3210 and 1610 cm⁻¹ for the NH and CO stretching modes respectively. This proves that in CHCl₃, 2a exists in the intramolecularly H-bonded *E* configuration. The ¹H NMR spectrum of this compound in CDCl₃ at 20°C exhibits sharp signals characteristic of a single conformer (*E*). On addition of DMSO-d6 to this solution, signals corresponding to the (*Z*) isomer appear. The population of the (*Z*) isomer increases with increasing DMSO-d6 content, reaching nearly 40% in pure DMSO-d6. This behaviour is reminiscent of that of 1, although in that case, the proportion of the *Z* conformer in DMSO-d6 reached 80%. The assignment of the peaks in pure CDCl₃ and DMSO-d6 to the *E* and *Z* isomers of 2 is shown in Table 1. The large chemical shift difference for NH between the intramolecular H-bonded *E* configuration and the *Z* form is noteworthy. The *para* substituted compounds 2b, 2c and 2d as well as the *ortho*-hydroxy derivative 2e and the methyl ketone 2h behave in a similar manner. However, in the case of *o*-methoxyphenyl 2f and *o*-chlorophenyl 2g derivatives, there is considerable line-broadening in DMSO-d6 are shown in Table 2. The ratio varies over a narrow margin.

Table 1

Compd	** 	NH		=CH		NCH ₂		SCH ₂	
		E	Z	E	Z	E	Z	E	Z
2a	CDCl ₃ DMSO-d6	10.55 10.40	8.00	5.90 6.00	6.30	3.90 3.90	3.59	3.20 3.30	3.10
2b	CDCl ₃ DMSO-d6	10.55 10.50	- 8.40	5.90 5.90	6.20	3.90 4.00	3.85	3.20 3.30	3.05
2c	CDCl3 DMSO-d6	10.60 10.33	8.30	6.00 6.00	6.33	3.95 3.90	3.60	3.30 3.10	3.20
2đ	CDCl3 DMSO-d6	10.80 10.50	8.75	5.90 6.30	6.05	4.00 3.90	3.65	3.30 3.65	3.40
2e	CDCl ₃ DMSO-d6	10.25 10.20	8.95	6.00 6.00	6.40	4.00 3.80	3.65	3.30 3.30	3.15
2f	CDCl ₃ DMSO-d6	10.60 10.25	8.30	5.90 **	- **	3.95 **	- **	3.25 **	- **
2 g	CDCl3 DMSO-d6	10.60 10.25	- 8.60	5.70 **	- **	4.05 **	- **	3.35 **	3.10
2h	CDCl3 DMSO-d6	10.90 9.90	8.10	5.30 5.20	5.60	3.85 3.80	3.50	3.20 3.20	3.00
2i	CDCl ₃ DMSO-d6	12.45 12.15	-	5.75 5.75	-	3.55 3.45	-	3.20 3.10	-
2j	CDCl3 DMSO-d6	11.75 11.90	-	5.75 5.75	-	3.55 3.50	-	3.15 3.10	-
2k	CDCl3 DMSO-d6	12.35 12.05	-	5.70 5.50	2	3.50 3.40	-	3.05 3.10	-

¹H NMR Chemical shifts (δ) for Compound 2

** :- Line broadening

There is no significant difference in the behaviour of 2c (E:Z = 65:35) and 2d (E:Z = 56:44). Thus, the electronic nature of the substituents on the phenyl ring has no influence on the relative population of the two isomers. The higher population of (Z) isomer in the case of 2e is to be expected, since it can still avail itself of an intramolecular H-bond with the phenolic OH being the donor.

Molecular geometry seems to play a crucial role in determining the magnitude of solvent induced shift of conformational equilibrium. This is obvious from a comparison of the two benzoyl derivatives 2a and 2i. The former has a 5-membered hetero ring as part of the keten-S,N-acetal, while the latter has a 6-membered ring. The thiazolidine derivative 2a, as mentioned above, exhibits solvent dependent conformational change. In contrast, the thiazine derivative 2i shows only one sharp set of peaks in both CDCl₃ and DMSO-d6. In all these cases, the *E*-configuration is assigned, based on IR spectral data and the chemical shift of the NH in the ¹H NMR spectrum. The NH signal in the thiazine is seen further downfield than in the thiazolidine derivatives; this may indicate a stronger intramolecular H-bond in the former. The comparison of the *ortho*-hydroxyphenyl derivatives 2e and 2j brings out the dramatic effect of changing the hetero-ring size. While in the former, in DMSO-d6 solution, the Z-conformer is populated to the extent of 52%, with the thiazine analog 2j, the Z-isomer is not observable at all.

Table 2

L/L Iano III DIVISO-u	E/Z	ratio	in	DMSO	-d6
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Compound	E	Z
2a	62	38
2b	65	35
2c	65	35
2d	56	44
2e	48	52
2 h	59	41
2i	< 95	>5
2j	100	-
2 k	100	-

The important conclusion therefore emerges that the relative energy of the E and Z isomers in 2 is critically dependent on the geometry of the molecule and especially on the local alignment at S and O. A similar observation had been made earlier with the nitro compounds.² An entropic price apparently has to be paid for orienting the molecule in the proper geometry. The open-chain analog 3^5 which has freedom of rotation around the N-CH₃ and S-CH₃ bonds, also prefers to remain in the E form in polar and nonpolar solvents.

Factors influencing E/Z ratios

In push-pull ethylene systems, such as those present in 1, 2 and 3, the barrier to rotation around the formal C-C double bond is considerably reduced⁶; typically, this could be of the order of 10-15 kcal. mole⁻¹. Interconversion of E and Z isomers should occur readily under the conditions studied experimentally. Hence the relative populations of conformers directly reflect their stabilities. As noted above, both 1a and 2a exist exclusively in the intramolecular hydrogen-bonded E form in non-polar solvents, while in polar solvents there is a significant population of the Z- conformer.

Three possible explanations can be considered for the increased stability of the Z-isomers in polar solvents.

i) Solvent effect

It is known that the barrier to rotation around the C-C double bond in push-pull systems decreases in solvents of high dielectric constant. Along with this, the difference in energy between E and Z forms also decreases with increasing solvent polarity.^{6,8} There may therefore be an increase in the population of the isomer with greater charge separation, viz., the one in which NH and C=O are *trans* to each other. This explanation assigns no role for the sulfur atom in the ring, and should therefore be valid for the isosters 4 and 5 of 2a. To assess this proposal, the pyrrolidine 4 and oxazolidine derivative 5 were synthesized^{3,9} and their ¹H NMR spectra in CDCl₃ and DMSO-d6 recorded. It was clear that in both cases, there was no change in configuration in going from non-polar to polar solvents. (Table 3). This





¹H NMR Data for the Pyrrolidine (4) and Oxazolidine (5) analogs of 2a

Compound		NH	=C H	хсн ₂	NCH ₂
4	CDCl ₃	13.30	5.80	1.90 a	3.60
	DMSO-d6	10.20	5.80	1.90	3.55
5	CDCl ₃	10.00	5.60	4.50 ^b	3.65
	DMSO-d6	9.85	5.55	4.50	3.75

a: $X = CH_2$; b: X = O

renders any explanation based exclusively on solvent polarity extremely unlikely. The same holds true for any presumed steric effect due to solvation of NH in DMSO-d6. The solvent induced conformational change in 1 and 2 must therefore involve an active role for sulfur.

ii) Hypervalent Sulfur.

The ability of sulfur to form hypervalent structures can be invoked to suggest that the Z-isomer of **2a-h** is in fact a structure as shown in **6**. This represents an extreme description of the S..O attractive interaction. Since the structure is expected to be highly polarized, it may be stabilized in DMSO. The geometric criteria for the proposed structure with T-shape at the hypervalent sulfur are likely to be quite stringent. Hence, the observed differences in the behaviour of thiazolidine **2a** and thiazine **2i** can be readily understood. The proposal can also be extended to thiones (7), as shown in (8) which would explain the intriguing results discussed below.

The above proposal may be questioned on a number of grounds. Hypervalent sulfur structures generally involve linear arrangements of X-S-Y units in which X and Y are highly electronegative atoms or polarizable sulfur⁷. Examples of structures with apical C-S-O units, as in 6, have not yet been characterized. Further, large electronic structural changes as in 6 should lead to larger effects on the chemical shifts than those observed for 2Z.

A proposal involving a mild attractive S..O interaction would best explain the observed results. iii) Non-bonded S..O interaction.

The idea of non-bonded attractive interaction between a divalent sulfur atom and a suitably located oxygen has been used by X-ray crystallographers to explain the unusual short contact observed in several solid state structures¹⁰. The essential sub-structure required for the interaction is S-A=B-Y=O in which A=B has the *cis*-configuration and B-Y has *s-cis* configuration. This condition is met in both 1Z and 2Z. It is therefore likely that such a non-bonded attractive force might be responsible for the observed behaviour of these compounds. The implication is that once the intramolecular H-bonds of the *E* isomers are broken by solvation, the weak attractive force manifests itself in populating the Z configuration. Obviously this also explains the absence of such behaviour in the case of the pyrrolidine 4 and the oxazolidine 5 analogs.

Another important aspect which has come to light from an X-ray crystallographic analysis is the co-linearity of the three atoms C-S..O; this arrangement might be essential for the interaction of the lone pair on oxygen with the σ^* antibonding orbital of the C-S bond. This in turn might explain the difference in behaviour between the thiazolidine 2a and the thiazine 2i.

Although (S,O) and a number of other atom pairs have been shown to exhibit such non-bonded attraction 11,12, all the evidence observed so far refer only to the solid state. To our knowledge, there has been no confirmed instance in which this has been observed in solution.

E/Z equilibria in thiones (7)

Table 4

Compound	Solvent	N	н	=(СН	NC	H ₂	SC	Н2	E/Z
		E	Z	E	<u>Z</u>	E	Z	E	<u>Z</u>	
7a	CDCl ₃ DMSO-d6	13.75 13.31	9.71	6.75 6.20	7.15	4.15 4.10	3.75	3.40 3.40	3.25	100/0 59/41
7c	CDCl3 DMSO-d6	13.70 13.20	9.60	6.70 6.75	7.25	4.15 **	- **	3.30 **	- **	100/0 56/44b
7d	CDCl3 DMSO-d6	13.30 13.20	10.50	6.75 **	- **	4.25 **	- **	3.50 **	- **	100/0 **
7f	CDC13 DMSO-d6	13.75 13.15	9.55	6.65 6.45	- **	4.10 **	- **	3.30 **	- **	100/0 **
7g	CDCl3 DMSO-d6	13.70 13.10	9.75	6.55 6.70	- 6.48	4.20 4.10	- **	3.45 **	- **	100/0 **
7h	CDC13 DMSO-d6	13.50 13.10	9.43	6.30 5.80	- 6.60	4.05 4.05	3.65	3.35 3.40	3.20	100/0 67/33
7i	CDCl3 DMSO-d6	15.00 15.20	-	6.50 6.45	-	3.55 3.60	-	3.20 3.20	-	100/0 100/0
7k	CDCl ₃ DMSO-d6	14.95 14.65	-	6.35 6.15	-	3.60 3.55	-	3.10 3.15	-	100/0 100/0

¹H NMR Data and E/Z ratios for the Enaminothiones^c 7

** :- Line broadening; b: Ratio calculated from NH integration c: 'a' to 'k' same as 2 except 'b' 'c' and 'j'

In a further extrapolation of this study, we have included the thiones 7 generated by Lawesson thionation²³ of the acylketen-S,N-acetals 2. The phenolic compound 2e and 2j did not yield any product in this reaction. The relevant ¹H NMR data and E/Z ratios are given in Table 4. Interestingly the behaviour of the thiones more or less parallels that of the oxo compounds 2. Thus 7a exists in the *E* form in CDCl₃; but in DMSO-d6, the E/Z ratio is 60:40. The same is true of 7c and the methyl compound 7h. As with the oxo compounds 2i and 2k, the thiobenzoyl derivatives 7i and 7k of the thiazine series exist only in the *E*-form even in pure DMSO-d6. The ortho-substituted derivatives 7f and 7g as well as the *p*-nitrophenyl compound 7d show considerable line broadening in DMSO-d6; the E/Z ratio could not therefore be determined in these cases.

The surprising similarity in the E/Z ratio of 2a and 7a in DMSO-d6 may appear to throw some doubt on the validity of the non-bonded S...O attractive forces as being operative in the former. One explanation could be that while the conformational equilibrium in 2a measures the strength of the S..O interaction relative to an intramolecular N-H...Ohydrogen bond, the corresponding equilibrium with 7a compares the weak S..Sinteraction with the N-H..Shydrogen bond (which is definitely known to be weaker than N-H..O hydrogen bond)¹³.

Theoretical studies -

To confirm the above interpretation, ab initio calculations¹⁴⁻¹⁶ were carried out on model systems. The magnitudes of S..O and S..S interactions were probed using 9 and 10. In order to obtain a direct comparison with N-H..O and N-H..S hydrogen bond strengths, the amino derivatives 11 and 12 were examined. Two conformations were considered in each case, of which only one has a potentially stabilizing intramolecular interaction. Geometry optimization was carried out with the 3-21G and 3-21G^{*} (augmented with d orbitals on sulfur) basis sets. Additional calculations were carried out with the 6-31G^{*} basis set (d functions on all non-hydrogen atoms) and also including electron correlation at the second order Moller-Plesset level using the 3-21G^{*} geometries

On the basis of the computed conformational energy differences (Table 5), the strongest intramolecular interaction among the systems studied is the N-H..O hydrogen bond in 11. A value of 6.5 k.cal. mol⁻¹ is obtained at the $6-31G^*$ level. The N-H..S interaction is weaker (5.0 k.cal. mol⁻¹). These values as well as their basis set dependence are comparable to earlier results on related hydrogen bonded systems. 16.17 Compared to the hydrogen bonds, the S..O interaction in 9 is quite weak. Even after inclusion of sulfur d orbitals, 9a is computed to be more stable than 9b by 3.1 k.cal. mol⁻¹. At the highest level employed, MP2/ $6-31G^*$, the magnitude of S..O interaction in 9 is estimated to be 2.4 k.cal. mol⁻¹. Although this represents a relatively modest attractive interaction, it can prove to be significant in determining conformations.



Among the systems considered, intramolecular interaction between divalent sulfur and the thiocarbonyl unit is the weakest. At uncorrelated level of theory, S..S interaction is computed to be mildly repulsive. However, at the MP2/6-31G^{*} level, a small stabilization is indicated.

The optimized geometries of 9-12 provided additional insights into the nature of interactions in these systems. The S. Odistance in 9a is 2.90 Å at the 6-31G^{*} level. It becomes shorter (2.84Å) with the inclusion of d orbitals on sulfur. This value is larger than that observed for 1 (2.68 Å)¹, consistent with the stronger S. O interaction expected for the nitro compound. A key structural feature in 9a is that the carbonyl oxygen is nearly collinear with the H-S bond (168°). Further, the computed O=C. Sangle is around 93°. The p-type oxygen lone pair is ideally placed for interaction with the H-S σ^* orbital. These results are similar to those computed earlier¹⁸ for model system 13 and to the preferred direction of nucleophilic approach towards sulfur noted on the basis of an analysis of a large number of crystal structures¹⁹. Chemical evidence also points to the preference for backside approach of nucleophiles towards sulfur²⁰.

The nonbonded S..S distance is quite large in **10a** (3-21G : 3.34Å;3-21G^{*} : 3.21Å). While the H-S..S unit is computed to be fairly collinear (171°), the relatively acute C=S..S angle (79°) suggests that the thiocarbonyl in-plane lone pair is not ideally aligned for interaction with the H-S σ^* orbital. The magnitude of S..S interaction may therefore be larger in unencumbered systems.

The computed geometries of **11a** and **12a** reveal the presence of hydrogen bonding. The H..O (2.01 A⁰) and H..S (2.38 A⁰) contacts are fairly short, but shorter distances have been noted in unconstrained systems^{16,17}. The favored collinear arrangement²¹ of N-H..O (126⁰) and N-H..S (131⁰) units are not achieved. The carbonyl group is better aligned than the thione for interaction on the basis of the computed C=O..H (100⁰) and C=S..H (84⁰) angles.

Interestingly, the presence of a hydrogen bond or S. O interaction does not produce significant reduction in the bond angles involving the heavy atoms. The largest reduction on removing potential intramolecular attraction is around 4° for 12a relative to 12b. In general, the angles are all greater than 120°. Angle distortions are not prerequisites or indicators of intramolecular interactions in these systems²².

Table 5.

Molecule	3-21G*		6-31G*		MP2/6-31G*		
	E	Rel E	E	Rel E	E	Rel E	
9a	-585.35840	0.0	-588.26818	0.0	-588.94231	0.0	
9b	-585.35349	3.1	-588.26786	0.2	-588.93844	2.4	
10a	-906.57509	1.1	910.90502	2.3	-911.56642	0.0	
10b	-906.57686	0.0	-910.90874	0.0	-911.56572	0.4	
11a	-244.43617	0.0	-245.80350	0.0			
11b	-244.42077	9.6	-245.79311	6.5			
12a	565.65498	0.0	568.44449	0.0			
1 2b	-565.64633	5.4	-568.43637	5.0a			

Calculated Total Energies (Hartree) and Relative energies (k.cal mole⁻¹) of 9-12^a.

a: Using 3-21G* optimized geometries

Conclusions

The present study of conformational equilibria in different solvent systems using NMR provides convincing evidence for the presence of an attractive intramolecular S...Ointeraction in the enaminoketones 2(a to h). The related S....Sinteraction in the enaminothiones 7 is weak. Greater attraction may be possible in conformationally less constrained systems. Ab initio calculations on models yield quantitative estimates of these interactions relative to intramolecular hydrogen bond strengths in related geometries.

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EXPERIMENTAL

General: Melting points are uncorrected. IR spectra were recorded in CHCl₃ solution or as nujol mulls on a Perkin-Elmer model 599B infrared spectrometer, using NaCl optics. PMR spectra were recorded on a Bruker WH90 or a Bruker AC-200 instrument; chemical shifts are expressed in ppm. downfield from Me₄Si used as internal standard.

Synthesis of enaminoketones 2. Method A Compounds $2a^4$, $2e^4$, 2f, 2i, 2j and 2k were prepared in two steps by the sulfide contraction route. The first step was S-alkylation of thiazolidine-2-thione or 1,3-thiazine-2-thione by the α -haloketone. This was followed by sulfur extrusion³ in the second step to give the enaminoketones 2.

2-Benzoylmethylenethiazolidine (2a⁴): Yield 69%; Light yellow crystalline solid, m.p. 168°C; ¹H NMR (CDCl₃): δ 3.20 (t,J=8Hz,2H,SCH₂), 3.90 (t,J=8Hz,2H,NCH₂), 5.90 (s,1H,=CH), 7.2-7.8 (m,5H,ArH), 10.55 (bs,1H,NH); **IR** (nujol): 3200, 1600, 1580cm⁻¹; **MS:** m/z 205 (M⁺,10%); 204 (100). **2-(2-Hydroxybenzoyl)methylenethiazolidine (2e):** Yield 80%; Yellow crystalline solid, m.p. 140°C; **1**H NMR (CDCl₃): δ 3.30 (t,J=8Hz,2H,SCH₂), 4.00 (t,J=8Hz,2H,NCH₂), 6.00 (s,1H,=CH), 6.6-7.6 (m,4H,ArH), 10.25 (bs,1H,NH), 13.55(s,1H,OH); **IR**(nujol): 3260, 3000, 1600, 1580, 1530 cm⁻¹; **MS:** m/z 221 (M⁺, 100%), 121 (60), 204 (45), 101 (30); Anal. Calcd. for C₁₁H₁₁NO₂S: C, 59.70; H, 5.00; N, 6.33; S, 14.47. Found: C, 60.12; H, 5.39; N, 6.33; S, 14.49.

2-(2-Methoxybenzoyl)methylenethiazolidine (2f): Yield 75%; Light yellow viscous liquid; ¹H NMR(CDCl₃): δ 3.25 (t,J=8Hz,2H,SCH₂), 3.90 (s,3H,OCH₃), 3.95 (t,J=8Hz,2H,NCH₂), 5.9 (s,1H,=CH), 6.95-7.6 (m,4H,ArH), 10.6 (bs,1H,NH); **IR**(neat): 1390, 1580,1600, 2940, 3200 cm⁻¹; MS: m/z 235 (M⁺ 21%), 135 (100), 204 (86). Compound was not stable enough for getting a good microanalysis.

2-Benzoylmethylenethiazine (2i): Yield 75%; Colourless crystalline solid, m.p. 104-105°C; ¹H NMR (CDCl₃): δ 2.25 (m,2H,CCH₂), 3.20 (t,J=8Hz,2H,SCH₂), 3.55 (t,J=8Hz,2H,NCH₂), 5.75 (s,1H,=CH), 6.40-7.9(m,5H,ArH), 12.45(bs,1H,NH); **IR**(nujol): 3000, 1580, 1470 cm⁻¹; **MS:** m/z 219 (M⁺,35%), 77 (100); Anal. Calcd. for C₁₂H₁₃NOS C, 65.72; H, 5.97; N, 6.38; S, 14.62. Found: C, 65.82; H, 6.75; N, 6.64; S, 14.56.

2-(2-Hydroxybenzoyl)methylenethiazine (2j): Yield 50%; Colourless crystline solid, m.p. 125-127°C; ¹H NMR (CDCl₃): δ 2.25(m,2H,CCH₂), 3.15(t,J=8Hz,2H,SCH₂), 3.55(t,J=8Hz,2H,NCH₂), 5.75 (s,1H,=CH), 6.70-7.50 (m,4H,ArH), 11.75 (bs,1H,NH), 13.75 (s,1H,OH); **IR**(CHCl₃) 3400, 3020, 1600, 1580 cm⁻¹; **MS:** m/z 235 (M⁺,93%), 188 (100); Anal. Calcd. for C₁₂H₁₃NO₂S: C, 61.28; H, 5.57; N, 5.95. Found: C, 62.00; H, 5.67; N, 6.07.

2-(2-Methoxybenzoyl)methylenethiazine (2k): Yield 62%; Colourless crystalline solid, m.p. 107-108°C; ¹H NMR (CDCl₃): $62.20(m,2H,CCH_2)$, $3.05(t,J=8Hz,2H,SCH_2)$, $3.50(t,J=8Hz,2H,NCH_2)$, $3.75(s,3H,OCH_3)$, 5.70(s,1H,=CH), 6.90-7.60(m,4H,ArH), 12.35(bs,1H,NH); **IR**(nujol+CHCl₃): 3400, 1600, 1610 cm⁻¹; **MS:** m/z 249 (M⁺,9%), 135 (100); Anal. Calcd. for C₁₃H₁₅NO₂S: C, 62.65; H, 6.00; N, 5.60. Found: C, 62.60; H, 62.2; N, 5.77.

Method B Compounds $2b^2$, $2c^4$, 2d, 2g were prepared by condensation of an acylketene dithioacetal with 2-aminoethanethiol in ethanol at reflux temperature⁴.

2-(4-Chlorobenzoyl)methylenethiazolidine (2b²): Yield 80%; Light yellow crystalline solid, m.p. 137-139°C; ¹H NMR (CDCl₃): δ 3.20 (t,J=8Hz,2H,SCH₂), 3.90 (t,J=8Hz,2H,NCH₂), 5.90 (s,1H,=CH), 7.30 (d,J=9Hz,2H,ArH), 7.70 (d,J=9Hz,2H,ArH), 10.55 (bs,1H,NH); **IR**(nujol): 3200, 1590 cm⁻¹; MS: m/z 239 (M⁺,79%).

2-(4-Methoxybenzoyl)methylenethiazolidine (2c⁴): Yield 73%; Light yellow crystlline solid, m.p. 154-156₀C; ¹H NMR (CDCl₃): δ 3.30(t,J=8Hz,2H,SCH₂), 3.75(s,3H,OCH₃), 3.95(t,J=8Hz,2H,NCH₂), 6.00(s,1H,=CH), 6.90-7.80(m,4H,ArH), 10.60(bs,1H,NH); **IR**(CHCl₃) 3260,2940,1610,1580 cm⁻¹; MS: m/z 235 (M⁺,64%).

2-(4-Nitrobenzoyl)methylenethiazolidine (2d): Yield 44%; Yellow crystalline solid, m.p. 120-122°C; ¹H NMR (CDCl₃): $\delta 3.30(t,J=8Hz,2H,SCH_2)$, 4.00 (t,J=8Hz,2H,NCH₂), 5.90 (s,1H,=CH), 8.00-8.30(m,4H,ArH), 10.80 (bs,1H,NH); **IR**(nujol): 2900, 1600, 1550 cm⁻¹; **MS**: m/z 250 (M⁺,45%), 128 (100); Anal. Calcd. for C₁₁H₁₀N₂O₃S: C, 52.78; H, 4.02; N, 11.20; S, 12.81. Found: C, 52.80; H, 4.11; N, 11.19; S, 12.67.

2-(2-Chlorobenzoyl)methylenethiazolidine (2g): Yield 58%; Light yellow crystalline solid, m.p. 138-140°C; ¹H NMR (CDCl₃): $\delta 3.35$ (t,J=8Hz,2H,SCH₂), 4.05 (t,J=8Hz,2H,NCH₂), 5.70 (s,1H,=CH), 7.40-7.70 (m,4H,ArH), 10.60 (bs,1H,NH); **IR**(nujol): 3250, 3000, 1600 cm⁻¹; **MS:** m/z 239 (M⁺,45%), 204 (100); Anal. Calcd. for C₁₁H₁₀ClNOS: C, 55.12; H, 4.20; N, 5.84. Found: C, 55.68; H, 4.43; N, 5.77.

1-Phenyl-2-(2-pyrrolidinylidene)ethanone (4): This compound was prepared by a reported procedure for 1-4'-bromophenyl2-(2-pyrrolidinylidine)-ethanone³; m.p 110°C; Anal. Calcd. for $C_{12}H_{13}NO$: C, 77.01; H, 6.95. Found: C, 77.52; H, 7.01.

General procedure for thionation

A mixture of, compound 2 (10 mmol) and Lawesson reagent²³ (6 mmol) was stirred and heated in benzene at 80°C under an inert atmosphere for 4h. The solvent was then removed in vacuo and the product purified by chromatography on silica gel column (petroleum ether-ethyl acetate)

2-Thiobenzoylmethylenethiazolidine (7a): Yield 75%; Yellow crystalline solid, m.p. 94-95°C; ¹H NMR (CDCl₃): δ 3.35 (t,J=8Hz,2H,SCH₂), 4.15 (t,J=8Hz,2H,NCH₂), 6.70 (s,1H,=CH), 7.30-7.80 (m,5H,ArH), 13.75 (bs,1H,NH); MS: m/z 221 (M⁺,83%), 128 (100); **IR**(nujol): 3000, 2800, 1570, 1550 cm⁻¹; Anal. Calcd. for C₁₁H₁₁NS₂: C, 59.72; H, 4.97. Found: C, 59.52; H: 4.89.

2-(4-Methoxythiobenzoyl)methylenethiazolidine (7c): Yield 80%; Yellow crystalline solid, m.p. 156-157°C; ¹H NMR (CDCl₃): δ 3.30(t,J=8Hz,2H,SCH₂), 3.85(s,3H,OCH₃), 4.15(t,J=8Hz,2H,NCH₂), 6.70(s,1H,=CH), 6.85-7.75(m,4H,ArH), 13.75(bs,1H,NH); **IR**(nujol): 2950, 1610, 1560, cm⁻¹; MS: m/z 251 (M⁺,83%), 128 (100); Anal. Calcd. for C₁₂H₁₃NOS₂: C, 57.33; H, Found: C, 58.02; H: 5.30.

2-(4-Nitrothiobenzoyl)methylenethiazolidine (7d): Yield 61%; Dark brown viscous liquid: ¹H NMR (CDCl₃): δ 3.50 (t,J=8Hz,2H,SCH₂), 4.25 (t,J=8Hz,2H,NCH₂), 6.75 (s,1H,=CH), 7.85-8.25 (m,4H,ArH), 13.80 (bs,1H,NH); **IR**(neat): 3080, 2920, 1570, 1520 cm⁻¹; **MS:** m/z 266 (M⁺,74%), 238 (100); Anal. Calcd. for C₁₁H₁₀N₂O₂S₂: C, 49.62; H, 3.75; N, 10.52. Found: C, 49.80; H, 4.11; N, 11.19.

2-(2-Methoxythiobenzoyl)methylenethiazolidine (7f): Yield 65%; Dark brown viscous liquid; ¹H NMR (CDCl₃): δ 3.30 (t,J=8Hz,2H,SCH₂), 3.85 (s,3H,OCH₃), 4.10 (t,J=8Hz,2H,NCH₂), 6.65 (s,1H,=CH), 6.90-7.40 (m,4H,ArH), 13.75 (bs,1H,NH); **IR**(neat): 3350, 1600, 1500, 1470 cm⁻¹; **MS**: m/z 251 (M⁺,6%), 234 (100), 135(42); Anal. Calcd. for C₁₂H₁₃NOS₂: C, 57.33; H, 5.17. Found: C, 57.63; H, 5.27.

2-(2-Chlorothiobenzoyl)methylenethiazolidine (7g): Yield 63%; Yellow crystalline solid, m.p. 157-159°C; ¹H NMR (CDCl₃): δ 3.45 (t,J=8Hz,2H,SCH₂), 4.20 (t,J=8Hz,2H,NCH₂), 6.55 (s,1H,=CH), 7.40-7.80 (m,4H,ArH), 13.70 (bs,1H,NH); **IR**⁻¹(nujol): 2940, 1560, 1500, 1380 cm⁻¹; **MS:** m/z 255 (M⁺,45%), 192 (100), 220(49); Anal. Calcd. for C₁₁H₁₀ClNS₂: C,51.65;H, 3.94;N,5.47;S,25.06.Found: C, 52.08; H, 3.77 N, 5.62; S, 25.15.

2-Thioacetylmethylenethiazolidine (7h): Yield 85%; Yellow crystalline solid, m.p. 100°C; ¹H NMR (CDCl₃): $\delta 2.54(s, 3H, CH_3)$, $3.34(t, J=8Hz, 2H, SCH_2)$, $4.10(t, J=8Hz, 2H, NCH_2)$, 6.30(s, 1H, =CH), 13.50 (bs,1H,NH); **IR**(nujol): 3400, 1570, 1470, 1390, 1280cm⁻¹; **MS**: m/z 159 (M⁺,80%), 131 (100). Compound was not stable enough for getting a good microanalysis.

2-Thiobenzoylmethylenethiazine (7i): Yield 67%; Yellow crystlline solid, m.p. 157-159°C; ¹H NMR (CDCl₃): δ 2.20 (m,2H,CCH₂), 3.15 (t,J=7Hz,2H,SCH₂), 3.65 (t,J=7Hz,2H,NCH₂), 6.50 (s,1H,=CH), 7.40-7.80(m,5H,ArH), 15.00(bs,1H,NH), **IR**(nujol): 2940,2860,1600,1510cm⁻¹; **MS**: m/z 235 (M⁺,70%), 178 (100), 202(76); Anal. Calcd. for C₁₂H₁₃NS₂: C, 61.27; H, 5.53. Found: C, 61.10; H, 5.56.

2-(2-Methoxythiobenzoyl)methylenethiazine (7k): Yield 59%; Dark brown viscous liquid; ¹H NMR (CDCl₃): $\delta 2.25 \text{ (m,2H,CCH}_2\text{)}$, 3.10 (t,J=7Hz,2H,SCH₂), 3.60 (t,J=7Hz,2H,NCH₂), 3.80 (s,1H,OCH₃), 6.35 (s,1H,=CH), 6.90-7.40 (m,4H,ArH), 14.95 (bs,1H,NH); **IR**(neat): 3350, 2940, 1620, 1600 cm⁻¹; MS: m/z 265 (M⁺,1%), 127 (100), 129(43). Compound was not stable enough for getting a good microanalysis.

References and Notes

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