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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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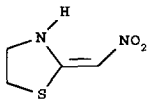
Abstract: PMR spectra of carbonyl compounds **2a-k** reveal significant variations in the population of *E* and *Z* isomers on changing the solvent from $CDCl_3$ to DMSO-d_6. In non-polar media, the intramolecular N-H....O hydrogen bonded form is exclusively observed. In DMSO-d_6, the alternative *Z* 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 involve an interplay of N-H....X hydrogen 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, ^{13}C and ^{15}N 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 well[2].

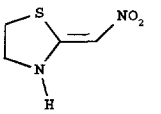
In the present article we establish the generality of the conformational behaviour for a number of carbonyl derivatives, **2a-k**. Various explanations for the observed population differences are discussed and evaluated using data obtained for the related models **9-12**. The conformational study has 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

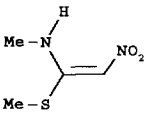
The enaminoketones **2** were prepared by using either one of the two known routes :(a) Condensation of an α-haloketone with a cyclic dithiocarbamate, followed by sulfur extrusion[3] or (b) condensation of an acylketen dithioacetal with the appropriate amimoalcohol or aminothiol[4]. The methyl ketone **2h** was prepared by the second method, using acetylacetone as the starting material; final mono deacetylation yielded **2h**[4]. Lawesson thionation of the enaminoketones led to the thioacylketen S,N-acetals[23].



1(E)



1(Z)



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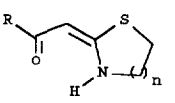
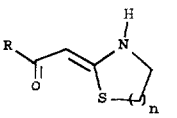


2(E)



2(Z)

	R	n
a:	Ph	1
b:	4-Cl-C_6H_4	1
c:	4-MeO-C_6H_4	1
d:	4-NO_2-C_6H_4	1
e:	2-HO-C_6H_4	1
f:	2-MeO-C_6H_4	1
g:	2-Cl-C_6H_4	1
h:	Me	1
i:	Ph	2
j:	2-HO-C_6H_4	2
k:	2-MeO-C_6H_4	2

Results and Discussion.

E/Z equilibria in carbonyl compounds 2.

The IR spectrum of **2a** in $CHCl_3$ exhibits concentration-independent bands at 3210 and 1610 cm^{-1} for the NH and CO stretching modes respectively. This proves that in $CHCl_3$, **2a** exists in the intramolecularly H-bonded *E* configuration. The ^1H NMR spectrum of this compound in $CDCl_3$ 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 $CDCl_3$ 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 solution, although the peaks are sharp in $CDCl_3$. The *E/Z* ratios of **2a-2e** and **2h** in DMSO-d6 are shown in Table 2. The ratio varies over a narrow margin.

Table 1

^{1}H NMR Chemical shifts (δ) for Compound **2**

Compd		NH		=CH		NCH_2		SCH_2	
		E	*Z*	*E*	*Z*	*E*	*Z*	*E*	*Z*
2a	$CDCl_3$	10.55	-	5.90	-	3.90	-	3.20	-
	DMSO-d6	10.40	8.00	6.00	6.30	3.90	3.59	3.30	3.10
2b	$CDCl_3$	10.55	-	5.90	-	3.90	-	3.20	-
	DMSO-d6	10.50	8.40	5.90	6.20	4.00	3.85	3.30	3.05
2c	$CDCl_3$	10.60	-	6.00		3.95		3.30	-
	DMSO-d6	10.33	8.30	6.00	6.33	3.90	3.60	3.10	3.20
2d	$CDCl_3$	10.80	-	5.90	-	4.00	-	3.30	-
	DMSO-d6	10.50	8.75	6.30	6.05	3.90	3.65	3.65	3.40
2e	$CDCl_3$	10.25	-	6.00	-	4.00	-	3.30	-
	DMSO-d6	10.20	8.95	6.00	6.40	3.80	3.65	3.30	3.15
2f	$CDCl_3$	10.60	-	5.90	-	3.95	-	3.25	-
	DMSO-d6	10.25	8.30	**	**	**	**	**	**
2g	$CDCl_3$	10.60	-	5.70	-	4.05	-	3.35	-
	DMSO-d6	10.25	8.60	**	**	**	**	**	3.10
2h	$CDCl_3$	10.90	-	5.30	-	3.85	-	3.20	-
	DMSO-d6	9.90	8.10	5.20	5.60	3.80	3.50	3.20	3.00
2i	$CDCl_3$	12.45	-	5.75	-	3.55	-	3.20	-
	DMSO-d6	12.15	-	5.75	-	3.45	-	3.10	-
2j	$CDCl_3$	11.75	-	5.75	-	3.55	-	3.15	-
	DMSO-d6	11.90	-	5.75	-	3.50	-	3.10	-
2k	$CDCl_3$	12.35	-	5.70	-	3.50	-	3.05	-
	DMSO-d6	12.05	-	5.50	-	3.40	-	3.10	-

** :- 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 $CDCl_3$ 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 ^{1}H 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

E/Z ratio in DMSO-d6

Compound	*E*	*Z*
2a	62	38
2b	65	35
2c	65	35
2d	56	44
2e	48	52
2h	59	41
2i	<95	>5
2j	100	-
2k	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-CH_3 and S-CH_3 bonds, also prefers to remain in the *E* form in polar and nonpolar solvents.

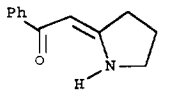
Factors influencing E/Z ratios

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 reduced[6]; 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 $CDCl_3$ 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



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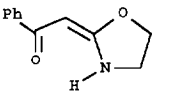

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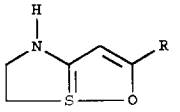

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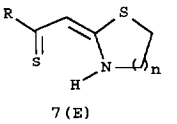
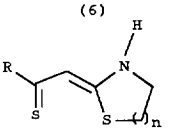
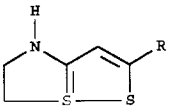


7(E)



7(Z)



(8)

Table 3

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

Compound		NH	=CH	XCH_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 sulfur[7]. 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 structures[10]. 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 **1***Z* and **2***Z*. 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

^{1}H NMR Data and *E/Z* ratios for the Enaminothiones[c] **7**

Compound	Solvent	NH		=CH		NCH_2		SCH_2		*E/Z*
	-	*E*	*Z*	*E*	*Z*	*E*	*Z*	*E*	*Z*	
7a	$CDCl_3$	13.75	-	6.75	-	4.15	-	3.40	-	100/0
	DMSO-d6	13.31	9.71	6.20	7.15	4.10	3.75	3.40	3.25	59/41
7c	$CDCl_3$	13.70	-	6.70	-	4.15	-	3.30	-	100/0
	DMSO-d6	13.20	9.60	6.75	7.25	**	**	**	**	56/44[b]
7d	$CDCl_3$	13.30	-	6.75	-	4.25	-	3.50	-	100/0
	DMSO-d6	13.20	10.50	**	**	**	**	**	**	**
7f	$CDCl_3$	13.75	-	6.65	-	4.10	-	3.30	-	100/0
	DMSO-d6	13.15	9.55	6.45	**	**	**	**	**	**
7g	$CDCl_3$	13.70	-	6.55	-	4.20	-	3.45	-	100/0
	DMSO-d6	13.10	9.75	6.70	6.48	4.10	**	**	**	**
7h	$CDCl_3$	13.50	-	6.30	-	4.05	-	3.35	-	100/0
	DMSO-d6	13.10	9.43	5.80	6.60	4.05	3.65	3.40	3.20	67/33
7i	$CDCl_3$	15.00	-	6.50	-	3.55	-	3.20	-	100/0
	DMSO-d6	15.20	-	6.45	-	3.60	-	3.20	-	100/0
7k	$CDCl_3$	14.95	-	6.35	-	3.60	-	3.10	-	100/0
	DMSO-d6	14.65	-	6.15	-	3.55	-	3.15	-	100/0

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

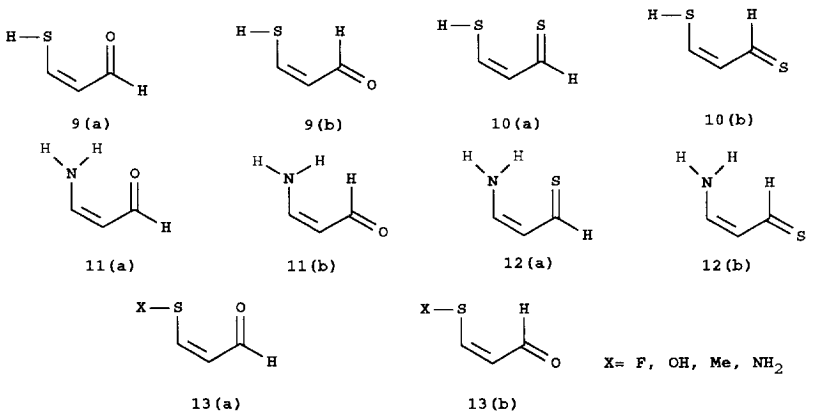
In a further extrapolation of this study, we have included the thiones **7** generated by Lawesson thionation[23] of the acylketen-S,N-acetals **2**. The phenolic compound **2e** and **2j** did not yield any product in this reaction. The relevant ^{1}H NMR data and *E/Z* ratios are given in Table 4. Interestingly the behaviour of the thiones more or less parallels that of the oxo compounds **2**. Thus **7a** exists in the *E* form in $CDCl_3$; 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...O hydrogen bond, the corresponding equilibrium with **7a** compares the weak S..S interaction with the N-H..S hydrogen bond (which is definitely known to be weaker than N-H..O hydrogen bond)[13].

Theoretical studies -

To confirm the above interpretation, ab initio calculations[14-16] 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..O distance 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..S angle 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 earlier[18] 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 structures[19]. Chemical evidence also points to the preference for backside approach of nucleophiles towards sulfur[20].

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 A°) and H..S (2.38 A°) contacts are fairly short, but shorter distances have been noted in unconstrained systems[16,17]. The favored collinear arrangement[21] of N-H..O (126°) and N-H..S (131°) units are not achieved. The carbonyl group is better aligned than the thione for interaction on the basis of the computed C=O..H (100°) and C=S..H (84°) 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 systems[22].

Table 5.

Calculated Total Energies (Hartree) and Relative energies (k.cal mole^{-1}) of **9-12**[a].

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		
12b	-565.64633	5.4	-568.43637	5.0a		

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...O interaction in the enaminoketones **2**(**a** to **h**). The related S....S interaction 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 $CHCl_3$ 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 Me_4Si 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 extrusion[3] in the second step to give the enaminoketones **2**.

2-Benzoylmethylenethiazolidine (2a[4]): Yield 69%; Light yellow crystalline solid, m.p. 168°C; **^{1}H NMR** ($CDCl_3$)**:** δ 3.20 (t,J=8Hz,2H,SCH_2), 3.90 (t,J=8Hz,2H,NCH_2), 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** ($CDCl_3$): δ 3.30 (t,J=8Hz,2H,SCH_2), 4.00 (t,J=8Hz,2H,NCH_2), 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 $C_{11}H_{11}NO_2S$: 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; **^{1}H NMR**($CDCl_3$): δ 3.25 (t,J=8Hz,2H,SCH_2), 3.90 (s,3H,OCH_3), 3.95 (t,J=8Hz,2H,NCH_2), 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; **^{1}H NMR** ($CDCl_3$): δ 2.25 (m,2H,CCH_2), 3.20 (t,J=8Hz,2H,SCH_2), 3.55 (t,J=8Hz,2H,NCH_2), 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 $C_{12}H_{13}NOS$ 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 crystlline solid, m.p. 125-127°C; **^{1}H NMR** ($CDCl_3$): δ2.25(m,2H,CCH_2), 3.15(t,J=8Hz,2H,SCH_2), 3.55(t,J=8Hz,2H,NCH_2), 5.75 (s,1H,=CH), 6.70-7.50(m,4H,ArH), 11.75 (bs,1H,NH), 13.75 (s,1H,OH); **IR**($CHCl_3$) 3400, 3020, 1600, 1580 cm^{-1}; **MS:** m/z 235 (M^+,93%), 188 (100); Anal. Calcd. for $C_{12}H_{13}NO_2S$: 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; **^{1}H NMR** ($CDCl_3$): δ2.20(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+$CHCl_3$): 3400, 1600, 1610 cm^{-1}; **MS:** m/z 249 (M^+,9%), 135 (100); Anal. Calcd. for $C_{13}H_{15}NO_2S$: 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 temperature[4].

2-(4-Chlorobenzoyl)methylenethiazolidine (2b[2]**):** Yield 80%; Light yellow crystalline solid, m.p. 137-139°C; **^{1}H NMR** ($CDCl_3$): δ3.20(t,J=8Hz,2H,SCH_2), 3.90(t,J=8Hz,2H,NCH_2), 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 (2c[4]**):** Yield 73%; Light yellow crystlline solid, m.p. 154-156$_0$C; **^{1}H NMR** ($CDCl_3$): δ3.30(t,J=8Hz,2H,SCH_2), 3.75(s,3H,OCH_3), 3.95(t,J=8Hz,2H,NCH_2), 6.00(s,1H,=CH), 6.90-7.80(m,4H,ArH), 10.60(bs,1H,NH); **IR**($CHCl_3$) 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; **^{1}H NMR** ($CDCl_3$): δ3.30(t,J=8Hz,2H,SCH_2), 4.00(t,J=8Hz,2H,NCH_2), 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 $C_{11}H_{10}N_2O_3S$: 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; **^{1}H NMR** ($CDCl_3$): δ3.35(t,J=8Hz,2H,SCH_2), 4.05(t,J=8Hz,2H,NCH_2), 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 $C_{11}H_{10}ClNOS$: 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)-ethanone[3]; 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.

(E)-2-(Benzoylmethylene)oxazolidine (5)[9]: was prepared by the reported method[9] m.p. 103-104; Anal. Calcd. for $C_{11}H_{11}NO_2$: C, 69.82; H, 5.86; N, 7.40. Found: C, 69.91; H, 5.78; N, 7.21.

General procedure for thionation

A mixture of, compound **2** (10 mmol) and Lawesson reagent[23] (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; **^{1}H NMR** ($CDCl_3$): δ 3.35 (t,J=8Hz,2H,SCH_2), 4.15 (t,J=8Hz,2H,NCH_2), 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 $C_{11}H_{11}NS_2$: 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; **^{1}H NMR** ($CDCl_3$): δ 3.30(t,J=8Hz,2H,SCH_2), 3.85(s,3H,OCH_3), 4.15(t,J=8Hz,2H,NCH_2), 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 $C_{12}H_{13}NOS_2$: C, 57.33; H, Found: C, 58.02; H: 5.30.

2-(4-Nitrothiobenzoyl)methylenethiazolidine (7d): Yield 61%; Dark brown viscous liquid; **^{1}H NMR** ($CDCl_3$): δ 3.50 (t,J=8Hz,2H,SCH_2), 4.25 (t,J=8Hz,2H,NCH_2), 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 $C_{11}H_{10}N_2O_2S_2$: 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; **^{1}H NMR** ($CDCl_3$): δ 3.30 (t,J=8Hz,2H,SCH_2), 3.85 (s,3H,OCH_3), 4.10 (t,J=8Hz,2H,NCH_2), 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 $C_{12}H_{13}NOS_2$: 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; **^{1}H NMR** ($CDCl_3$): δ3.45(t,J=8Hz,2H,SCH_2), 4.20(t,J=8Hz,2H,NCH_2), 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 $C_{11}H_{10}ClNS_2$: 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; **^{1}H NMR** ($CDCl_3$): δ2.54(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; **^{1}H NMR** ($CDCl_3$): δ 2.20 (m,2H,CCH_2), 3.15 (t,J=7Hz,2H,SCH_2), 3.65 (t,J=7Hz,2H,NCH_2), 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 $C_{12}H_{13}NS_2$: C, 61.27; H, 5.53. Found: C, 61.10; H, 5.56.

2-(2-Methoxythiobenzoyl)methylenethiazine (7k): Yield 59%; Dark brown viscous liquid; **^{1}H NMR** ($CDCl_3$): δ2.25 (m,2H,CCH_2), 3.10 (t,J=7Hz,2H,SCH_2), 3.60 (t,J=7Hz,2H,NCH_2), 3.80 (s,1H,OCH_3), 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.

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