Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron
Tetrahedron 63 (2007) 10054–10058

A novel four-component tandem protocol for the stereoselective synthesis of highly functionalised thiazoles

Subbiah Renuga,[a,*] Michael Gnanadeebam,[a] Beer Mohamed Vinosha[a] and Subbu Perumal[b]

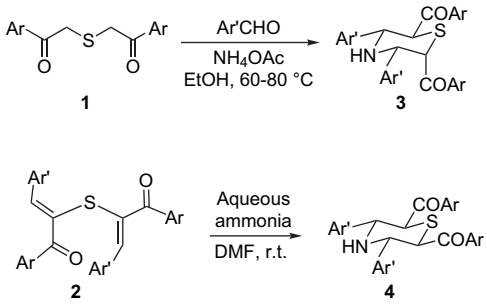
[a]*Department of Chemistry, Fatima College, Madurai 625018, India*
[b]*School of Chemistry, Madurai Kamaraj University, Madurai 625021, India*

Received 24 April 2007; revised 28 June 2007; accepted 12 July 2007
Available online 19 July 2007

Abstract—The reaction of bis(aroylmethyl) sulfides with aromatic aldehydes and ammonium acetate in 1:2:1 molar ratio under solvent-free microwave irradiation afforded predominantly a series of thiazoles, viz., 1-aryl-2-[5(*Z*)-5-arylmethylidene-2,4-diaryl-2,5-dihydrothiazol-2-yl]ethanones stereoselectively. This reaction presumably occurs via a Knoevenagel condensation–Michael addition–cyclocondensation–ring opening–ring closing Michael addition sequence. The intermediacy of (*Z*,*Z*)-2,2′-thiobis(1,3-diarylprop-2-en-1-ones) in the above transformation is demonstrated by their conversion to the thiazoles upon reaction with ammonium acetate under solvent-free microwave irradiation.

1. Introduction

Thiazines are known for their important biological activities such as anti-HIV,[1] anti-fungal, anthelmintic, anti-inflammatory[2] and anti-psoriatic.[3] Previously, diastereomeric 2,6-diaroyl-3,5-diaryltetrahydro-1,4-thiazines (**3** and **4**) have been obtained, respectively, from the reaction of aromatic aldehydes and ammonium acetate with bis(aroylmethyl) sulfides **1**,[4] and from the reaction of (*Z*,*Z*)-2,2′-thiobis(1,3-diarylprop-2-en-1-ones) **2** with ammonia[5] in moderate yields (Scheme 1).



Scheme 1. Formation of diastereomeric tetrahydro-1,4-thiazines.

In the present work, the reaction of bis(aroylmethyl) sulfides with aromatic aldehydes and ammonium acetate has been effected under solvent-free microwave irradiation, as it is not uncommon to get different products from reactions under solvent-free microwave irradiation and in solution under conventional heating. This is ascribable to the fact that under solvent-free conditions the transition state, being surrounded by only reactant molecules in place of solvent, is bound to have an environment with different polarity than that in solution. This, in turn, can enable quite different reactions under solventless condition and in solution. Microwave irradiation also, in general, favours reactions involving more polar transition states and often leads to different product selectivities than the thermal reactions.[6–10] Further, reactions under microwave irradiation often proceed more rapidly than the conventional thermal reactions with diminished decomposition of the reactants and/or products thus minimising the waste and enhancing the yield.

It is pertinent to note that, in accord with the above observations, in the present investigation, the reaction of bis(aroylmethyl) sulfides **1** with aromatic aldehydes and ammonium acetate in 1:2:1 molar ratio under solvent-free microwave irradiation, afforded predominantly tetrasubstituted thiazoles via tandem reactions instead of the 1,4-thiazines previously reported in solution.[4,5] The results of these investigations are presented in this paper. Incidentally, tandem reactions fall under green synthetic protocols as they lead to convergent, elegant, efficient and eco-friendly construction of complex molecules without isolating and purifying the intermediates thus minimising waste, labour and cost.[11,12]

Keywords: Tandem reactions; Bis(aroylmethyl) sulfides; Microwave irradiation; Solvent-free; Thiazole.
* Corresponding author. Tel.: +91 452 2668016; fax: +91 452 2668437; e-mail: s.renuga@gmail.com

0040–4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.07.040

Moreover, this investigation, affording hitherto unknown thiazoles serendipitously, assumes importance since the thiazoles display numerous biological activities such as anti-inflammatory,[13] anti-tumour,[14] anti-fungal[15] and anti-microbial.[16]

2. Results and discussion

In the present investigation, bis(aroylmethyl) sulfide **1**, an aromatic aldehyde and ammonium acetate were thoroughly mixed in a borosilicate boiling tube kept partially immersed in a silica bath, which, in turn, was placed in a microwave oven (750 W and frequency of 2450 MHz) and irradiated at power level 4 of a total scale of 6. Completion of the reaction (TLC) requires 10 min of microwave irradiation in one stretch without intermittent cooling. This reaction led to the formation of three products (Scheme 2), which were obtained in a pure form by column chromatography on silica gel with ethyl acetate–petroleum ether mixture [2:98 (v/v)] as eluent.

The major product was identified as a thiazole derivative **5** from elemental analysis and ^{1}H, ^{13}C and 2D NMR spectroscopic data. The yields and melting points of **5a**–**5g** are given in Table 1. Of the two minor products, the one obtained in 7–10% yields was found to be the already known (*Z*,*Z*)-2,2′-thiobis(1,3-diarylprop-2-en-1-ones) **2**, while the other formed in negligible amounts was identified as 2-[(2-oxo-2-phenylethyl)sulfanyl]-1,3-diphenylprop-2-en-1-one **6** (Scheme 2).

The elucidation of the structure of **5** using one- and two-dimensional NMR spectroscopic data is discussed with **5f** as an example. The 1H doublets at 4.44 and 3.85 ppm (J=17.1 Hz) due to the diastereotopic methylene hydrogens have an HMBC correlation with the carbonyl at 194.8 ppm disclosing their proximity (Fig. 1). That the ^{13}C signal at 92.6 ppm is due to C-2 of the thiazole is evident from its

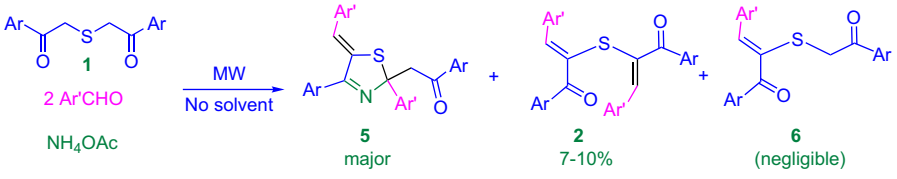
Table 1. Yields and melting points of thiazoles[a] **5**

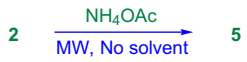
5	Ar	Ar′	Yields[a] (%)		Mp (°C)
			Method 1[b]	Method 2[c]	
a	C_6H_5	C_6H_5	70	80	176—178
b	C_6H_5	*p*-Cl–C_6H_4	73	76	165—167
c	C_6H_5	*o*-Cl–C_6H_4	62	79	166—168
d	*p*-Cl–C_6H_4	C_6H_5	68	84	150—152
e	*p*-Cl–C_6H_4	*p*-Cl–C_6H_4	71	82	158—160
f	*p*-Cl–C_6H_4	*p*-Me–C_6H_4	63	81	136—138
g	*p*-Me–C_6H_4	C_6H_5	66	85	138—140

[a] After purification by column chromatography.
[b] Obtained from the reaction of **1** with ArCHO and NH_4OAc.
[c] Obtained from the reaction of **2** with NH_4OAc.

HMBC correlation with (i) the methylene protons, and (ii) the aromatic protons at 7.58 ppm of the *p*-tolyl ring. The methyls of the tolyl rings give ^{1}H signals at 2.31 and 2.35 ppm and ^{13}C signals at 21.4 and 21.0 ppm. These ^{13}C signals have HMBC correlations with aromatic hydrogens at 7.14 and 7.19 ppm, respectively. The signals at 7.58 and 7.14 ppm, related by an H,H-COSY correlation, are due to the protons *meta* and *ortho* to the methyl of *p*-tolyl ring at C-2. The signals at 7.19 and 7.43 ppm having an H,H-COSY correlation are assigned to the protons *ortho* and *meta* to the methyl group in the other tolyl group. The DEPT spectrum of **5f** confirms the presence of one methylene carbon and one quaternary carbon in the aliphatic region (C-3).

The imine carbon (C-4) signal at 168.6 ppm has an HMBC correlation with the singlet at 6.74 ppm assigning it to arylmethylidene hydrogen. The latter has a C,H-COSY correlation with the carbon signal at 125.7 ppm, which in turn correlates with the H signal at 7.43 ppm (HMBC) due to the Hs of the tolyl ring, suggesting that the second *p*-tolyl ring is present in the arylmethylidene function. The signals due to the other protons and carbons of **5f** are also assigned similarly. The important HMBC correlations and the ^{1}H and ^{13}C chemical shifts of **5f** are given in Figures 1 and 2, respectively.





2 & 5	Ar	Ar'
a	C_6H_5	C_6H_5
b	C_6H_5	*p*-Cl-C_6H_4
c	C_6H_5	*o*-Cl-C_6H_4
d	*p*-Cl-C_6H_4	C_6H_5
e	*p*-Cl-C_6H_4	*p*-Cl-C_6H_4
f	*p*-Cl-C_6H_4	*p*-Me-C_6H_4
g	*p*-Me-C_6H_4	C_6H_5

Scheme 2. Formation of thiazoles **5** by tandem reactions.

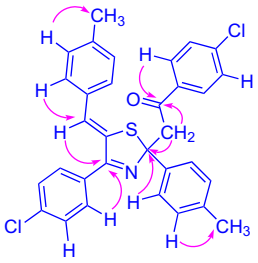


Figure 1. HMBC correlations of **5f**.

The ^{1}H and ^{13}C spectroscopic features of **5a**–**5e** and **5g** are also similar to **5f**, except for the substituent effects. The structure for **5b** in solid state deduced from X-ray crystallographic studies is similar to **5f** (Fig. 3).

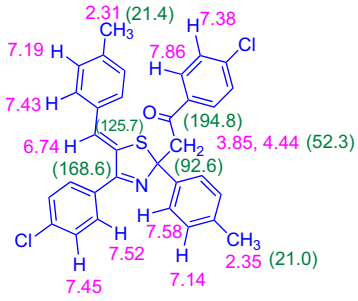


Figure 2. ^{1}H and ^{13}C chemical shifts of **5f**.

The mechanism (Scheme 3) envisages an initial Knoevenagel condensation of bis(aroylmethyl) sulfide with two molecules of aromatic aldehyde to give **2**. This is presumably followed by Michael addition of ammonia with concomitant cyclocondensation to give **7**. Base catalysed ring opening of **7** to **8** and ring closing Michael addition of **8** to **3** complete the tandem sequence. Presumably, the ring opening of **7** to **8** is driven by the stability of the fully conjugated azatrienone system **8**. The formation of minor products **2** and **6** is also in consonance with the mechanism.

The involvement of (*Z*,*Z*)-2,2′-thiobis(1,3-diarylprop-2-en-1-ones) **2** as an intermediate in this reaction is evident from the reaction of an equimolar mixture of (*Z*,*Z*)-2,2′-thiobis(1,3-diarylprop-2-en-1-ones) **2** and ammonium acetate furnishing **5** as the major product under the conditions

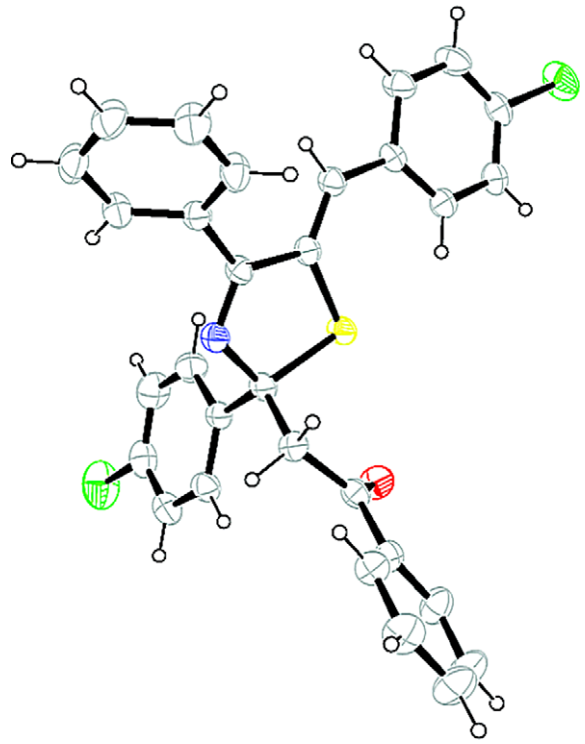
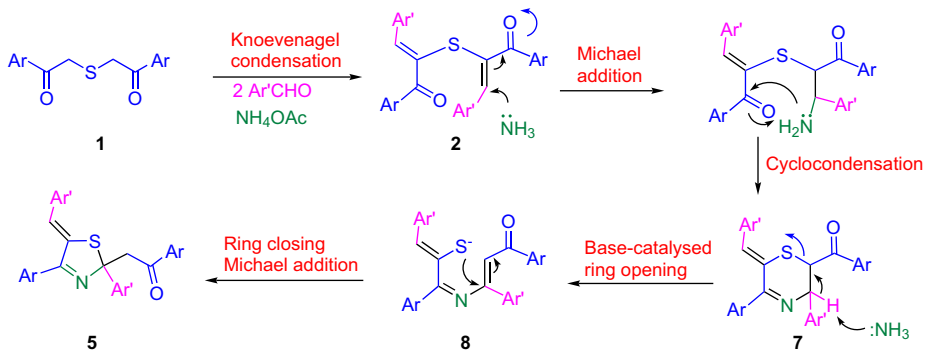


Figure 3. X-ray crystal structure of **5b**.

employed for the reaction of bis(aroylmethyl) sulfide **1** (Scheme 2). The yields of **5** (76–85%) obtained in the transformation of **2** to **5** are better than those obtained from **1** (62–73%) (Table 1).

3. Conclusions

The present work describes the predominant formation of highly functionalised thiazoles under solvent-free microwave irradiation presumably via a tandem sequence of reactions. This study discloses the complementary nature of the present protocol to the solution state chemistry, which demonstrates that the product selectivity can be tuned by employing appropriate reaction conditions. Further investigations on the utility of these thiazoles as synthons in the construction of novel heterocycles are being currently explored in our group.



Scheme 3. Mechanism for the formation of thiazoles **5**.

4. Experimental section

4.1. General methods

The melting points are uncorrected. A domestic microwave oven (IFB, model-electron of 750 W capacity and microwave frequency of 2450 MHz) was employed for microwave irradiation. NMR spectra were recorded at 20 °C on a Bruker AMX 300 instrument operating at 300 MHz for ^{1}H and at 75 MHz for ^{13}C. Solutions (in $CDCl_3$) were approximately 0.05 M and chemical shifts were referenced internally to TMS in all cases and expressed in δ scale (ppm). Two-dimensional NMR measurements H,H-COSY, C,H-COSY and HMBC have also been measured using the above instrument. Standard Bruker software (UXNMR) was used throughout. The single crystal X-ray data for **5b** were collected on an Enraf-Nonius MACH 3 four-circle diffractometer (Mo Kα radiation, λ=0.71073 Å). Elemental analyses were performed on a Perkin–Elmer 2400 Series II Elemental CHNS Analyser.

4.2. Synthesis of 1-aryl-2-[5(*Z*)-5-arylmethylidene-2,4-diaryl-2,5-dihydrothiazol-2-yl]ethanones—general procedure

Method 1: by the reaction of bis(aroylmethyl) sulfide, aromatic aldehyde and ammonium acetate. A mixture of bis(benzoylmethyl) sulfide (0.54 g, 2 mmol), benzaldehyde (0.4 mL, 4 mmol) and ammonium acetate (0.154 g, 2 mmol) was taken in a glass mortar and ground to a homogeneous paste with a pestle. This paste was then transferred to a borosilicate boiling tube, kept in a silica bath and placed in a domestic microwave oven at power level 4 for 10 min. The TLC analysis of the reaction mixture shows that the reaction goes to completion in 10 min affording three products. These products were separated by column chromatography using ethyl acetate–petroleum ether [2:98 (v/v)] mixture.

Among the two minor products, the one obtained in 7–10% yields was the known compound (*Z*,*Z*)-2,2′-thiobis-(1,3-diphenylprop-2-en-1-one) **2** and the other obtained in negligible amount was identified as 2-[(2-oxo-2-phenylethyl)sulfanyl]-1,3-diphenylprop-2-en-1-one **6**. The thiazole derivative was obtained as the major product, which was recrystallised from chloroform–alcohol mixture.

Method 2: by the reaction of (Z,Z)-2,2′-thiobis(1,3-diarylprop-2-en-1-ones) and ammonium acetate. The procedure is the same as the one described in method 1 except that in this method, the reactants are a mixture of (*Z*,*Z*)-2,2′-thiobis-(1,3-diarylprop-2-en-1-ones)[17] (1 mmol) and ammonium acetate (1 mmol).

4.2.1. 2-[(5*Z*)-5-Benzylidene-2,5-dihydro-2,4-diphenylthiazol-2-yl]-1-phenylethanone (5a). Obtained as a colourless solid (0.624 g, 70% in method 1 and 0.358 g, 80% in method 2), mp=176–178 °C; IR (KBr) ν 1695, 1586, 1485 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 3.90 (1H, d, *J*=17.4 Hz), 4.57 (1H, d, *J*=17.4 Hz), 6.83 (1H, s), 7.24–7.94 (20H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 52.2, 92.8, 125.6, 127.0, 127.7, 128.0, 128.1, 128.2, 128.5, 128.6, 128.9, 129.2, 129.9, 133.3, 133.5, 136.0, 136.7, 140.2, 143.3, 169.6, 195.9. Anal. Calcd for $C_{30}H_{23}NOS$: C, 80.87; H, 5.20; N, 3.14. Obsd: C, 81.01; H, 5.16; N, 3.10%.

4.2.2. 2-[(5*Z*)-5-(*p*-Chlorobenzylidene)-2-(*p*-chlorophenyl)-2,5-dihydro-4-phenylthiazol-2-yl]-1-phenylethanone (5b). Obtained as a colourless solid (0.750 g, 73% in method 1 and 0.392 g, 76% in method 2), mp=165–167 °C; IR (KBr) ν 1690, 1592, 1487 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 3.87 (1H, d, *J*=17.7 Hz), 4.55 (1H, d, *J*=17.7 Hz), 6.78 (1H, s), 7.27–7.99 (18H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 52.4, 92.6, 124.5, 128.1, 128.3, 128.5 (7), 128.5 (9), 128.6, 128.7, 129.0, 130.0, 130.1, 133.1, 133.5, 133.6, 134.4, 136.4, 140.5, 141.6, 169.6, 195.8. Anal. Calcd for $C_{30}H_{21}Cl_2NOS$: C, 70.04; H, 4.11; N, 2.72. Obsd: C, 69.97; H, 4.08; N, 2.76%.

4.2.3. 2-[(5*Z*)-5-(*o*-Chlorobenzylidene)-2-(*o*-chlorophenyl)-2,5-dihydro-4-phenylthiazol-2-yl]-1-phenylethanone (5c). Obtained as a colourless solid (0.639 g, 62% in method 1 and 0.408 g, 79% in method 2), mp=166–168 °C; IR (KBr) ν 1693, 1612, 1463 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 4.17 (1H, d, *J*=15.3 Hz), 4.43 (1H, d, *J*=15.3 Hz), 7.15–7.94 (19H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 48.1, 91.5, 121.6, 126.9, 127.0, 128.1, 128.3 (9), 128.4 (4), 128.6, 128.9 (6), 129.0 (4), 129.2, 129.5, 130.1, 130.9, 131.6, 132.8, 133.3, 134.2, 134.3, 137.8, 141.4, 142.6, 170.8, 195.9. Anal. Calcd for $C_{30}H_{21}Cl_2NOS$: C, 70.04; H, 4.11; N, 2.72. Obsd: C, 70.08; H, 4.14; N, 2.68%.

4.2.4. 2-[(5*Z*)-5-Benzylidene-4-(*p*-chlorophenyl)-2,5-dihydro-2-phenylthiazol-2-yl]-1-(*p*-chlorophenyl)ethanone (5d). Isolated as a colourless solid (0.700 g, 68% in method 1 and 0.433 g, 84% in method 2), mp=150–152 °C; IR (KBr) ν 1676, 1588, 1488 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 3.89 (1H, d, *J*=17.1 Hz), 4.47 (1H, d, *J*=17.1 Hz), 6.80 (1H, s), 7.25–7.89 (18H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 52.2, 92.8, 125.7, 126.8, 127.8, 128.2 (7), 128.3 (2), 128.6, 128.8, 128.9, 129.6, 130.5, 131.8, 135.1, 135.7, 136.2, 139.7 (6), 139.7 (9), 143.2, 168.8, 194.7. Anal. Calcd for $C_{30}H_{21}Cl_2NOS$: C, 70.04; H, 4.11; N, 2.72. Obsd: C, 69.99; H, 4.09; N, 2.76%.

4.2.5. 2-[(5*Z*)-5-(*p*-Chlorobenzylidene)-2,4-bis(*p*-chlorophenyl)-2,5-dihydrothiazol-2-yl]-1-(*p*-chlorophenyl)-ethanone (5e). Obtained as a colourless solid (0.830 g, 71% in method 1 and 0.480 g, 82% in method 2), mp=158–160 °C; IR (KBr) ν 1680, 1576, 1478 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 3.83 (1H, d, *J*=17.5 Hz), 4.44 (1H, d, *J*=17.5 Hz), 6.73 (1H, s), 7.26–7.86 (16H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 52.4, 92.6, 124.6, 128.4 (0), 128.4 (3), 128.8, 128.9, 129.0, 129.5, 130.0, 130.5, 133.8, 133.9, 134.1, 134.8, 140.1, 141.5, 168.8, 194.5. Anal. Calcd for $C_{30}H_{19}Cl_4NOS$: C, 61.77; H, 3.28; N, 2.40. Obsd: C, 61.62; H, 3.26; N, 2.43%.

4.2.6. 2-[(5*Z*)-5-(*p*-Methylbenzylidene)-4-(*p*-chlorophenyl)-2,5-dihydro-2-(*p*-methylphenyl)thiazol-2-yl]-1-(*p*-chlorophenyl)ethanone (5f). Obtained as a colourless solid (0.684 g, 63% in method 1 and 0.441 g, 81% in method

2), mp=136–138 °C; IR (KBr) ν 1675, 1575, 1483 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 2.31 (3H, s), 2.35 (3H, s), 3.85 (1H, d, J=17.1 Hz), 4.44 (1H, d, J=17.1 Hz), 6.74 (1H, s), 7.14–7.87 (16H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 21.0, 21.4, 52.3, 92.6, 125.7, 126.7, 128.7, 128.8, 129.0, 129.3, 129.6, 130.6, 132.0, 133.0, 135.2, 136.1, 137.6, 138.5, 138.8, 139.7, 140.3, 168.6, 194.8. Anal. Calcd for $C_{32}H_{25}Cl_2NOS$: C, 70.84; H, 4.64; N, 2.58. Obsd: C, 70.75; H, 4.67; N, 2.55%.

4.2.7. 2-[(5*Z*)-5-Benzylidene-2,5-dihydro-4-(*p*-methylphenyl)-2-phenylthiazol-2-yl]-1-(*p*-methylphenyl)ethanone (5g). Obtained as a colourless solid (0.626 g, 66% in method 1 and 0.404 g, 85% in method 2), mp=138–140 °C; IR (KBr) ν 1678, 1585, 1473 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 2.39 (3H, s), 2.44 (3H, s), 3.86 (1H, d, J=17.4 Hz), 4.56 (1H, d, J=17.4 Hz), 6.86 (1H, s), 7.14–7.85 (18H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 21.4, 21.6, 52.2, 92.7, 125.3, 127.0, 127.5, 127.9, 128.1, 128.3, 128.5, 128.8, 129.1, 129.2, 130.6, 134.3, 136.1, 140.1, 140.3, 143.4, 144.1, 169.5, 195.7. Anal. Calcd for $C_{32}H_{27}NOS$: C, 81.15; H, 5.75; N, 2.96. Obsd: C, 81.05; H, 5.69; N, 2.98%.

4.3. X-ray crystallographic determination of compound 5b

Data were collected at room temperature on an Enraf-Nonius MACH 3 four-circle diffractometer (Mo Kα radiation, λ=0.71073 Å) for compound **5b**. The data collection, integration and data reduction for **5b** were performed using CAD-4 EXPRESS[18] and XCAD4[19] programs and an empirical absorption correction was applied using ψ scan method.[20] The unit cell parameters were determined by a least square fitting of 25 randomly selected strong reflections and an empirical absorption correction was applied using the azimuthal scan method. The structures were solved by direct methods (SHELXS 97)[21] and subsequent Fourier synthesis and refined by full matrix least squares on SHELX 97[22] for all non-hydrogen atoms of 5**b**. All hydrogen atoms were placed in calculated positions.

4.3.1. Compound 5b. $C_{30}H_{21}Cl_2NOS$, M=514.44, triclinic, space group P-1, a=10.355(6) Å, b=10.5240(11) Å, c=13.6390(12) Å, V=1293.1(8) $Å^3$, Z=2, F(000)=532, μ=0.355 mm^{-1}, D_c=1.321 $Mg\,m^{-3}$. The reflections collected were 5365 of which 4540 were unique [$R_{(int)}$=0.0121]; 3372 reflections $I>2\sigma(I)$, R_1=0.0499 and wR_2=0.1277 for 3372 [$I>2\sigma(I)$] and R_1=0.0753 and wR_2=0.1419 for all (4540) intensity data. Goodness of fit=1.040, residual electron density in the final Fourier map was 0.536 and −0.398 e $Å^{-3}$. CCDC number is 643988.

Acknowledgements

S.R. and M.G. thank UGC for the financial support under Major Research Project and also thank the Correspondent and the Principal, Fatima College, Madurai-18 for providing facilities.

Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.07.040.

References and notes

1. Arranz, M. E.; Diaz, J. A.; Ingate, S. T.; Witvrouw, M.; Pannecouque, C.; Balzarini, J.; De Clercq, E.; Vega, S. *Bioorg. Med. Chem.* **1999**, *7*, 2811.
2. Srivastava, S. K.; Yadav, R.; Srivastav, S. D. *Indian J. Chem., Sect. B* **2004**, *43*, 399.
3. Moriyama, H.; Tsukida, T.; Inoue, Y.; Yokota, K.; Yoshino, K.; Kondo, H.; Miura, N.; Nishimura, S. *J. Med. Chem.* **2004**, *47*, 1930.
4. Selvaraj, S.; Dhanabalan, A.; Mercypushphalatha, A.; Arumugam, N. *Phosphorus, Sulfur Silicon Relat. Elem.* **1991**, *63*, 295.
5. Selvaraj, S.; Dhanabalan, A. Madurai Kamaraj University, unpublished results.
6. Regnier, T.; Lavastre, O. *Tetrahedron* **2006**, *62*, 155.
7. Quiroga, J.; Cruz, S.; Insuasty, B.; Abonía, R.; Nogueras, M.; Cobo, J. *Tetrahedron Lett.* **2006**, *47*, 27.
8. Castagnolo, D.; Renzulli, M. L.; Galletti, E.; Corelli, F.; Botta, M. *Tetrahedron: Asymmetry* **2005**, *16*, 2893.
9. Ju, Y.; Varma, R. S. *Tetrahedron Lett.* **2005**, *46*, 6011.
10. Kabalka, G. W.; Mereddy, A. R. *Tetrahedron Lett.* **2005**, *46*, 6315.
11. (a) Posner, G. H. *Chem. Rev.* **1986**, *86*, 831; (b) Tietze, L. F.; Beifuss, U. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 131; (c) Bunce, R. A. *Tetrahedron* **1995**, *48*, 13103; (d) Ho, T.-L. *Tandem Organic Reactions*; Wiley Interscience: New York, NY, 1992; (e) Tietze, L. F.; Brasche, C.; Gericke, K. M. *Domino Reactions in Organic Synthesis*; Wiley-VCH: Weinheim, 2006.
12. (a) Gnanadeepam, M.; Selvaraj, S.; Perumal, S.; Renuga, S. *Tetrahedron* **2002**, *58*, 2227; (b) Srinivasan, M.; Perumal, S. *Tetrahedron* **2006**, *62*, 7726; (c) Alex Raja, V. P.; Perumal, S. *Tetrahedron* **2006**, *62*, 4892; (d) Savitha Devi, N.; Perumal, S. *Tetrahedron* **2006**, *62*, 5931; (e) Kamal Nasar, M.; Ranjith Kumar, R.; Perumal, S. *Tetrahedron Lett.* **2007**, *48*, 2155; (f) Karthikeyan, S. V.; Perumal, S. *Tetrahedron Lett.* **2007**, *48*, 2261.
13. Kumar, A.; Rajput, C. S.; Bhati, S. K. *Bioorg. Med. Chem.* **2007**, *15*, 3089.
14. Popsavin, M.; Spaić, S.; Svirčev, M.; Kojić, V.; Bogdanović, G.; Popsavin, V. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 5317.
15. Cukurovali, A.; Yilmaz, I.; Gur, S.; Kazaz, C. *Eur. J. Med. Chem.* **2006**, *41*, 201.
16. Vicini, P.; Geronikaki, A.; Anastasia, K.; Incerti, M.; Zani, F. *Bioorg. Med. Chem.* **2006**, *14*, 3859.
17. Gnanadeebam, M.; Renuga, S.; Selvaraj, S.; Perumal, S. *Phosphorus, Sulfur Silicon Relat. Elem.* **2004**, *179*, 203.
18. Enraf-Nonius. *CAD-4 EXPRESS Version 5.0*; Enraf-Nonius: Delft, The Netherlands, 1994.
19. Harms, K.; Wocadio, S. *XCAD4*; University of Marburg: Marburg, Germany, 1995.
20. North, A. C. T.; Philips, D. C.; Mathews, F. S. *Acta Crystallogr., Sect. A* **1968**, *24*, 351.
21. Sheldrick, G. M. *Acta Crystallogr., Sect. A* **1990**, *46*, 467.
22. Sheldrick, G. M. *SHELX97*; University of Gottingen: Gottingen, Germany, 1997.