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4-{3-DIMETHYLAMINO-1-(2-DIMETHYLAMINOVINYL)PROP-2-ENYLIDENE}-2-PHENYL-1,3-OXAZOL-5(4*H*)-ONE AND 5-{3-DIMETHYLAMINO-1-[2-DIMETHYLAMINOVINYL)PROP-2-ENYLIDENE}-3-METHYL-2-THIOXO-1,3-THIAZOLIDIN-4-ONE IN THE SYNTHESIS OF 1,4-DIHYDROPYRIDINE DERIVATIVES

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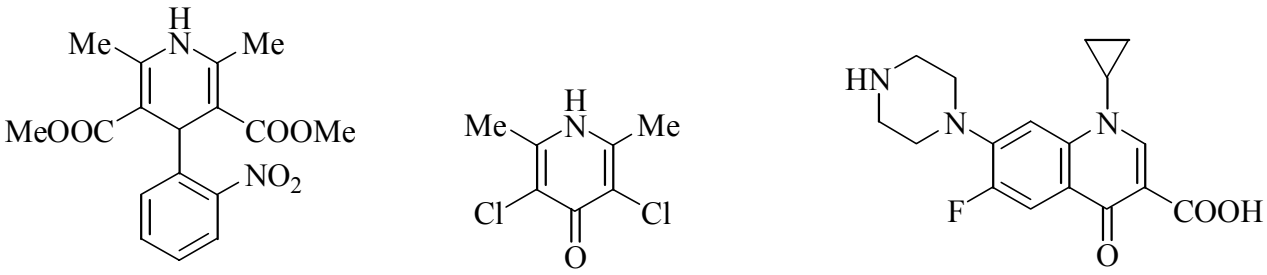
Dedicated to Emeritus Professor Miha Tišler, University of Ljubljana, on the occasion of his 75th birthday

Abstract – 4-{3-Dimethylamino-1-[2-(dimethylamino)vinyl]prop-2-enylidene}-2-phenyl-1,3-oxazol-5(4*H*)-one (**3**) and 5-{3-dimethylamino-1-[2-(dimethylamino)vinyl]prop-2-enylidene}-3-methyl-2-thioxo-1,3-thiazolidin-4-one (**15**) were prepared from 4-(1-methylethylidene)-2-phenyl-1,3-oxazol-5(4*H*)-one (**2**) and 5-(1-methylethylidene)-2-thioxo-1,3-thiazolidin-4-one (**11**), respectively. Treatment of compounds (**3**) and (**15**) with primary amines afforded 1,4-dihydropyridine derivatives (**5**) and (**16**) in 19–94% yields. Reactions of oxazolones (**5**) with hydrazine hydrate gave the corresponding imidazolones (**6**), while upon base- or acid-catalysed methanolysis of **5** methyl (benzoylamino)(1-substituted pyridin-4(1*H*)-ylidene)acetates (**7**) were obtained. Catalytic hydrogenation of **7a** furnished α-(piperidin-4-yl)glycine derivative (**8**) and/or α-(pyridin-2-yl)glycine derivative (**9**).

The interest in dihydropyridines is due to the unique ability of these compounds to act as NAD(P)H analogues of 1,4-dihydronicotinamide.[1] They are most extensively studied as calcium antagonists,[2] however, they also exhibit hepatoprotective,[3] antitumor,[4] antidiabetic,[5] bronchodilating,[6] and other pharma-

cological activities[7–9] (Figure 1).

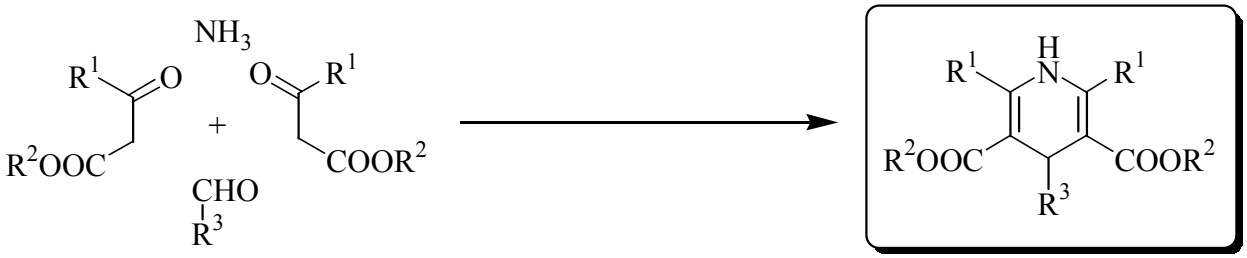
Figure 1. Examples of Pharmacologically Important 1,4-Dihydropyridine Derivatives.



Nifedipine (calcium channel blocker) | Clopidol (antiparasitic) | Ciprofloxacin (antibiotic)

There are several methods for the preparation of 1,4-dihydropyridine derivatives described in the literature.[10–13] The most widely used method is Hantzsch-type cyclocondensation reaction[11,12] (Scheme 1).

Scheme 1. Hantzch Three-Component Synthesis of 1,4-Dihydropyridines.



Various modifications of this reaction have also been described in the literature. For example, 1,4-dihydropyridines can be formed from diaminoacrylates,[14] by the condensation of aldehydes with amidines[15] or β-aminocrotonates,[16] and from acetoacetate or aminocrotonate by condensation with aldehydes forming the unsymmetrical 1,4-dihydropyridines.[17] The other methods for preparation of 1,4-dihydropyridines are various reductions of pyridines and pyridinium salts[18] and nucleophilic additions to pyridines and pyridinium salts.[19] Some *N*-substituted 1,4-dihydropyridines have been prepared by reaction of 2-amino-5-formyl-4*H*-pyran with primary amines.[20] In recent years, interest has also been focused on the aza-analogues, such as 1,4-dihydropyrimidines.[21]

Recently, alkyl 2-acylamino-3-dimethylaminopropenoates and their analogues, as masked α-formyl-α-amino, and α-formyl-α-hydroxy acids, and their derivatives have been used as reagents for the preparation of a variety of heterocyclic systems.[22] Among them, dialkyl 4-oxo-1,4-dihydropyridin-3,5-dicarboxylates have been prepared from dialkyl 2,4-bis[(dimethylamino)methylene]-3-oxopentanedioates.[23] As an extension of this research, we report here the synthesis of the two bifunctional

3-dimethylaminopropenoate analogues, 4-{3-(dimethylamino)-1-[2-(dimethylamino)-vinyl]prop-2-en-ylidene}-2-phenyl-1,3-oxazol-5(4*H*)-one (**3**) and 5-{3-(dimethylamino)-1-[2-(dimethylamino)vinyl]-prop-2-enylidene}-3-methyl-2-thioxo-1,3-thiazolidin-4-one (**15**), and their utilisation in the synthesis of 1,4-dihydropyridine derivatives.

The first starting compound, (**3**), was prepared in two steps from hippuric acid (**1**) as shown in Scheme 2. The acid (**1**) was first transformed into 4-(1-methylethylidene)-2-phenyl-1,3-oxazol-5(4*H*)-one (**2**) according to the procedure described in the literature.[24] Both methyl groups of **2** reacted with *N*,*N*-dimethylformamide dimethyl acetal (DMFDMA) by heating in DMF to give **3** in 80% yield. Treatment of **3** with hydrochlorides of various aliphatic and aromatic primary amines (**4a–f**) afforded the corresponding 4-[1-substituted pyridin-4(1*H*)-ylidene]-2-phenyl-1,3-oxazol-5(4*H*)-ones (**5a**–**f**) in 53–75% yield.

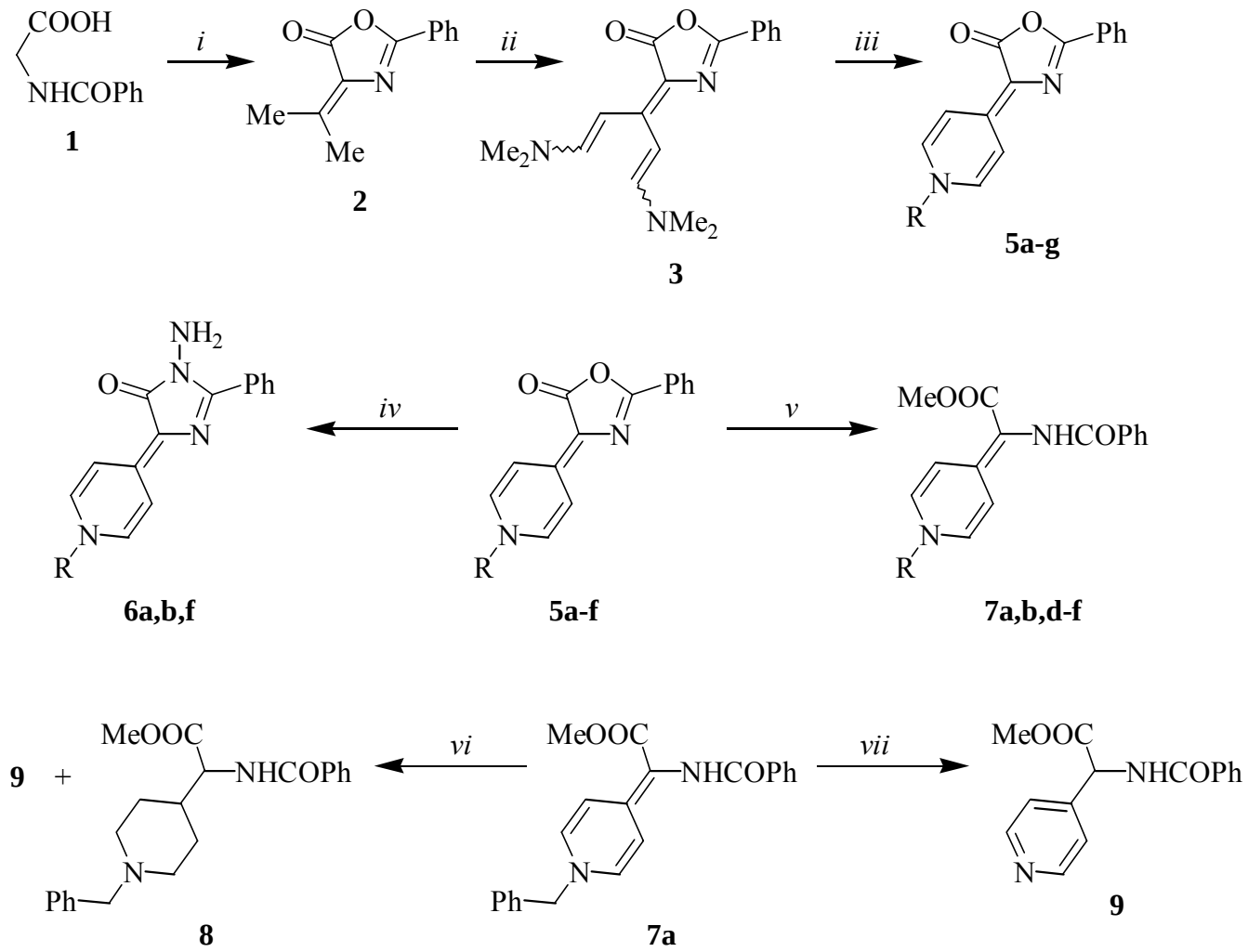
Similarly, the reaction of **3** with 1 equivalent of hydrazine hydrate furnished the corresponding 4-(1-aminopyridin-4(1*H*)-ylidene)-2-phenyl-1,3-oxazol-5(4*H*)-one (**5g**) in 19% yield.

In the reaction of compounds (**5a,b,f**) with hydrazine hydrate, the oxazolone ring was transformed into 3-amino-3,5-dihydro-4*H*-imidazol-4-one derivatives (**6a,b,f**) in 31–75% yield. When compounds (**5a,b,d–f**) were treated with methanol in the presence of sodium methoxide or sulfuric acid at reflux, the oxazolone ring was cleaved to give methyl (benzoylamino)(1-substituted pyridin-4(1*H*)-ylidene)acetates (**7a,b,d–f**) in good yields.

Catalytic hydrogenation of **7a** in formic acid in the presence of 10% Pd–C afforded methyl (benzoylamino)(1-benzylpiperidin-4-yl)acetate (**8**) in 48% yield and methyl (benzoylamino)(pyridin-4-yl)acetate (**9**) in 11% yield, while by catalytic hydrogenation in methanol in the presence of ammonium formate and 10% Pd–C only the debenzylation took place and methyl (benzoylamino)(pyridin-4-yl)acetate (**9**) was obtained in 99% yield (Scheme 2).

5-(1-Methylethylidene)-2-thioxo-1,3-thiazolidin-4-one (**11**), prepared from 2-thioxo-1,3-thiazolidin-4-one (**10**) and acetone according to the procedure described in the literature,[25] was treated with bis(dimethylamino)-*tert*-butoxymethane (Bredereck's reagent) in toluene in an inert atmosphere at room temperature to give 5-[3-dimethylamino-1-methylprop-2-enylidene]-2-thioxo-1,3-thiazolidin-4-one (**12**) in 66% yield. Upon treatment of **11** with DMFDMA, also the methylation at the ring nitrogen atom took place to give the corresponding *N*-methylated derivative (**13**) in 65% yield. Attempts to convert compound (**12**) by heating with Bredereck's reagent at 100–120°C into bis(dimethylamino) compound (**14**) failed, while the reaction of compound (**13**) with Bredereck's reagent gave 5-{3-dimethylamino-1-[2-(dimethylamino)vinyl]prop-2-enylidene}-3-methyl-2-thioxo-1,3-thiazolidin-4-one (**15**) in 94% yield. Compound (**15**) was transformed with various aliphatic (**4a–c**), aromatic (**4e,h,i**), and heteroaromatic primary amines (**4j–n**) and with α-amino acid derivatives (**4o,p**) into 3-methyl-5-(1-substituted pyridin-4(1*H*)-ylidene)-2-thioxo-1,3-thiazolidin-4-ones (**16a–c,e,h–p**) in 22–94% yields. (Scheme 3).

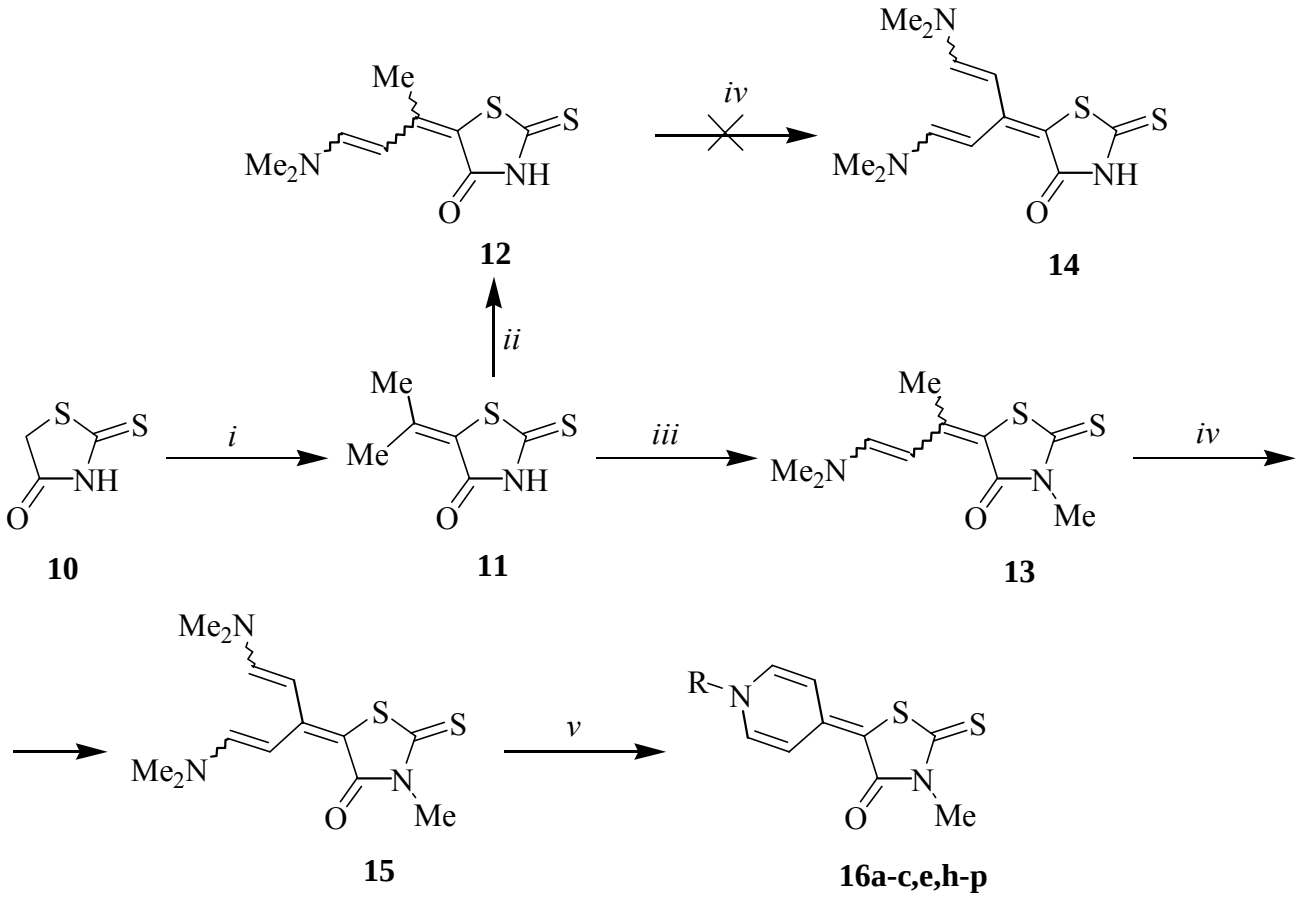
Scheme 2



Compound	R
4a–**7a**	benzyl
4b–**7b**	methyl
4c,**5c**	2-hydroxyethyl
4d, **5d**, **7d**	cyclohexyl
4e, **5e**, **7e**	phenyl
4f–**7f**	4-methylphenyl
4g, **5g**	amino

Reagents and conditions: *i*) acetone, Ac_2O, AcONa, reflux; *ii*) DMFDMA, DMF, reflux; *iii*) RNH_2 (**4a–g**), EtOH, HCl, reflux; *iv*) N_2H_4 x H_2O, reflux; *v*) MeOH, MeONa, rt or MeOH, H_2SO_4, reflux; *vi*) H_2, 10% Pd–C, HCOOH, rt; *vii*) $HCOONH_4$, 10% Pd–C, MeOH, reflux.

Scheme 3



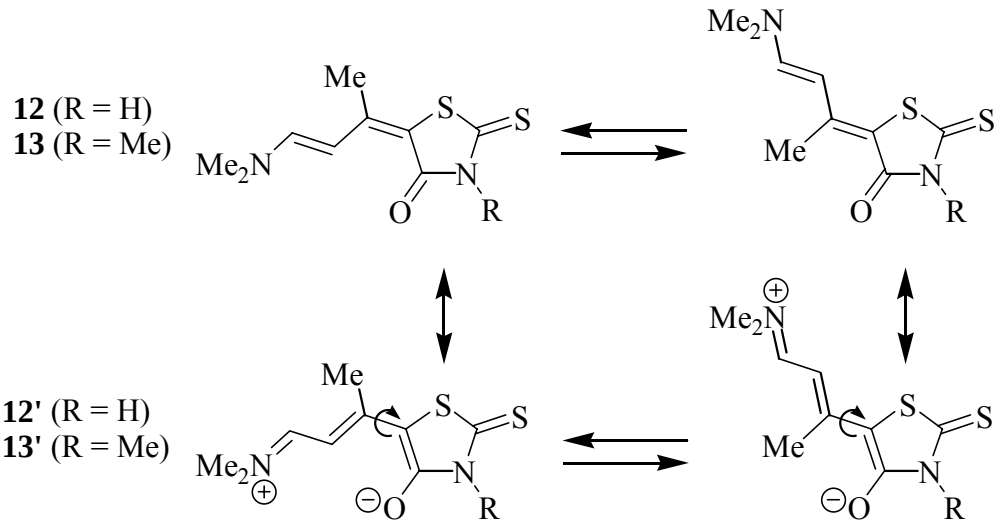
Compound	R
4a, **16a**	benzyl
4b, **16b**	methyl
4c, **16c**	2-hydroxyethyl
4e, **16e**	phenyl
4h, **16h**	4-fluorophenyl
4i, **16i**	3-nitrophenyl
4j, **16j**	pyridin-2-yl
4k, **16k**	5-chloropyridin-2-yl
4l, **16l**	isoxazol-3-yl
4m, **16m**	thiazol-2-yl
4n, **16n**	benzothiazol-2-yl
4o, **16o**	methoxycarbonylmethyl
4p, **16p**	ethoxycarbonylmethyl

Reagents and conditions: *i*) acetone, NH_3(aq.), NH_4Cl, reflux; *ii*) *t*-BuOCH(NMe_2)$_2$, toluene, rt; *iii*) DMFDMA, toluene, rt; *iv*) *t*-BuOCH(NMe_2)$_2$, toluene, reflux; *v*) RNH_2 (**4a–c,e,h–p**), EtOH, HCl, reflux.

The structure determination of the products is based on ^{1}H NMR spectra, MS spectra, and X-Ray analysis. The DMFDMA methylation of heterocyclic compounds with a thioamide structural element gives in most cases the *S*-methylated product.[26] In the reaction of **11** with DMFDMA the compound (**13**) was formed. The chemical shift for the methyl group, δ = 3.47 ppm, clearly indicates that methylation occurred at ring nitrogen atom. Also the chemical shifts for the methyl group in compounds (**16**) in the range δ = 3.34–3.77 ppm indicate that the methyl group is attached at the thiazolidine ring nitrogen atom, since the typical chemical shift of the *S*-methyl groups in azole series is usually within the range δ = 2.5–3.0 ppm. Finally, the *N*-methylation was unambiguously confirmed by X-Ray analysis of compound (**16a**) (Figure 2, Table 1).

Both, **12** and **13**, exist in DMSO–d_6 solution as mixtures of isomers in a ratio of 53:47 and 59:41, respectively. On the other hand, **13** exists in $CDCl_3$ solution as a single isomer, since only one set of signals was observed by ^{1}H NMR spectrum. A more detailed structural study has not yet been carried out, however, according to previous studies in some related 3-(dimethylamino)propenoates,[22a] isomerization around the exocyclic C=C double bond in compounds (**12**) and (**13**) is feasible *via* the mesomeric structures (**12'**) and (**13'**) (Scheme 4).

Scheme 4 Isomerisation of compounds (**12**) and (**13**) in DMSO–d_6 solution.



X-Ray Crystallography. A thin orange plate-like crystal with approximate dimensions of 0.22 x 0.11 x 0.06 mm was mounted on a glass fibre. Diffraction data were collected on a Nonius Kappa CCD diffractometer[27,28] with graphite monochromated Mo*Kα* radiation (λ=0.71073 Å). Crystal data: $C_{16}H_{14}N_2OS_2$, M_r=314.41, monoclinic space group $P2_1/n$, *a*=4.159(2), *b*=28.7708(11), *c*=9612(6) Å, *β*=93.908(2)°, *V*=1428.0(1) Å^3, *Z*=4, T=200 K. Structure was solved by direct methods (SHELXS-97[29])

and refined by full-matrix least squares on F^2 using SHELXL-97.[30] Non-hydrogen atoms were refined anisotropically, hydrogen atoms were placed at calculated positions with appropriate thermal parameters and allowed to ride on their parent atoms. Final refinement cycle was based on 5595 measured reflections [3095 independent, 1688 observed with $I>2\sigma(I)$]. Final agreement factors on observed reflections are $R_1=0.061$ and $wR_2=0.144$ for 191 refined parameters. Relevant crystal data and data collection summary are quoted in Table 1. Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. A copy can be obtained on request, free of charge, by quoting the publication citation and the deposition number CCDC 167052.

Figure 2. ORTEP view of compound (**16a**) with atomic numbering scheme. Thermal ellipsoids are drawn at 50% probability level.

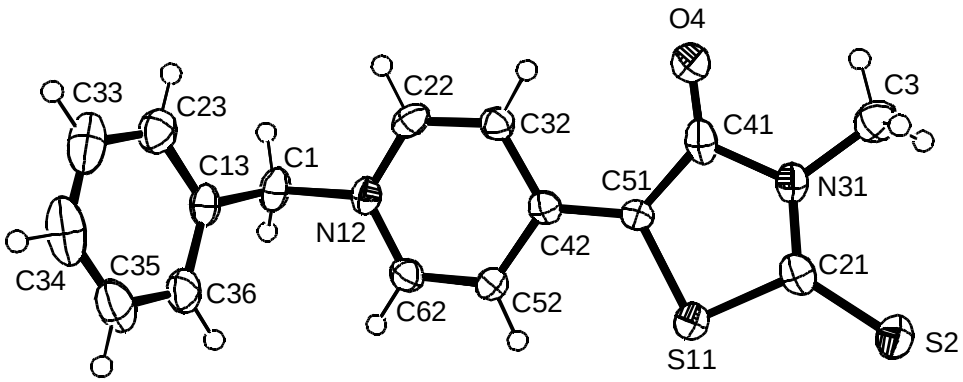
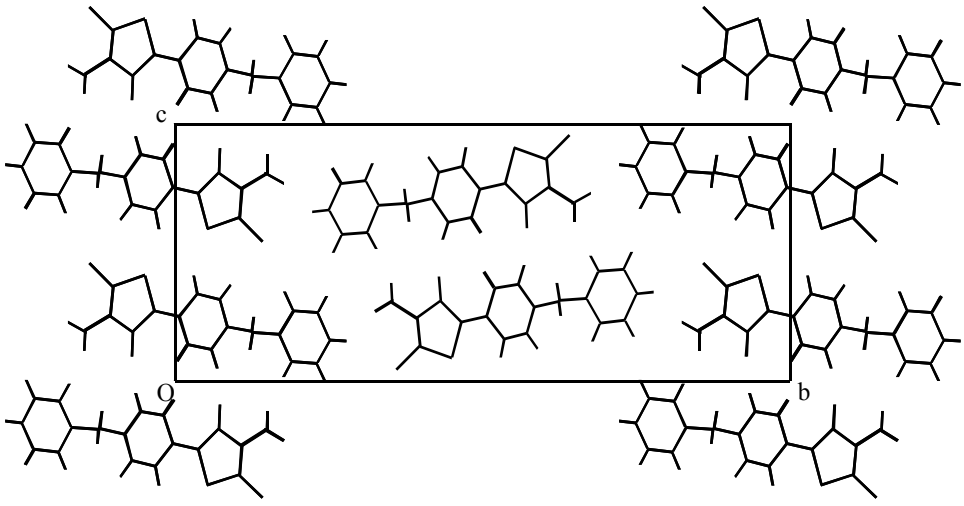


Figure 3. Crystal packing of compound (**16a**) viewed along a axis.



Description of the structure. The molecular geometry[31] and crystal packing[32] are depicted in Figures 2 and 3, respectively. Bond lengths and angles are normal and in agreement with related compounds. The distances S11-C21 and S11-C51 of 1.720(5) and 1.767(4) Å suggest a single C-S bond, whereas the distance S2-C21 of 1.675(5) indicates a double bond character. The torsion angles S11-C51-C42-C52 and C41-C51-C42-C32 are -1.2(5) and -3.8(7)˚, respectively. There are no significant intermolecular contacts.

Table 1. Relevant crystal data and data collection summary for compound (**16a**).

Formula	$C_{16}H_{14}N_2OS_2$
Formula weight	314.41
Colour	Orange
Size (mm)	0.22 x 0.11 x 0.06
Crystal system	Monoclinic
Space group	$P2_1/n$
a (Å)	4.1592(2)
b (Å)	28.7708(11)
c (Å)	11.9612(6)
β (°)	93.9084(16)
V (Å^3)	1427.99(11)
Z	4
$D_{calc.}$ (g·cm^{-3})	1.462
μ (mm^{-1})	0.372
Diffractometer	Nonius Kappa CCD
Temperature (K)	200
$\theta_{min},\theta_{max}$ (˚)	2.22, 28.81
Scan type	1.5˚ φ and ω scans
Total data	5595
Unique data	3095
Observed data [I>2(σI)]	1688
$R_{int.}$	0.076
R_1 [I>2(σI)]	0.061
wR_2 [I>2(σI)]	0.144

EXPERIMENTAL

Melting points were taken on a Kofler micro hot stage. The ^{1}H NMR spectra were obtained on a Varian EM360L (60 MHz) spectrometer and Bruker Avance DPX 300 (300 MHz) spectrometer with TMS as the internal standard, MS spectra on an AutoSpecQ spectrometer, IR spectra on a Perkin-Elmer 1310 infrared spectrophotometer and microanalyses for C, H and N on a Perkin-Elmer CHN Analyser 2400.
4-(1-Methylethylidene)-2-phenyl-1,3-oxazol-5(4*H*)-one (**2**)[24] and 5-(1-methylethylidene)-2-thioxo-1,3-thiazolidin-4-one (**11**)[25] were prepared according to the procedures described in the literature.

4-{3-Dimethylamino-1-[2-(dimethylamino)vinyl]prop-2-enylidene}-2-phenyl-1,3-oxazol-5(4*H*)-one (3).
Procedure A. A mixture of **2** (0.378 g, 2 mmol), DMFDMA (1.2 mL, 8 mmol), and DMF (3 mL) was heated under reflux for 3 h. The volatile components were evaporated *in vacuo*, a mixture of water and ethanol (4 mL, 3:1) was added, and the precipitate was collected by filtration to give **3**. Yield: 0.498 g (80%); mp 57–60°C (from ethanol/water). MS: (EI) *m/z* = 311 (M^+). ^{1}H NMR (60 MHz, $CDCl_3$) δ: 3.05 (12H, s, 2 NMe_2), 6.04 (2H, d, *J* = 13 Hz, 2 C*H*NMe_2), 7.31–7.59 (3H, m, 3H of Ph), 7.58 (2H, d, *J* = 13 Hz, 2 C*H*=CH–NMe_2), 7.92–8.20 (2H, m, 2H of Ph). *Anal.* Calcd for $C_{18}H_{21}N_3O_2$ x 1.5 H_2O: C, 63.89; H, 7.15; N, 12.42. Found: C, 64.30; H, 7.02; N, 12.59.
Procedure B. A mixture of **2** (0.402 g, 2 mmol), DMFDMA (0.9 mL, 6 mmol), and DMF (2 mL) was heated under reflux for 2 h. The volatile components were evaporated *in vacuo*, the residue was suspended in water (3 mL) and extracted with chloroform (3 x 10 mL). Organic phases were combined, dried over anhydrous sodium sulphate, filtered, and evaporated *in vacuo* to give the crude compound (**3**) which was used for further transformations without purification.

General Procedure for the Preparation of 4-(1-Substituted Pyridin-4(1*H*)-ylidene)-2-phenyl-1,3-oxazol-5(4*H*)-ones (5a–g). A mixture of compound (**3**) (0.622 g, 2 mmol), ethanol (3 mL) and amine hydrochloride (**4a–g**) (2 mmol) was heated under reflux for 2–6 h, cooled, and the precipitate was collected by filtration to give dihydropyridine derivatives (**5a–g**). (Compounds (**5d**) and (**5f**) were not prepared in analytically pure form, however, further transformations led to analytically pure compounds (**7d**) and (**6f**), respectively.)
The following compounds were prepared in this manner:

4-(1-Benzylpyridin-4(1*H*)-ylidene)-2-phenyl-1,3-oxazol-5(4*H*)-one (5a). This compound was prepared from benzylamine hydrochloride (**4a**); reflux for 5.5 h. Yield: 0.464 g (71%), mp 178–179°C (from ethanol), MS: (EI) *m/z* = 328 (M^+), ^{1}H NMR (60 MHz, $CDCl_3$) δ: 4.95 (2H, s, CH_2), 7.08–7.59 (11H, m,

8H of Ph, 3H of pyridine), 7.58–8.16 (3H, m, 2H of Ph, 1H of pyridine). *Anal.* Calcd for $C_{21}H_{16}N_2O_2$: C, 76.81; H, 4.91; N, 8.53. Found: C, 76.61; H, 4.82; N, 8.74.

4-(1-Methylpyridin-4(1*H*)-ylidene)-2-phenyl-1,3-oxazol-5(4*H*)-one (5b). This compound was prepared from methylamine hydrochloride (**4b**); reflux for 2.5 h. Yield: 0.283 g (56%); mp 220–222°C (from ethanol). ^{1}H NMR (60 MHz, DMSO–d_6) δ: 3.81 (3H, s, Me), 7.18–7.60 (4H, m, 2H of Ph and 2H of pyridine), 7.60–8.01 (5H, m, 3H of Ph and 2H of pyridine). *Anal.* Calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.19; H, 4.58; N, 11.21.

4-[1-(2-Hydroxyethyl)pyridin-4(1*H*)-ylidene]-2-phenyl-1,3-oxazol-5(4*H*)-one (5c). This compound was prepared from 2-aminoethanol hydrochloride (**4c**); reflux for 2 h. Yield: 0.425 g (75%); mp 198–200°C (from ethanol), ^{1}H NMR (60 MHz, DMSO–d_6) δ: 3.78 (2H, m, NCH_2), 4.11 (2H, m, OCH_2), 5.11 (1H, br s, OH), 7,26–7.63 (4H, m, 3H of Ph and 1H of pyridine), 7.67–8.06 (5H, m, 2H of Ph and 3H of pyridine). *Anal.* Calcd for $C_{16}H_{14}N_2O_3$: C, 68.07; H, 5.00; N, 9.92. Found: C, 67.80; H, 4.68; N, 10.01.

4-(1-Cyclohexylpyridin-4(1*H*)-ylidene)-2-phenyl-1,3-oxazol-5(4*H*)-one (5d). This compound was prepared from cyclohexylamine hydrochloride (**4d**); reflux for 6 h. Yield: 0.460 g (72%); mp 228–230°C (from ethanol), ^{1}H NMR (60 MHz, $CDCl_3$) δ: 0.98–2.20 (10H, m, 10H of cyclohexyl), 3.32–3.88 (1H, m, 1H of cyclohexyl), 7.20–7.56 (6H, m, 3H of Ph and 3H of pyridine), 7.82–8.15 (3H, m, 2H of Ph and 1H of pyridine). *Anal.* Calcd for $C_{20}H_{20}N_2O_2$: C, 74.98; H, 6.29; N, 8.74. Found: C, 75.45; H, 6.22; N, 8.30.

4-(1-Phenylpyridin-4(1*H*)-ylidene)-2-phenyl-1,3-oxazol-5(4*H*)-one (5e). This compound was prepared from aniline hydrochloride (**4e**); reflux for 5 h. Yield: 0.334 g (53%); mp 194–196°C (from methanol), ^{1}H NMR (60 MHz, $CDCl_3$) δ: 7.30–7.70 (11H, m, 8H of Ph and 3H of pyridine), 7.84–8.19 (3H, m, 2H of Ph and 1H of pyridine). *Anal.* Calcd for $C_{20}H_{14}N_2O_2$: C, 76.42; H, 4.49; N, 8.91. Found: C, 76.10; H, 4.15; N, 9.17.

4-[1-(4-Methylphenyl)pyridin-4(1*H*)-ylidene]-2-phenyl-1,3-oxazol-5(4*H*)-one (5f). This compound was prepared from 4-methylaniline hydrochloride (**4f**); reflux for 2.5 h. Yield: 0.490 g (75%); mp 267–269°C (from DMF). MS: *m/z* = 328 (M^+). ^{1}H NMR (60 MHz, CF_3COOD) δ: 1.57 (3H, s, Me), 6.55 (4H, br s, C_6H_4), 6.67–6.96 (3H, m, 3H of Ph), 7.05–7.63 (6H, m, 2H of Ph and 4H of pyridine). *Anal.* Calcd for $C_{21}H_{16}N_2O_2$: C, 76.81; H, 4.91; N, 8.53. Found: C, 76.19; H, 4.76; N, 8.26.

4-[1-Aminopyridin-4(1*H*)-ylidene]-2-phenyl-1,3-oxazol-5(4*H*)-one (5g). This compound was prepared

from hydrazine hydrochloride (**4g**), reflux for 5 h. Yield: 0.098 g (19%); mp 233–234°C (from ethanol), ^{1}H NMR (60 MHz, DMSO–d_6) δ: 6.88 (2H, s, NH_2), 7.18–8.00 (9H, m, 5H of Ph and 4H of pyridine). *Anal.* Calcd for $C_{14}H_{11}N_3O_2$: C, 66.40; H, 4.38; N, 16.59. Found: C, 66.76; H, 4.05; N, 16.88.

General Procedure for the Preparation of 3-Amino-5-(1-substituted pyridin-4(1*H*)-ylidene)-2-phenyl-3,5-dihydro-4*H*-imidazol-4-ones (6a,b,f). A mixture of oxazolone (**5a,b,f**) (1 mmol) and hydrazine hydrate (99%, 3 mL, 59 mmol) was heated under reflux for 1–16 h, cooled, and the precipitate was collected by filtration to give **6a,b,f**.

The following compounds were prepared in this manner:

3-Amino-5-(1-benzylpyridin-4(1*H*)-ylidene)-2-phenyl-3,5-dihydro-4*H*-imidazol-4-one (6a). This compound was prepared from **5a**, reflux for 12.5 h. Yield: 0.182 g (53%); mp 213–216°C (from ethanol/water). ^{1}H NMR (60 MHz, DMSO–d_6) δ: 5.13 and 5.20 (4H, 2s, 1:1, CH_2 and NH_2), 7.21–7.67 (9H, m, 8H of Ph and 1H of pyridine), 7.83–8.47 (5H, m, 2H of Ph and 3H of pyridine). *Anal.* Calcd for $C_{21}H_{18}N_4O$: C, 73.67; H, 5.30; N, 16.36. Found: C, 73.47; H, 5.24; N, 16.55.

3-Amino-5-(1-methylpyridin-4(1*H*)-ylidene)-2-phenyl-3,5-dihydro-4*H*-imidazol-4-one (6b). This compound was prepared from **5b**; reflux for 8 h. Yield: 0.199 g (75%); mp 273–278°C (decomp) (from ethanol), ^{1}H NMR (60 MHz, DMSO–d_6) δ: 3.70 (3H, s, Me), 5.08 (2H, s, NH_2), 7.12–7.50 (4H, m, 3H of Ph and 1H of pyridine), 7.55–8.39 (5H, m, 2H of Ph and 3H of pyridine). *Anal.* Calcd for $C_{15}H_{14}N_4O$: C, 67.65; H, 5.30; N, 21.04. Found: C, 67.43; H, 5.01; N, 21.43.

3-Amino-5-[1-(4-methylphenyl)pyridin-4(1*H*)-ylidene]-2-phenyl-3,5-dihydro-4*H*-imidazol-4-one (6f). This compound was prepared from **5f**; reflux for 16 h. Yield: 0.105 g (31%); mp 246–249°C (from methanol), ^{1}H NMR (60 MHz, $CDCl_3$) δ: 2.40 (3H, s, Me), 4.40 (2H, s, NH_2), 7.08–7.62 (10H, m, C_6H_4, 3H of Ph, and 3H of pyridine), 7.89–8.37 (3H, m, 2H of Ph and 1H of pyridine). *Anal.* Calcd for $C_{21}H_{18}N_4O$: C, 73.67; H, 5.30; N, 16.36. Found: C, 73.61; H, 5.34; N, 16.22.

General Procedures for the Preparation of Methyl (Benzoylamino)[1-Substituted Pyridin-4(1*H*)-ylidene]acetates (7a,b,d–f).

Procedure A. A mixture of compound (**5**) (1 mmol) and a solution of sodium (92 mg, 4 mmol) in methanol (5 mL) was heated under reflux for 0.25–2 h, cooled, and the precipitate was collected by filtration to give **7**.

Procedure B. A mixture of compound (**5**) (1 mmol) and a solution of sulfuric acid (96%, 0.3 mL) in

methanol (2 mL) was heated under reflux for 1–1.5 h, cooled, neutralised with 5% aqueous solution of sodium hydrogen carbonate, and the product was extracted with chloroform (5 mL). The organic phase was dried over anhydrous sodium sulphate, filtered, and the filtrate was evaporated *in vacuo*. The oily residue was triturated with an appropriate solvent and the precipitate was collected by filtration to give **7**. The following compounds were prepared in this manner:

Methyl (Benzoylamino)[1-Benzylpyridin-4(1*H*)-ylidene]acetate (7a). This compound was prepared from **5a**; Procedure A, reflux for 2 h. Yield: 0.356 g (99%); mp 230–232°C (from acetonitrile), ^{1}H NMR (60 MHz, DMSO–d_6) δ: 3.49 (3H, s, OMe), 4.93 (2H, s, CH_2), 6.00–6.18 (1H, m, 1H of pyridine), 7.12–7.63 (10H, m, 8H of Ph and 2H of pyridine), 7.69–8.00 (3H, m, 2H of Ph and 1H of pyridine), 8.91 (1H, s, NH). *Anal.* Calcd for $C_{22}H_{20}N_2O_3$: C, 73.32; H, 5.59; N, 7.77. Found: C, 73.12; H, 5.43; N, 7.81.

Methyl (Benzoylamino)[1-Methylpyridin-4(1*H*)-ylidene]acetate (7b). This compound was prepared from **5b**; Procedure B, reflux for 1 h, trituration with acetone. Yield: 0.189 (66%); mp 210°C (from methanol). ^{1}H NMR (60 MHz, DMSO–d_6) δ: 3.25 (6H, br s, OMe and NMe), 6.02–6.20 (1H, m, 1H of pyridine), 7.14–7.40 (2H, m, 2H of pyridine), 7.45–7.66 (3H, m, 3H of Ph), 7.77–8.09 (3H, m: 2H of Ph and 1H of pyridine), 8.95 (1H, s, NH). *Anal.* Calcd for $C_{16}H_{16}N_2O_3$: C, 67.59; H, 5.67; N, 9.85. Found: C, 67.57; H, 5.54; N, 9.79.

Methyl (Benzoylamino)[1-Cyclohexylpyridin-4(1*H*)-ylidene]acetate (7d). This compound was prepared from **5d**; Procedure B, reflux for 1.5 h, trituration with acetone. Yield: 0.260 g (74%); mp 229–231°C (from methanol), ^{1}H NMR (60 MHz, DMSO–d_6) δ: 0.95–2.03 (10H, m, 10H of cyclohexyl), 3.28–3.94 (1H, m, 1H of cyclohexyl), 3.59 (3H, s, OMe), 6.02–6.19 (1H, m, 1H of pyridine), 7.28–7.65 (5H, m, 3H of Ph and 2H of pyridine), 7.78–8.09 (3H, m, 2H of Ph and 1H of pyridine), 8.95 (1H, s, NH). *Anal.* Calcd for $C_{21}H_{24}N_2O_3$: C, 71.57; H, 6.86; N, 7.95. Found: C, 71.46; H, 6.68; N, 7.99.

Methyl (Benzoylamino)[1-Phenylpyridin-4(1*H*)-ylidene]acetate (7e). This compound was prepared from **5e**; Procedure A, reflux for 15 min. Yield: 0.314 g (91%); mp 244–247°C (from methanol/acetonitrile). ^{1}H NMR (60 MHz, DMSO–d_6) δ: 3.56 (3H, s, OMe), 6.14–6.31 (1H, m, 1H of pyridine), 7.18–7.70 (10H, m, 8H of Ph and 2H of pyridine), 7.81–8.10 (3H, m, 2H of Ph and 1H of pyridine), 9.09 (1H, s, NH). *Anal.* Calcd for $C_{21}H_{18}N_2O_3$: C, 72.82; H, 5.24; N, 8.09. Found: C, 72.67; H, 4.90; N, 8.40.

Methyl (Benzoylamino)[1-(4-Methylphenyl)pyridin-4(1*H*)-ylidene]acetate (7f). This compound was

prepared from **5f**; Procedure B, reflux for 1.5 h, trituration with water/methanol (2:1). Yield: 0.138 g (38%); mp 237–240°C (from methanol), ^{1}H NMR (60 MHz, DMSO–d_6) δ: 2.34 (3H, s, Ar–*Me*), 3.56 (3H, s, COOMe), 6.17–6.33 (1H, m, 1H of pyridine), 7.22–7.77 (9H, m, C_6H_4, 3H of Ph, and 2H of pyridine), 7.87–8.11 (3H, m, 2H of Ph and 1H of pyridine), 9.13 (1H, s, NH). *Anal.* Calcd for $C_{22}H_{20}N_2O_3$: C, 73.32; H, 5.59; N, 7.77. Found: C, 73.51; H, 5.68; N, 8.05.

Methyl (Benzoylamino)(1-Benzylpiperidin-4-yl)acetate (8) and Methyl (Benzoylamino)(Pyridin-4-yl)acetate (9). A mixture of compound (**7a**) (720 mg, 2 mmol), formic acid (6 mL), and 10% Pd–C (150 mg) was hydrogenated at rt for 48 h at 340 kPa pressure of hydrogen. The mixture was filtered through Vulkasil®, washed with formic acid (2 x 5 mL), and the filtrate was evaporated *in vacuo*. The oily residue was triturated with methanol/water and the precipitate was collected by filtration to give **9**; yield: 0.065 g (12%). The filtrate was evaporated *in vacuo*, the residue was triturated with diisopropyl ether/methanol, and the precipitate was collected by filtration to give **8**. Yield: 0.352 g (48%); mp 122–125°C (from acetone), ^{1}H NMR (60 MHz, $CDCl_3$) δ: 1.25–2.18 (7H, m, 7H of piperidine), 2.86 and 3.04 (2H, 2m, 1:1, 2H of piperidine), 3.48 (2H, s, C*H*$_2$Ph), 3.68 (3H, s, COOMe), 4.37 (1H, dd, *J* = 4.0, 8.0 Hz, C*H*NH), 7.35 (5H, s, Ph), 7.46–7.68 (3H, m, 3H of Ph), 7.73–8.08 (2H, m, 2H of Ph), 8.71 (1H, br d, *J* = 8.0 Hz, NH). *Anal.* Calcd for $C_{22}H_{26}N_2O_3$: C, 72.11; H, 7.15; N, 7.64. Found: C, 71.96; H, 7.05; N, 7.56.

Methyl (Benzoylamino)(Pyridin-4-yl)acetate (9). A mixture of compound (**7a**) (2.090 g, 5.93 mmol), methanol (20 mL), ammonium formate (1.096 g, 17.4 mmol), and 10% Pd–C (1.450 g) was heated under reflux for 30 min. The mixture was filtered through Vulkasil®, washed with hot methanol, and the filtrate was evaporated *in vacuo*. The oily residue was triturated with methanol/water (1:3, 4 mL) and the precipitate was collected by filtration to give **9**. Yield: 1.586 g (99%); mp 117–119°C (from diisopropyl ether/methanol), ^{1}H NMR (60 MHz, DMSO–d_6) δ: 3.72 (3H, s, OMe), 5.82 (1H, d, *J* = 8.0 Hz, C*H*NH), 7.30–7.69 (5H, m, 3H of Ph, 3'–H, and 5'–H), 7.72–8.12 (2H, m, 2H of Ph), 8.61 (2H, m, 2'–H, 6'–H), 9.36 (1H, d, *J* = 8.0 Hz, NH). *Anal.* Calcd for $C_{15}H_{14}N_2O_3$: C, 66.66; H, 5.22; N, 10.36. Found: C, 66.35; H, 4.86; N, 10.74.

5-[3-Dimethylamino-1-methylprop-2-enylidene]-2-thioxo-1,3-thiazolidin-4-one (12). A solution of compound (**11**) (1.733 g, 10 mmol) and Bredereck's reagent (8.3 mL, 40 mmol) in anhydrous toluene (20 mL) was stirred at rt under argon atmosphere for 84 h. The volatile components were evaporated *in vacuo*, ethanol (10 mL) was added to the residue, and the precipitate was collected by filtration to give **12**. Yield: 1.516 g (66%); mp 257–259°C (from ethanol/toluene), MS: (EI) *m/z* = 228 (M^+), (FAB) *m/z* = 229 (MH^+). IR (KBr) 3110, 2998, 2837, 1651, 1592, 1518 cm^{-1}. ^{1}H NMR (300 MHz, DMSO–d_6) Major

isomer δ: 2.03 (3H, s, Me), 3.02 (6H, br s, NMe_2), 6.97 (1H, d, J = 13.2 Hz, C*H*=CHNMe$_2$), 7.64 (1H, d, J = 13.2 Hz, CH=C*H*NMe$_2$). 12.71 (1H, br s, NH); Minor isomer δ: 2.43 (3H, s, Me), 4.71 (1H, d, J = 12.4 Hz, C*H*=CHNMe$_2$), 7.54 (1H, d, J = 12.4 Hz, CH=C*H*NMe$_2$). *Anal.* Calcd for $C_9H_{12}N_2OS_2$: C, 47.34; H, 5.30; N, 12.27. Found: C, 47.50; H, 5.31; N, 12.19.

5-[3-Dimethylamino-1-methylprop-2-enylidene]-3-methyl-2-thioxo-1,3-thiazolidin-4-one (13). A solution of compound (**11**) (1.970 g, 11.4 mmol) and DMFDMA (9.1 mL, 68.4 mmol) in anhydrous toluene (20 mL) was stirred at rt under argon atmosphere for 24 h. The volatile components were evaporated *in vacuo*, ethanol (10 mL) was added to the residue, and the precipitate was collected by filtration to give **13**. Yield: 1.800 g (65%); mp 195–198°C (from ethanol/toluene). MS: (EI) *m/z* = 242 (M^+), (FAB) *m/z* = 243 (MH^+). IR (KBr) 2905, 1660, 1601, 1521, 1400, 1260 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.09 (3H, s, Me), 3.06 (6H, s, NMe_2), 3.47 (3H, s, Me–N(3)), 7.19 (2H, s, CH=CH). ^{1}H NMR (300 MHz, DMSO–d_6) Major isomer δ: 2.10 (3H, s, Me), 3.18 (6H, br s, NMe_2), 3.31 (3H, s, Me–N(3)), 7.09 (1H, d, J = 12.8 Hz, C*H*=CHNMe$_2$), 7.75 (1H, d, J = 12.8 Hz, CH=C*H*NMe$_2$); Minor isomer δ: 2.94 (6H, br s, NMe_2), 3.29 (3H, s, Me–N(4)), 4.84 (1H, d, J = 12.1 Hz, C*H*=CHNMe$_2$), 7.64 (1H, d, J = 12.1 Hz, CH=C*H*NMe$_2$). *Anal.* Calcd for $C_{10}H_{14}N_2OS_2$: C, 49.56; H, 5.82; N, 11.56. Found: C, 49.49; H, 5.75; N, 11.31.

5-{3-Dimethylamino-1-[2-(dimethylamino)vinyl]prop-2-enylidene}-3-methyl-2-thioxo-1,3-thiazolidin-4-one (15). A solution of compound (**13**) (0.528 g, 2.4 mmol) and Bredereck's reagent (1 mL, 4.8 mmol) in anhydrous toluene (10 mL) was stirred at 110–120°C under argon atmosphere for 1 h. The volatile components were evaporated *in vacuo*, ethanol (5 mL) was added to the residue, and the precipitate was collected by filtration to give **15**. Yield: 0.670 g (94%); mp 198–199°C (from ethanol/toluene). MS: (EI) *m/z* = 297 (M^+), (FAB) *m/z* = 298 (MH^+). HRMS: Calcd for $C_{13}H_{19}N_3OS_2$: 297.096956. Found: 297.098050. IR (KBr) 2905, 2808, 1649, 1586, 1503, 1259 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.98 (12H, s, 2 NMe_2), 3.47 (3H, s, Me–N(3)), 5.72 (2H, br s, 2 C*H*=CHNMe$_2$), 6.97 (2H, d, J = 12.8 Hz, 2 CH=C*H*NMe$_2$). *Anal.* Calcd for $C_{13}H_{19}N_3OS_2$: C, 52.49; H, 6.44; N, 14.13. Found: C, 52.46; H, 6.35; N, 14.02.

General Procedure for the Preparation of 3-Methyl-5-[1-Substituted Pyridin-4(1*H*)-ylidene]-2-thioxo-1,3-thiazolidin-4-ones (16a–c,e,h–p). A mixture of compound (**15**) (0.149 g, 0.5 mmol), amine hydrochloride (**4**) (0.5 mmol), and ethanol (1 mL) was stirred under reflux for 15 min–3 h. The volatile components were evaporated *in vacuo*, ethanol (0.5 mL) was added to the residue, and the precipitate was collected by filtration to give **16**.

The following compounds were prepared in this manner:

5-[1-Benzylpyridin-4(1*H*)-ylidene]-3-methyl-2-thioxo-1,3-thiazolidin-4-one (16a). This compound was prepared from benzylamine hydrochloride (**4a**), reflux for 2 h. Yield: 0.148 g (94%); mp 287–288°C (from ethanol). IR (KBr) 3036, 1660, 1616, 1526, 1406, 1270 cm^{-1}. ^1H NMR (300 MHz, DMSO–d_6) δ: 3.28 (3H, s, Me), 5.23 (2H, s, CH_2), 6.46 (1H, dd, *J* = 2.5, 7.2 Hz, 5'–H), 7.33–7.45 (5H, m, Ph), 7.98–8.02 (2H, m, 2'–H and 6'–H), 8.25 (1H, dd, *J* = 2.5, 7.5 Hz, 3'–H). *Anal.* Calcd for $C_{16}H_{14}N_2OS_2$: C, 61.12; H, 4.49; N, 8.91. Found: C, 61.29; H, 4.62; N, 8.64.

3-Methyl-5-[1-methylpyridin-4(1*H*)-ylidene]-2-thioxo-1,3-thiazolidin-4-one (16b). This compound was prepared from methylamine hydrochloride (**4b**), reflux for 1 h. Yield: 0.093 g (78%); mp 315–316°C (from ethanol/DMF). IR (KBr) 3046, 2936, 1663, 1618, 1530, 1263 cm^{-1}. ^1H NMR (300 MHz, DMSO–d_6) δ: 3.32 (3H, s, Me–N(3)), 3.77 (3H, s, Me–N(1')), 6.45 (1H, ddd, *J* = 0.6, 2.6, 7.1 Hz, 5'–H), 7.84–7.87 (2H, m, 2'–H and 6'–H), 8.25 (1H, ddd, *J* = 0.6, 2.6, 7.3 Hz, 3'–H). *Anal.* Calcd for $C_{10}H_{10}N_2OS_2$: C, 50.39; H, 4.23; N, 11.75. Found: C, 50.43; H, 4.11; N, 11.59.

5-[1-(2-Hydroxyethyl)pyridin-4(1*H*)-ylidene]-3-methyl-2-thioxo-1,3-thiazolidin-4-one (16c). This compound was prepared from 2-aminoethanol hydrochloride (**4c**), reflux for 1 h. Yield: 0.121 g (90%); mp 290–294°C (from ethanol/DMF). IR (KBr) 3345, 1656, 1580, 1509, 1396, 1275 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 3.34 (3H, s, Me), 3.69 (2H, dt, *J* = 5.1, 5.2 Hz, C*H*$_2$OH), 4.05 (2H, t, *J* = 5.1 Hz, H_2C–N(1')), 5.07 (1H, t, *J* = 5.2 Hz, OH), 6.46 (1H, dd, *J* = 2.5, 7.3 Hz, 5'–H), 7.85–7.89 (2H, m, 2'–H and 6'–H), 8.26 (1H, dd, *J* = 2.5, 7.4 Hz, 3'–H). *Anal.* Calcd for $C_{11}H_{12}N_2O_2S_2$: C, 49.23; H, 4.51; N, 10.44. Found: C, 49.09; H, 4.41; N, 10.15.

3-Methyl-5-[1-phenylpyridin-4(1*H*)-ylidene]-2-thioxo-1,3-thiazolidin-4-one (16e). This compound was prepared from aniline hydrochloride (**4e**), reflux for 3 h. Yield: 0.125 g (83%); mp 312–314°C (from ethanol/DMF). IR (KBr) 3051, 1657, 1620, 1532, 1489, 1265 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 3.51 (3H, s, Me), 6.29 (1H, dd, *J* = 2.5, 7.5 Hz, 5'–H), 7.34–7.37 (2H, m, 2H of Ph), 7.45–7.50 (3H, m, 3H of Ph), 7.53–7.56 (2H, m, 2'–H, 6'–H), 8.44 (1H, dd, *J* = 2.5, 7.9 Hz, 3'–H). *Anal.* Calcd for $C_{15}H_{12}N_2OS_2$: C, 59.97; H, 4.03; N, 9.33. Found: C, 60.03; H, 3.98; N, 9.13.

5-[1-(4-Fluorophenyl)pyridin-4(1*H*)-ylidene]-3-methyl-2-thioxo-1,3-thiazolidin-4-one (16h). This compound was prepared from 4-fluoroaniline hydrochloride (**4h**), reflux for 2 h. Yield: 0.148 g (93%); mp 320–322°C (from ethanol/DMF). IR (KBr) 3051, 1663, 1622, 1509, 1277 cm^{-1}. ^1H NMR (300 MHz,

$CDCl_3$) δ: 3.50 (3H, s, Me), 6.26 (1H, dd, *J* = 2.4, 7.3 Hz, 5'–H), 7.22–7.27 (2H, m, 2H of Ph), 7.32–7.37 (2H, m, 2H of Ph), 7.39–7.42 (2H, m, 2'–H and 6'–H), 8.42 (1H, dd, *J* = 7.7, 2.4 Hz, 3'–H). *Anal.* Calcd for $C_{15}H_{11}N_2OFS_2$: C, 56.58; H, 3.48; N, 8.80. Found: C, 56.45; H, 3.51; N, 8.60.

3-Methyl-5-[1-(3-nitrophenyl)pyridin-4(1*H*)-ylidene]-2-thioxo-1,3-thiazolidin-4-one (16i). This compound was prepared from 3-nitroaniline hydrochloride (**4i**), reflux for 1 h. Yield: 0.096 g (56%); mp 347–350°C (from ethanol/DMF). IR (KBr) 3063, 1665, 1626, 1528, 1352, 1271 cm^{-1}. ^1H NMR (300 MHz, DMSO–d_6) δ: 3.35 (3H, s, Me), 6.50–6.55 (1H, m, 5'–H), 7.86–7.91 (1H, m, 1H of Ar), 8.10–8.14 (1H, m, 1H of Ar), 8.21–8.25 (2H, m, 2H of Ar), 8.29–8.35 (2H, m, 2'–H and 6'–H), 8.51–8.53 (1H, m, 3'–H). *Anal.* Calcd for $C_{15}H_{11}N_3O_3S_2$: C, 52.16; H, 3.21; N, 12.17. Found: C, 52.42; H, 3.24; N, 11.97.

3-Methyl-5-[1-(pyridin-2-yl)pyridin-4(1*H*)-ylidene]-2-thioxo-1,3-thiazolidin-4-one (16j). This compound was prepared from 2-aminopyridine hydrochloride (**4j**), reflux for 30 min. Yield: 0.073 g (48%); mp 345–347°C (from ethanol/DMF). IR (KBr) 1663, 1619, 1528, 1431, 1267 cm^{-1}. ^1H NMR (300 MHz, DMSO–d_6) δ: 3.35 (3H, s, Me), 6.53 (1H, ddd, *J* = 0.5, 2.6, 7.5 Hz, 5'–H), 7.52 (1H, ddd, *J* = 0.9, 4.8, 7.4 Hz, 5"–H), 7.88 (1H, deg dt, *J* = 0.9, 7.3 Hz, 3"–H), 8.11 (1H, ddd, *J* = 1.9, 7.3, 7.4 Hz, 4"–H), 8.30 (1H, ddd, *J* = 0.5, 2.6, 7.9 Hz, 3'–H), 8.53–8.57 (2H, m, 2'–H and 6'–H), 8.60 (1H, ddd, *J* = 0.9, 1.9, 4.8 Hz, 6"–H). *Anal.* Calcd for $C_{14}H_{11}N_3OS_2$: C, 55.79; H, 3.68; N, 13.94. Found: C, 56.04; H, 3.69; N, 13.64.

5-[1-(5-Chloropyridin-2-yl)pyridin-4(1*H*)-ylidene]-3-methyl-2-thioxo-1,3-thiazolidin-4-one (16k). This compound was prepared from 2-amino-5-chloropyridine hydrochloride (**4k**), reflux for 1 h. Yield: 0.053 g (32%); mp 339–341°C (from ethanol/DMF), IR (KBr) 3092, 1663, 1622, 1531, 1275 cm^{-1}. ^1H NMR (300 MHz, DMSO–d_6) δ: 3.35 (3H, s, Me), 6.52 (1H, dd, *J* = 2.5, 7.9 Hz, 5'–H), 7.93 (1H, dd, *J* = 0.8, 8.9 Hz, 3"–H), 8.25 (1H, dd, *J* = 2.5, 8.9 Hz, 4"–H), 8.27 (1H, dd, *J* = 2.5, 8.1 Hz, 3'-H), 8.47–8.52 (2H, m, 2'–H and 6'–H), 8.65 (1H, dd, *J* = 0.8, 2.5 Hz, 6"–H). *Anal.* Calcd for $C_{14}H_{10}N_3OClS_2$: C, 50.07; H, 3.00; N, 12.51. Found: C, 50.13; H, 2.84; N, 12.41.

5-[1-(Isoxazol-3-yl)pyridin-4(1*H*)-ylidene]-3-methyl-2-thioxo-1,3-thiazolidin-4-one (16l). This compound was prepared from 3-aminoisoxazole hydrochloride (**4l**), reflux for 1 h. Yield: 0.062 g (43%); mp 224–226°C (from ethanol/DMF). IR (KBr) 3108, 2362, 1674, 1630, 1464, 1273 cm^{-1}. ^1H NMR (300 MHz, DMSO–d_6) δ: 3.34 (3H, s, Me), 6.47 (1H, dd, *J* = 1.3, 7.9 Hz, 5'–H), 7.27 (1H, d, *J* = 1.8 Hz, 4"–H), 8.18–8.21 (3H, m, 2'–H, 3'–H, and 6'–H), 9.12 (1H, d, *J* = 1.8 Hz, 5"–H). *Anal.* Calcd for $C_{12}H_9N_3O_2S_2$: C, 49.47; H, 3.11; N, 14.42. Found: C, 49.32; H, 2.89; N, 14.29.

3-Methyl-5-[1-(thiazol-2-yl)pyridin-4(1*H*)-ylidene]-2-thioxo-1,3-thiazolidin-4-one (16m). This compound was prepared from 2-aminothiazole hydrochloride (**4m**), reflux for 1 h. Yield: 0.102 g (66%); mp 228–229°C (from ethanol/DMF). IR (KBr) 3073, 1672, 1628, 1499, 1409, 1269 cm^{-1}. ^1H NMR (300 MHz, DMSO–d_6) δ: 3.35 (3H, s, Me), 6.45 (1H, dd, *J* = 2.6, 7.9 Hz, 5'–H), 7.69 (1H, d, *J* = 3.4 Hz, 4''–H), 7.72 (1H, d, *J* = 3.4 Hz, 5''–H), 8.21 (1H, dd, *J* = 2.6, 7.9 Hz, 3'–H), 8.29–8.34 (2H, m, 2'–H and 6'–H). *Anal.* Calcd for $C_{12}H_9N_3OS_3$: C, 46.88; H, 2.95; N, 13.67. Found: C, 46.99; H, 2.73; N, 13.48.

5-[1-(Benzothiazol-2-yl)pyridin-4(1*H*)-ylidene]-3-methyl-2-thioxo-1,3-thiazolidin-4-one (16n). This compound was prepared from 2-aminobenzothiazole hydrochloride (**4n**), reflux for 1 h. Yield: 0.076 g (43%); mp >350°C (from ethanol/DMF). IR (KBr) 1675, 1618, 1501, 1404, 1259 cm^{-1}. ^1H NMR (300 MHz, DMSO–d_6) δ: 3.36 (3H, s, Me), 6.50 (1H, dd, *J* = 2.5, 7.7 Hz, 5'–H), 7.48 (1H, ddd, *J* = 1.2, 6.5, 8.3 Hz, 6''–H), 7.58 (1H, ddd, *J* = 1.3, 6.5, 7.9 Hz, 5''–H), 7.96 (1H, ddd, *J* = 0.8, 1.2, 7.9 Hz, 4''–H), 8.18 (1H, dd, *J* = 1.3, 8.3 Hz, 7''–H), 8.23 (1H, dd, *J* = 2.5, 7.9 Hz, 3'–H), 8.37–8.41 (2H, m, 2'–H and 6'–H). *Anal.* Calcd for $C_{16}H_{11}N_3OS_3$: C, 53.76; H, 3.10; N, 11.75. Found: C, 53.75; H, 2.87; N, 11.55.

5-[1-Methoxycarbonylmethylpyridin-4(1*H*)-ylidene]-3-methyl-2-thioxo-1,3-thiazolidin-4-one (16o). This compound was prepared from methyl glycinate hydrochloride (**4o**), reflux for 15 min. Yield: 0.070 g (47%); mp 223–225°C (from toluene). IR (KBr) 2949, 1744, 1670, 1618, 1530 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 3.48 (3H, s, Me), 3.84 (3H, s, COOMe), 4.49 (2H, s, CH_2), 6.17 (1H, dd, *J* = 2.5, 7.4 Hz, 5'–H), 7.04–7.11 (2H, m, 2'–H and 6'–H), 8.33 (1H, dd, *J* = 2.5, 7.4 Hz, 3'–H). *Anal.* Calcd for $C_{12}H_{12}N_2O_3S_2$: C, 48.63; H, 4.08; N, 9.45. Found: C, 48.39; H, 3.90; N, 9.23.

5-[1-Ethoxycarbonylmethylpyridin-4(1*H*)-ylidene]-3-methyl-2-thioxo-1,3-thiazolidin-4-one (16p). This compound was prepared from ethyl glycinate hydrochloride (**4p**), reflux for 15 min. Yield: 0.078 g (50%); mp 229–231°C (from toluene/DMF). MS: (EI) *m/z* = 310 (M^+), (FAB) *m/z* = 311 (MH^+). IR (KBr) 2986, 1738, 1660, 1617, 1532 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.32 (3H, t, *J* = 7.1 Hz, CH_2CH_3), 3.48 (3H, s, Me), 4.29 (2H, q, *J* = 7.1 Hz, CH_2CH_3), 4.48 (2H, s, CH_2COOEt), 6.17 (1H, dd, *J* = 2.3, 7.2 Hz, 5'–H), 7.07–7.13 (2H, m, 2'–H and 6'–H), 8.33 (1H, dd, *J* = 2.3, 7.5 Hz, 3'–H). *Anal.* Calcd for $C_{13}H_{14}N_2O_3S_2$: C, 50.30; H, 4.55; N, 9.03. Found: C, 49.99; H, 4.51; N, 8.86.

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