

# SYNTHESIS AND SPECTRAL STUDIES OF 4H-1,4-BENZOTHAZINE

Savita Choudhary\* and Vibha Shrivastav#

\*Department of Chemistry, S. K. Govt. Girls College, Sikar

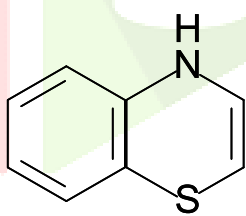
#Department of Chemistry, S. K. Govt. Girls College, Sikar

## Abstract

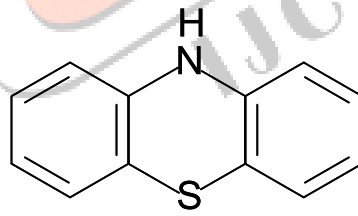
4H-1,4-Benzothiazines constitute an important class of heterocycles containing 1,4-thiazine ring fused to benzene. As a part of an ongoing programme in the development of novel synthetic methodology for the preparation of biologically active substances, we had been interested in the synthesis of various thiazine ring containing heterocyclic structures because they are the integral part of many naturally occurring and biologically active compounds.

**Key Words** - 4H-1,4-Benzothiazine, 2-aminobenzenethiol, 4H-1,4-Benzothiazines.

4H-1,4-Benzothiazine (I) is an analog of phenothiazine (II) replacing an o-phenylene group by an ethylene linkage in phenothiazine. It has structural resemblance with phenothiazines in having fold along N-S axis.



I



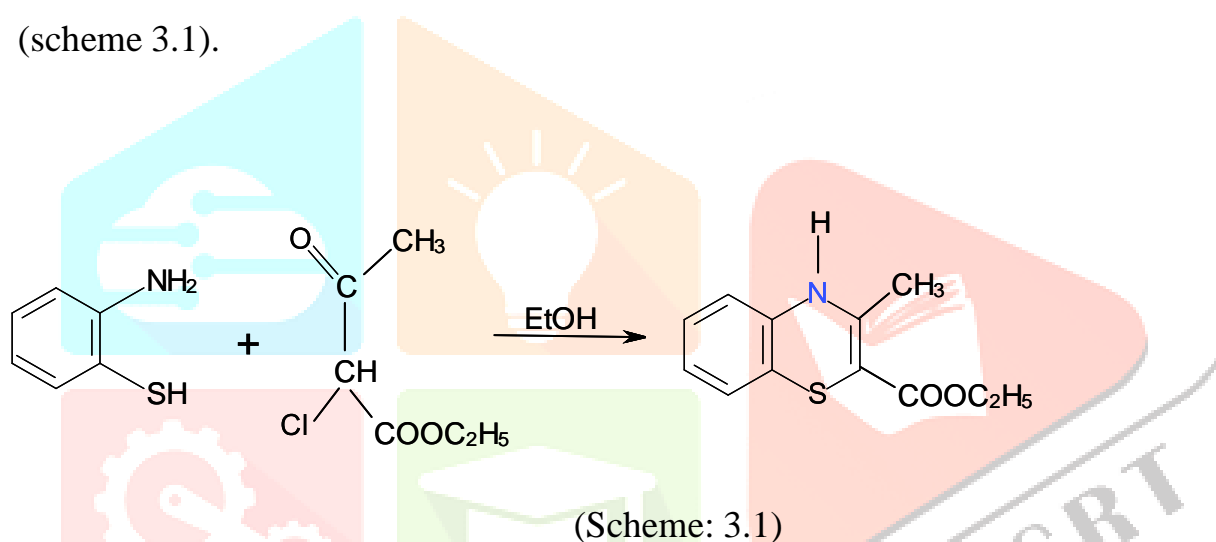
II

4H-1,4-Benzothiazine derivatives exhibit a wide range of pharmacological and biological activities including antifungal, immune-stimulating, anti-aldose-reductase, anti-rheumatic, anti-allergic, vasorelaxant, anti-arrhythmic, neuroprotective, cytotoxic, anti-parasitic, anti-bacterial, antiviral, antioxidant, anti-inflammatory, anti-hypertensive, anti-anginal drug, antidepressant, anti-tumor, anti-pyretic, diuretic and anti-tubercular activities etc<sup>1-11</sup>. These properties indicate that 1,4-benzothiazine is a template that may be potentially useful in medicinal chemistry and therapeutic applications<sup>12</sup>. 1,4-Benzothiazine derivatives also have

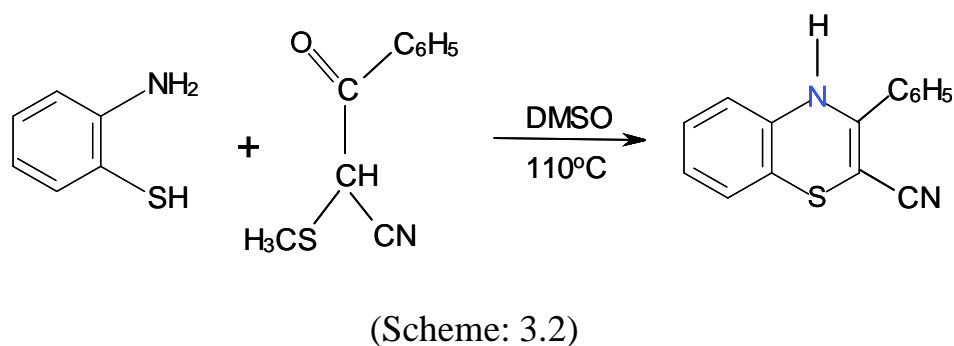
application in areas including dyestuff and photography. Their normal preparation route involves either lachrymatory halo organic substrates or toxic and expensive solvents<sup>13-20</sup>. In view of multifarious applications of these bioactive thiazine derivatives, our main aim is to develop environmentally benign and eco-friendly method for synthesis of 4H-1,4-benzothiazine derivatives<sup>21-28</sup>. Microwave assisted synthesis of 4H-1,4-benzothiazine has been reported by many workers<sup>29-33</sup>.

The literature methods for the synthesis of 4H-[1,4]-benzothiazines are reviewed below-

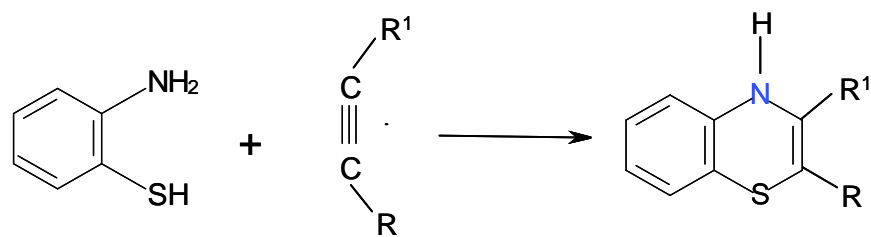
- (1). 4H-1,4-Benzothiazines have been prepared by the reaction of 2-aminobenzenethiol with ethyl 2-chloroacetoacetate in ethanol<sup>34-35</sup> (scheme 3.1).



2. The reaction of 2-aminobenzenethiol with  $\alpha$ -cyano- $\alpha'$ -thiomethylacetophenone in the presence of dimethylsulfoxide<sup>36</sup> at 110°C has yielded 2,3-disubstituted-4H-1,4-benzothiazine (scheme 3.2).

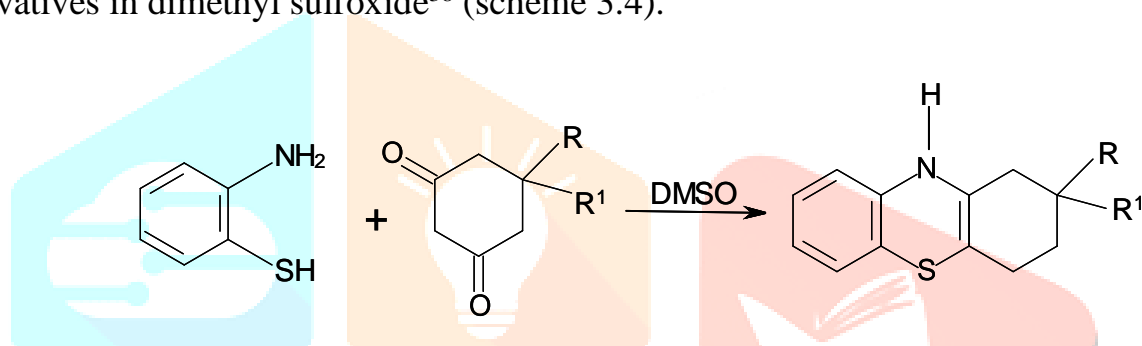


- (3). The Reaction of 2-aminobenzenethiol with acetylenic nitriles/esters<sup>37</sup> yield 4H-1,4-benzothiazines (scheme 3.3).



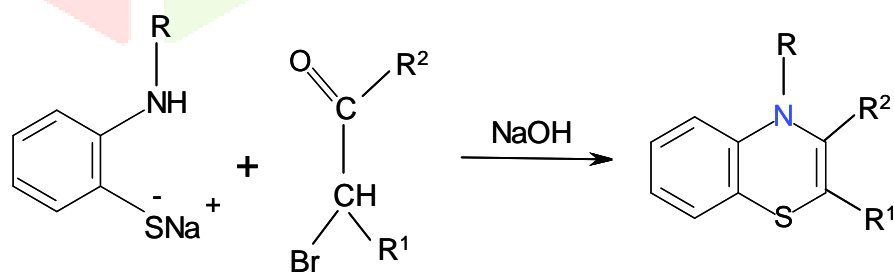
(Scheme: 3.3)

- (4). 4H-1,4-Benzothiazines have been prepared by the reaction of 2-aminobenzenethiols with cyclohexane-1,3-dione and its derivatives in dimethyl sulfoxide<sup>38</sup> (scheme 3.4).



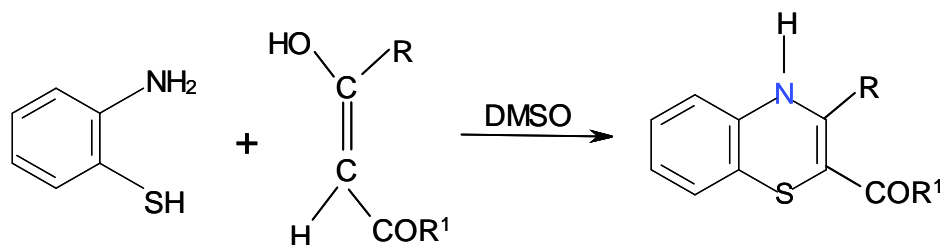
(Scheme: 3.4)

- (5). N-Substituted-1,4-benzothiazines<sup>39</sup> have been synthesized by the reaction of sodium salt of N-substituted-2-aminobenzenethiols with  $\beta$ -bromoketones (scheme 3.5).



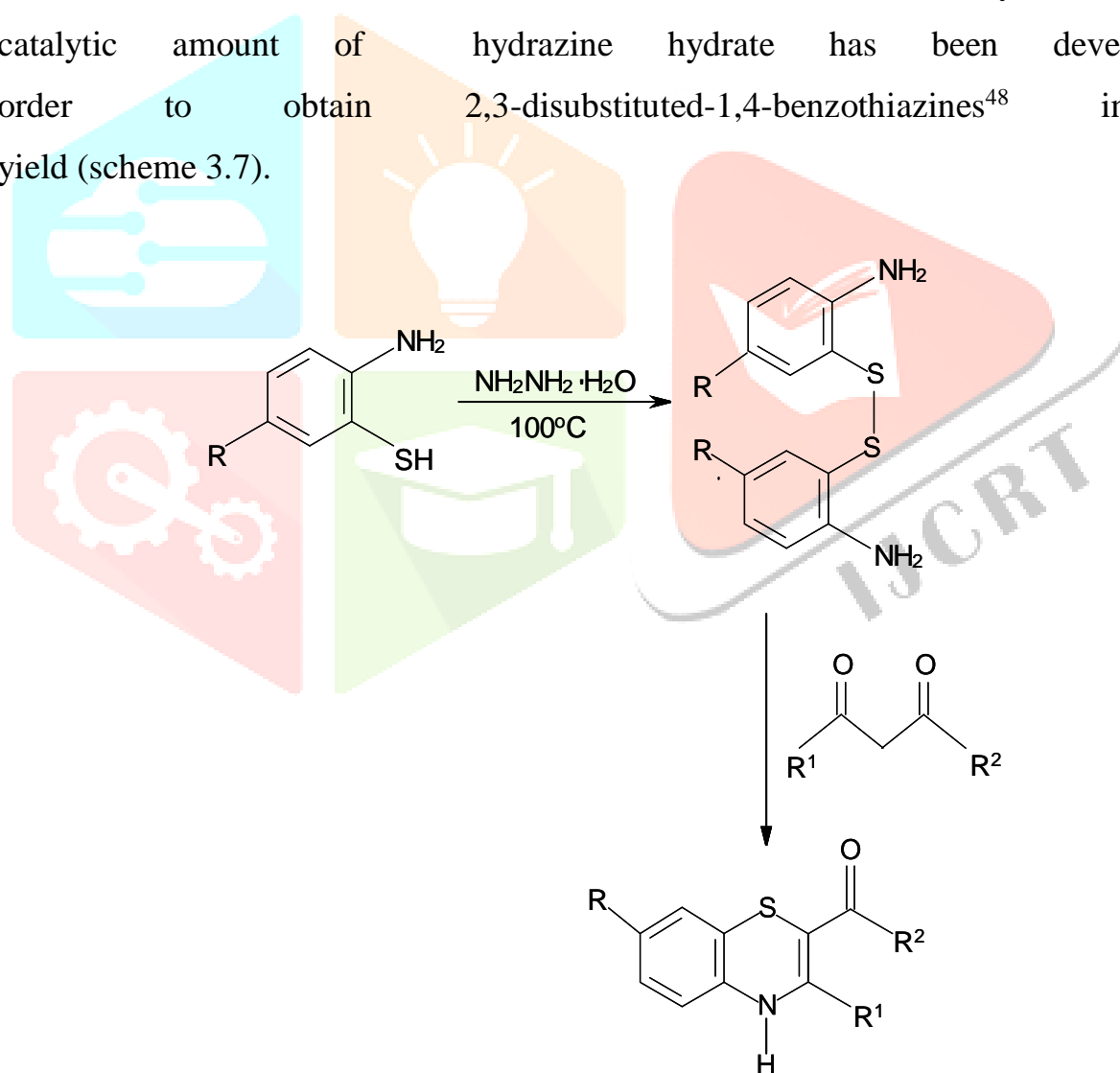
(Scheme: 3.5)

- (6). 4H-1,4-Benzothiazines<sup>40-47</sup> have been synthesized by the condensation of 2-aminobenzenethiol with  $\beta$ -ketoesters/ $\beta$ -diketones in DMSO (scheme 3.6).



(Scheme: 3.6)

(7). A rapid, solvent free synthetic strategy for the oxidative cyclocondensation of 2-aminobenzenethiol and 1,3-dicarbonyls using a catalytic amount of hydrazine hydrate has been developed in order to obtain 2,3-disubstituted-1,4-benzothiazines<sup>48</sup> in high yield (scheme 3.7).



(Scheme: 3.7)

Generally 1,4-benzothiazines were being synthesized by the reaction of 2-aminobenzenethiol with  $\alpha$ -haloketones/  $\alpha$ -haloesters but the lachrymatory nature of the latter was the main drawback of that method. Latterly slightly improved method is being used by which 1,4-benzo-thiazines are prepared by oxidative condensation of substituted 2-aminobenzenethiol with  $\beta$ -diketones/ $\beta$ -ketoesters in presence of DMSO. The latter is an aprotic dipolar solvent which acts as solvent and oxidant. It has several unfavourable properties and the product is difficult to separate out from it. Therefore, this method needs to be improved. Mechanism of the reaction of substituted 2-aminobenzenethiols with  $\beta$ -diketones/  $\beta$ -ketoesters reveals that the reaction proceeds in two steps. In the first step DMSO oxidizes 2-aminobenzenethiols<sup>49</sup> to the corresponding disulfides derivatives and the latter condense with  $\beta$ -diketones/  $\beta$ -ketoesters yielding 4H-1,4-benzothiazines in the second step. From the literature survey it was observed that 2-aminobenzenethiols can be oxidized easily by hydrogen peroxide<sup>50</sup>, DMSO-iodine<sup>51</sup>, thallium acetate<sup>52</sup>, sodium perborate<sup>53</sup>, mixture of NO<sub>2</sub> and NO<sub>3</sub><sup>54</sup> and even environmental oxygen on standing in presence of small amount of base<sup>55</sup>.

The literature survey<sup>56</sup> also reveals that benzenethiols are uncreative but in presence of catalytic amount of hydrazine hydrate and environmental oxygen at room temperature a quantitative amount of disulfide is obtained. In present investigation keeping this fact in mind a new method was developed in which the condensation of substituted 2-aminobenzenethiols was carried out with  $\beta$ -diketones/  $\beta$ -ketoesters in presence of catalytic amount of hydrazine hydrate in air. The reaction was accelerated by microwave irradiation under solvent free conditions in presence of an energy transfer agent DMF to get 4H-1,4-benzothiazine derivatives.

## EXPERIMENTAL

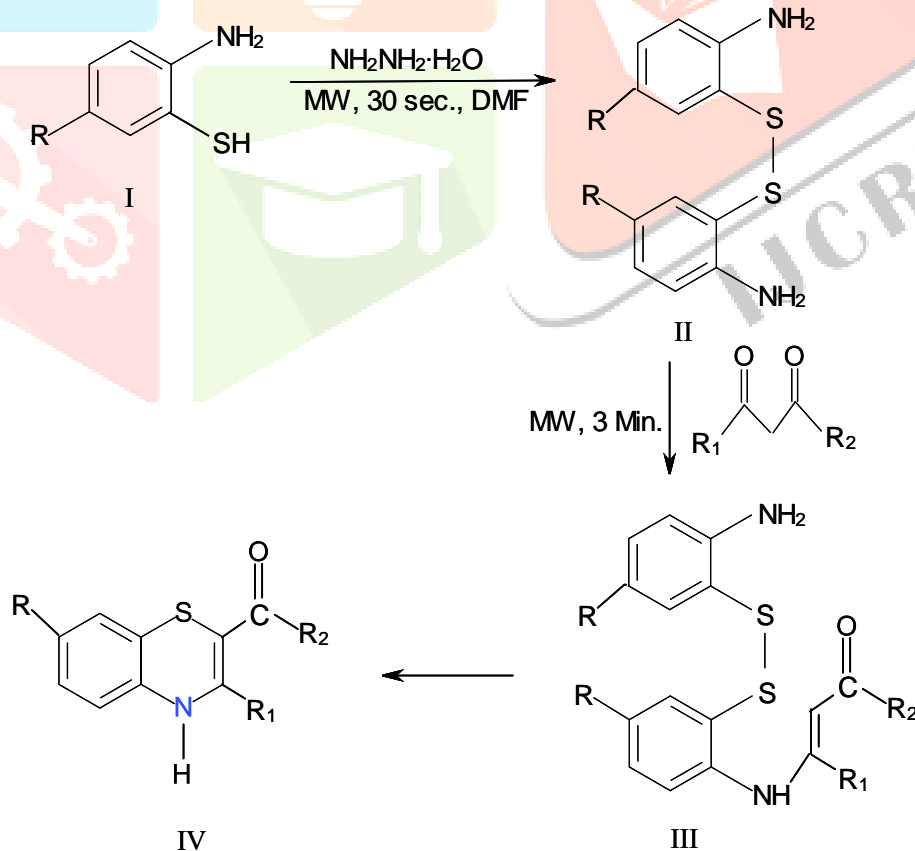
All the melting points are uncorrected. The purity of the compounds was checked on thin layer of silica gel in various non-aqueous solvent systems. Infrared spectra of all the synthesized compound have been scanned in KBr on Shimadzu FTIR Affinity-1 and their NMR spectra were scanned on Varian Gemini 400 spectrometer (300 MHz) using TMS as an internal standard. The mass spectra were recorded on Jeol SX 102 spectrometer at 70 eV. The reactions were carried in domestic microwave oven. All the analytical and physical data of the synthesized compounds are in good agreement with their literature<sup>57-58</sup> values.

## 1. Synthesis of substituted 2-aminobenzenethiols

Synthesis of substituted 2-aminobenzenethiols required for the preparation of 4H-1,4-benzothiazines has been given in part (A) of chapter-2.

## 2. Synthesis of substituted 4H-1,4-benzothiazines

A mixture of substituted 2-aminobenzenethiol (10 mmol), catalytic amount of hydrazine hydrate (1 mmol) and DMF (5 mmol) as an energy transfer medium was exposed to microwave irradiation for 30 sec. Now add  $\beta$ -diketone/ $\beta$ -ketoester (10 mmol) to the reaction mixture and again exposed to the microwave irradiation intermittently at 30 seconds for 3 min. After completion of reaction as monitored by TLC, the reaction mixture was cooled and transferred to crushed ice. The solid separated out was filtered, washed with 50% ethanol and crystallized from ethanol (Scheme 3.8).



(Scheme: 3.8)

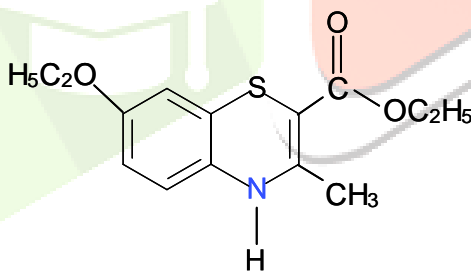
In present investigation following 4H-1,4-benzothiazines have been synthesized:

- (1). 7-Ethoxy-2-ethoxycarbonyl-3-methyl-4H-1,4-benzothiazine.
- (2). 2-Ethoxycarbonyl-7-methoxy-3-methyl-4H-1,4-benzothiazine.
- (3). 2-Benzoyl-7-methoxy-3-phenyl-4H-1,4-benzothiazine.
- (4). 2-Ethoxycarbonyl-3,7-dimethyl-4H-1,4-benzothiazine.
- (5). 2-Benzoyl-7-methyl-3-phenyl-4H-1,4-benzothiazine.
- (6). 7-Chloro-2-ethoxycarbonyl-3-methyl-4H-1,4-benzothiazine.
- (7). 2-Benzoyl-7-chloro-3-phenyl-4H-1,4-benzothiazine.
- (8). 2-Benzoyl-7-chloro-3-methyl-4H-1,4-benzothiazine.
- (9). 2-Benzoyl-3,7-dimethyl-4H-1,4-benzothiazine.

Physical and spectral data of the synthesized 4H-1,4-benzothiazines :

**(1). 7-Ethoxy-2-ethoxycarbonyl-3-methyl-4H-1,4-benzothiazine.**

Molecular Formula :  $C_{14}H_{17}O_3NS$



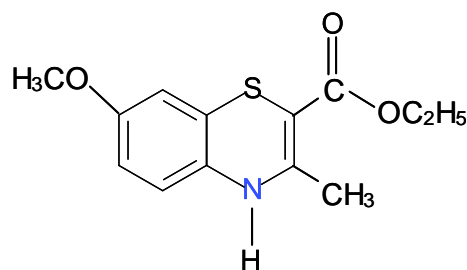
Yield:70%, M.P. 103<sup>o</sup>C

IR (KBr,  $\nu_{max}$ ,  $cm^{-1}$ ): 3410 (N-H), 1685 ( $>C=O$ ), 1460, 1350 (C-CH<sub>3</sub>), 1230, 1035 (C-O-C), 855, 835 (adj. 2H in ring), 3000 (C-H aliph.);

<sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 6.85-6.3 (3H, m, Ar.), 4.10 (2H, q, CH<sub>2</sub> at C-2), 1.20 (3H, t, CH<sub>3</sub> at C-2), 2.2 (3H, s, CH<sub>3</sub> at C-3), 3.95 (2H, q, CH<sub>2</sub> at C-7), 1.40 (3H, t, CH<sub>3</sub> at C-7), 8.75 (1H, s, N-H);

MS( m/z): 279 (M<sup>+</sup>), 278 (M<sup>+</sup>-H), 251 (M<sup>+</sup>-C<sub>2</sub>H<sub>4</sub>), 250 (M<sup>+</sup>-C<sub>2</sub>H<sub>5</sub>), 233 (M<sup>+</sup>-C<sub>2</sub>H<sub>5</sub>OH), 234 (M<sup>+</sup>-OC<sub>2</sub>H<sub>5</sub>), 222 (M<sup>+</sup>-COC<sub>2</sub>H<sub>5</sub>), 205 (M<sup>+</sup>-C<sub>2</sub>H<sub>5</sub>OH, CO).

Anal. Calculated (%) for C<sub>14</sub>H<sub>17</sub>O<sub>3</sub>NS: C, 60.21; H, 6.09; N, 5.01. Found (%): C, 60.11; H, 6.08; N, 5.02.

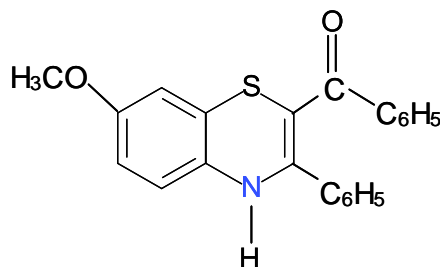
**(2). 2- Ethoxycarbonyl-7-methoxy-3- methyl-4H-1,4-benzothiazine.**Molecular Formula :  $C_{13}H_{15}O_3NS$ Yield:65%, M.P. 119<sup>0</sup>C

IR (KBr,  $\nu_{max}$ ,  $cm^{-1}$ ): 3340 (N-H), 1685 ( $>C=O$ ), 1465, 1340 (C-CH<sub>3</sub>), 1245, 1035 (C-O-C), 850, 820 (adj. 2H in ring);

<sup>1</sup>H NMR (CDCl<sub>3</sub>) $\delta$ : 6.8-6.4 (3H, m, Ar.), 3.95 (2H, q, CH<sub>2</sub> at C-2), 2.25 (3H, s, CH<sub>3</sub> at C-3), 1.25 (3H, t, CH<sub>3</sub> at C-2), 4.4 (3H, s, O-CH<sub>3</sub>), 8.8 (1H, s, N-H);

MS( m/z): 265 (M<sup>+</sup>), 264 (M<sup>+</sup>-H), 235 (M<sup>+</sup>-CH<sub>2</sub>O), 206 (M<sup>+</sup>-CH<sub>2</sub>O, C<sub>2</sub>H<sub>5</sub>), 178 (M<sup>+</sup>-CH<sub>2</sub>O, COC<sub>2</sub>H<sub>5</sub>), 250 (M<sup>+</sup>-CH<sub>3</sub>), 222 (M<sup>+</sup>-CH<sub>3</sub>, CO), 193 (M<sup>+</sup>-CH<sub>3</sub>, CO, C<sub>2</sub>H<sub>5</sub>), 165 (M<sup>+</sup>-CH<sub>3</sub>, CO, COC<sub>2</sub>H<sub>5</sub>).

Anal. Calculated (%) for :  $C_{13}H_{15}O_3NS$ : C, 58.86; H, 5.66; N, 5.28. Found (%): C, 58.84; H, 5.67; N, 5.30.

**(3). 2-Benzoyl-7-methoxy-3-phenyl-4H-1,4-benzothiazine.**Molecular Formula :  $C_{22}H_{17}O_2NS$ Yield:82%, M.P. 172<sup>0</sup>C

IR (KBr,  $\nu_{max}$ ,  $cm^{-1}$ ): 3400 (N-H), 1665 ( $>C=O$ ), 1230, 1050 (C-O-C), 855, 820 (adj. 2H in ring), 2920 (C-H, aliph.);

<sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 7.8-6.95 (13H, m, Ar.), 4.5 (3H, s, OCH<sub>3</sub>), 8.7 (1H, s, N-H);

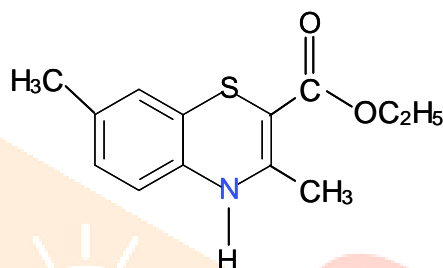


MS( m/z): 359 (M<sup>+</sup>), 358 (M<sup>+</sup>-H), 254 (M<sup>+</sup>-COC<sub>6</sub>H<sub>5</sub>), 282 (M<sup>+</sup>-C<sub>6</sub>H<sub>5</sub>), 329 (M<sup>+</sup>-CH<sub>2</sub>O), 344 (M<sup>+</sup>-CH<sub>3</sub>), 316 (M<sup>+</sup>-CH<sub>3</sub>, CO), 252 (M<sup>+</sup>-CH<sub>2</sub>O, C<sub>6</sub>H<sub>5</sub>), 224 (M<sup>+</sup>-CH<sub>2</sub>O, COC<sub>6</sub>H<sub>5</sub>).

Anal. Calculated (%) for C<sub>22</sub>H<sub>17</sub>O<sub>2</sub>NS: C, 70.19; H, 4.73; N, 3.90. Found (%): C, 70.20; H, 4.69; N, 3.88.

#### (4). 2-Ethoxycarbonyl-3,7-dimethyl-4H-1,4-benzothiazine

Molecular Formula : C<sub>13</sub>H<sub>15</sub>O<sub>2</sub>NS



Yield:75%, M.P. 178<sup>0</sup>C

IR (KBr,  $\nu_{\max}$ , cm<sup>-1</sup>): 3460 (N-H), 1680 (>C=O), 1465, 1345 (C-CH<sub>3</sub>), 1230, 1035 (C-O-C), 855, 825 (adj. 2H in ring), 2980 (C-H aliph.);

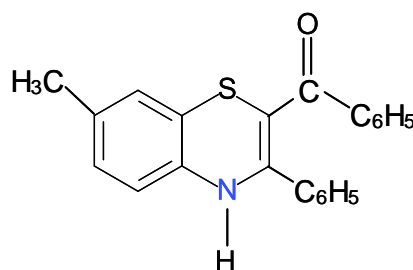
<sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 6.7-6.4 (3H, m, Ar.), 4.15 (2H, q, CH<sub>2</sub> at C-2), 2.25 (3H, s, CH<sub>3</sub> at C-3), 1.95 (3H, s, CH<sub>3</sub> at C-7), 1.25 (3H, t, CH<sub>3</sub> at C-2), 8.8 (1H, s, N-H);

MS( m/z): 249 (M<sup>+</sup>), 248 (M<sup>+</sup>-H), 220 (M<sup>+</sup>-C<sub>2</sub>H<sub>5</sub>), 204 (M<sup>+</sup>-OC<sub>2</sub>H<sub>5</sub>), 192 (M<sup>+</sup>-COC<sub>2</sub>H<sub>5</sub>), 221 (M<sup>+</sup>-C<sub>2</sub>H<sub>4</sub>), 203 (M<sup>+</sup>-C<sub>2</sub>H<sub>5</sub>OH), 175 (M<sup>+</sup>-C<sub>2</sub>H<sub>5</sub>OH, CO).

Anal. Calculated (%) for C<sub>13</sub>H<sub>15</sub>O<sub>2</sub>NS: C, 62.65; H, 6.02; N, 5.62. Found (%): C, 62.63; H, 6.63; N, 5.60.

#### (5). 2- Benzoyl-7-methyl-3-phenyl-4H-1,4-benzothiazine.

Molecular Formula : C<sub>22</sub>H<sub>17</sub>ONS



Yield:80%, M.P. 194<sup>0</sup>C

IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3345 (N-H), 1695 (>C=O), 1470, 1330 (C-CH<sub>3</sub>), 865, 820 (adj. 2H in ring), 3055 (C-H, Ar);

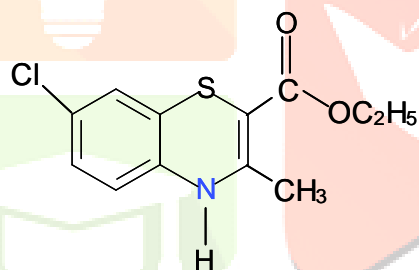
<sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 7.3-7.0 (13H, m, Ar.), 2.35 (3H, s, CH<sub>3</sub> at C-7), 8.8 (1H, s, NH);

MS( m/z): 343 (M<sup>+</sup>), 342 (M<sup>+</sup>-H), 238 (M<sup>+</sup>-COC<sub>6</sub>H<sub>5</sub>), 266 (M<sup>+</sup>-C<sub>6</sub>H<sub>5</sub>), 161 (M<sup>+</sup>-COC<sub>6</sub>H<sub>5</sub>, C<sub>6</sub>H<sub>5</sub>).

Anal. Calculated (%) for C<sub>22</sub>H<sub>17</sub>ONS: C, 73.46; H, 4.95; N, 4.08. Found (%): C, 73.75; H, 4.90; N, 4.06.

#### (6). 7-Chloro-2-ethoxycarbonyl-3-methyl-4H-1,4-benzothiazine.

Molecular Formula : C<sub>12</sub>H<sub>12</sub>O<sub>2</sub>NSCl



Yield:75%, M.P. 181<sup>0</sup>C

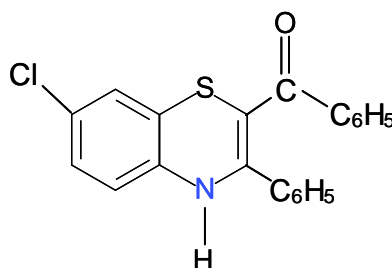
IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3380 (N-H), 1690 (>C=O), 1465, 1360 (C-CH<sub>3</sub>), 735 (C-Cl), 1240, 1040 (C-O-C), 860, 825 (adj. 2H in ring), 2985 (C- Haliph.);

<sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 6.85-6.4 (3H, m, Ar.), 4.05 (2H, q, CH<sub>2</sub> at C-2),

2.25 (3H, s, CH<sub>3</sub> at C-3), 1.25 (3H, t, CH<sub>3</sub> at C-2), 8.7 (1H, s, N-H);

MS( m/z): 269 (M<sup>+</sup>), 268 (M<sup>+</sup>-H), 241 (M<sup>+</sup>-C<sub>2</sub>H<sub>4</sub>), 224 (M<sup>+</sup>-C<sub>2</sub>H<sub>4</sub>, OH) or (M<sup>+</sup>-OC<sub>2</sub>H<sub>5</sub>), 196 (M<sup>+</sup>-COOC<sub>2</sub>H<sub>5</sub>), 240 (M<sup>+</sup>-C<sub>2</sub>H<sub>5</sub>), 223 (M<sup>+</sup>-C<sub>2</sub>H<sub>5</sub>OH), 212 (M<sup>+</sup>-C<sub>2</sub>H<sub>5</sub>, CO).

Anal. Calculated (%) for C<sub>12</sub>H<sub>12</sub>O<sub>2</sub>NSCl: C, 53.43; H, 4.45; N, 5.19. Found (%): C, 53.39; H, 4.42; N, 5.20.

**(7). 2-Benzoyl-7-chloro-3-phenyl-4H-1,4-benzothiazine.**Molecular Formula :  $C_{21}H_{14}ONSCl$ 

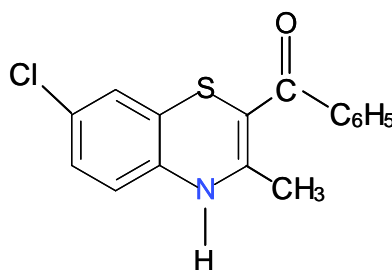
Yield:85%, M.P. 87°C

IR (KBr,  $\nu_{max}$ ,  $cm^{-1}$ ): 3360 (N-H), 1690 ( $>C=O$ ), 740 (C-Cl), 850, 820 (adj. 2H in ring), 3060 (C-H, Ar);

$^1H$  NMR ( $CDCl_3$ )  $\delta$ : 7.5-6.85 (13H, m, Ar), 8.6 (H, s, N-H);

MS( m/z):363 ( $M^+$ ), 362 ( $M^+-H$ ), 258 ( $M^+-COC_6H_5$ ), 286 ( $M^+-C_6H_5$ ), 77 ( $M^+-C_6H_5$ ), 181 ( $M^+-COC_6H_5$ ,  $C_6H_5$ ), 146 ( $M^+-COC_6H_5$ ,  $C_6H_5$ , Cl).

Anal. Calculated (%) for  $C_{21}H_{14}ONSCl$ : C, 69.32; H, 3.85; N, 3.85. Found (%): C, 69.30; H, 3.90; N, 3.90.

**(8). 2-Benzoyl-7-chloro-3-methyl-4H-1,4-benzothiazine.**Molecular Formula :  $C_{16}H_{12}ONSCl$ 

Yield:85%, M.P. 245°C

IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3365 (N-H), 1675 ( $>\text{C}=\text{O}$ ), 1460, 1340 (C-CH<sub>3</sub>), 725 (C-Cl), 850, 830 (adj. 2H in ring), 3020 (C-H, Ar);

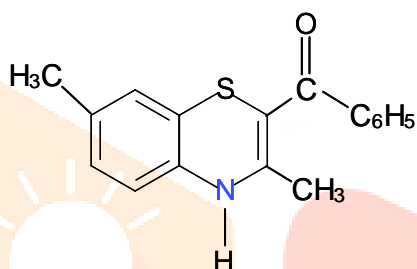
<sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 7.6-7.0 (8H, m, Ar.), 2.25 (3H, s, CH<sub>3</sub> at C-3), 8.7 (1H, s, NH);

MS( m/z): 301(M<sup>+</sup>), 300 (M<sup>+</sup>-H), 196 (M<sup>+</sup>-COC<sub>6</sub>H<sub>5</sub>), 224 (M<sup>+</sup>- C<sub>6</sub>H<sub>5</sub>), 161 (M<sup>+</sup>-COC<sub>6</sub>H<sub>5</sub>, Cl).

Anal. Calculated (%) for: C<sub>16</sub>H<sub>12</sub>ONSCl: C, 59.70; H, 4.97; N, 4.64. Found (%): C, 59.68; H, 4.89; N, 4.60.

### (9). 2-Benzoyl-3,7-dimethyl-4H-1,4-benzothiazine.

Molecular Formula : C<sub>17</sub>H<sub>15</sub>ONS



Yield:90%, M.P. 207<sup>o</sup>C

IR (KBr  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3380 (N-H), 1680 ( $>\text{C}=\text{O}$ ), 1460, 1340 (C-CH<sub>3</sub>), 860, 825 (adj. 2H in ring), 2930 (C-H, aliph.), 3030 (C-H, Ar.);

<sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 7.4-6.6 (8H, m, Ar.), 2.15 (3H, s, CH<sub>3</sub> at C-3), 1.95 (3H, s, CH<sub>3</sub> at C-7), 8.8 (1H, s, NH);

MS( m/z): 281 (M<sup>+</sup>), 280 (M<sup>+</sup>-H), 204 (M<sup>+</sup>-C<sub>6</sub>H<sub>5</sub>), 176 (M<sup>+</sup>-COC<sub>6</sub>H<sub>5</sub>), 131 (M<sup>+</sup>-COC<sub>6</sub>H<sub>5</sub>, HCS), 144 (M<sup>+</sup>-COC<sub>6</sub>H<sub>5</sub>, S).

Anal. Calculated (%) for C<sub>17</sub>H<sub>15</sub>ONS: C, 72.59; H, 5.33; N, 4.98. Found (%): C, 72.60; H, 5.35; N, 4.95.

### Spectral analysis

The infrared spectra of all the synthesized 4H-1,4-benzothiazines invariably showed a N-H stretching absorption peak in the region of 3410-3340  $\text{cm}^{-1}$  and for C=O stretching absorption peak in the region of 1695-1665  $\text{cm}^{-1}$ . The weak absorption bands in the region 1470-1330  $\text{cm}^{-1}$  are attributed to C-CH<sub>3</sub> bending vibrations. In compound 1,2,4 and 6 bands appearing in the region 1240-1225  $\text{cm}^{-1}$  and 1030-1040  $\text{cm}^{-1}$  are attributed to C-O-C asymmetric and symmetric

vibrations respectively. In compound 6,7 and 8 a band in the region  $725-740\text{ cm}^{-1}$  is assigned to C-Cl stretching vibrations.

In NMR spectra a broad singlet peak in the region of  $8.70-8.80\ \delta$  is observed in all the synthesized compounds for N-H proton and multiplets in the region of  $6.4-7.6\ \delta$  are due to aromatic ring protons. A singlet peak at about  $4.4\ \delta$  is observed in methoxy derivatives due to  $\text{OCH}_3$  group. Peaks for  $\text{CH}_3$  and  $\text{C}_2\text{H}_5$  groups are also observed in expected region and multiplicity.

In mass spectra all 1,4-benzothiazines having benzoyl group showed peak at  $m/z = M^+ - 105$  (with high intensity) and  $105$  ( $\text{C}_6\text{H}_5\text{CO}^+$ , base peak) by the loss of benzoyl group. The 2-ethoxycarbonyl derivatives gave peaks at  $m/z = M^+ - \text{C}_2\text{H}_4$ ,  $M^+ - \text{C}_2\text{H}_5$ ,  $M^+ - \text{COC}_2\text{H}_5$  and  $M^+ - \text{OC}_2\text{H}_5$ .

## REFERENCES

1. A. K. Pareek, P. E. Joseph, D. S. Seth, Orient J.Chem., **26(3)** 1147-1150 (2010).
2. B. R. Chaudhari, D. B. Shinde, M. S. Shingare, Indian Journal of Heterocyclic Chem., **04**, 187-190 (1995).
3. B. R. Chaudhari, D. B. Shinde, M. S. Shingare, Polish J. Chem., **70**, 1250-1256 (1996).
4. C. Studenik, R. Lemmens-Gruber, P. Heistraacher, Pharmazie, Chem. Abstr., **131**, 195 (1999).
5. H. Li, G. Dryhurst, J. Neurochem., **69(4)**, (1997).
6. B. Koidl, N. Miyawaki, H. A. Tritthart, Eur. J. Pharmacol., **322**, 2-3, (1997).
7. D. A. Oren, A. Zhang, H. Nesvadha, B. Rosenwirth, E. Arnold, J. Mol. Biol., **259(1)**, (1996).
8. S. K. Kwon, M. S. Park, Arzneimittelforschung., **46(10)**, (1996).

9. B. R. Chaudhari, D. B. Shinde, M. S. Shingare, Indian J. Heterocycl. Chem., **4(3)**, 87-90 (1995).
10. N. Kulkarni, E. Zang, G. Kelloff, B. S. Reddy, Carcinogenesis, **13(6)**, 995-1000 (1992).
11. D. Rai, V. Gupta, R. R. Gupta, Hererocycl. Commun., **2**, 273 (1996).
12. R. Fringuelli, L. Milanese, F. Schiaffella, Rev. Med. Chem.,**5**, 1061(2005).
13. J. Krapcho, C. F. Turk, J. Med. Chem.,**16**, 776 (1973).
14. J. Krapcho, Ger. Offen.,**2**, 152-282, Chem., Abstr., **77**, 34541 (1972).
15. R. R. Gupta, R. Kumar, R. K. Gautam, J. Fluor. Chem., **28(4)**, 381 (1985).
16. J. G. Lombardino, U.S. Pat., 3,954,786 (1976), Chem. Abstr., **85**, 46723 (1976).
17. A. Mackie, G. M. Stewart, A. A. Cutler, A. L. Mishra, Brit. J. Pharmacol. Chemother., **10**, 7 (1955).
18. O. Aki, Y. Nakagawa, Jap. Kokai, **7**, 332,976 (1973), Chem. Abste., **79**, 18735 (1973).
19. J. Krapcho, U. S. Pat., **3**, 089, 872 (1963) , Chem. Abstr., **61**, 9507 (1964).
20. R. N. Prasad, J. Med. Chem., **12(1)**, 290 (1969).
21. H. Y. Kogyo, Jap. Pat., **59**,187,170 (1984). Chem.Abstr.,**102**, 45965 (1985).
22. M. Muehlstaedt, R. Widera, H. Meinhold, K. Hollmann, Ger. (East) Pat., **214**, 128 (1984). Chem. Abstr., **102** 203979 (1985).

23. C. F. Turk, P. Eligiand, J. Krapcho, J. Heterocycl. Chem., **14**, 1135 (1977).
24. R. J. Charvat, U. S. Pat., 4,223, 136 (1976). Chem. Abstr., **94**, 103398 (1981).
25. S. Umio, H. Noguchi, Jap. Pat., **6**, 927, 588 (1969). Chem. Abstr., **72**, 66965 (1970).
26. J. Lwao, I. Iso, M. Oya, Eup. Pat., **166**, 386 (1984). Chem. Abstr., **102**, 24637 (1985).
27. D. R. Shridhar, M. Jogibhukta, K. S. Rao, V. S. H. Krishnan, A. N. Singh, K. Rastogi, M. L. Jian, Ind. IN 158,841 (1987). Chem. Abstr., **107**, 154344 (1987).
28. C. Sastry, V. Reddy, B. Ram, M. Jogibhukta, V. S. H. Krishnan, A. N. Singh, J. G. Kedy, S. C. Chaturvedi, S. P. Rao, D. R. Shridhar, Ind. J. Chem., **28B(1)**, 52 (1989)
29. A. Loupy (Ed.), Microwaves in Organic Synthesis, Wiley-VCH Verlag, Weinheim (2002).
30. B. L. Hayes, in Microwave Synthesis CEM Publishing : Matthews, USA (2002).
31. P. Lidstrom, J. Tierney, B. Wathey, J. Westman, Tetrahedron, 9225 (2001).
32. K. Mogilaiah , N. V. Reddy, Synth. Commun., **33**, 1067 (2003).
33. S. Paul, R. Gupta, A. Loupy, B. Rani, A. Dandia, Synthetic Commun., **31(5)**, 711-717 (2001).
34. F. Duro, P. Condarilli, G. Ronsisvalle, Ann. Chem., **63**, 45 (1973).
35. Y. Maki, M. Suzuki, T. Yamada, Chem. Pharm., **63**, 45 (1973). Chem. Abstr., **80**, 95856 (1974).

36. R. R. Gupta, R. K. Gautam, R. Kumar, *Heterocycles*, **22(5)**, 1143 (1984).
37. G. Liso, G. Trapani, V. Berardi, A. Latrofa, P. Marchini, *J. Heterocycl. Chem.*, **17(4)**, 793 (1980).  
*Chem. Abstr.*, **94**, 30681 (1981).
38. R. R. Gupta, G. S. Kalwania, R. Kumar, *Bull. Chem. Soc. Jap.*,  
**57(8)**, 4810 (1984).
39. R. R. Gupta, A. Thomas, R. K. Gupta, V. Gupta, *J. Fluor. Chem.*, **44**, 1 (1989).
40. R. Rajagopal, S. I. Bhatia, S. Seshadri, *Ind. J. Chem.*, **30(7)**, 655  
(1991).
41. N. Gautam, D. C. Gautam, R. R. Gupta, *Heterocycl. Commun.*, **3**, 401 (1997).
42. V. Gupta, R. R. Gupta, *J. Prakt. Chem.*, **333(1)**, 153 (1991).
43. D. Armenise, T. Trapani, V. Arrivo, F. Morlacchi, *J. Heterocycl. Chem.*, **27**, 1521 (1990).
44. M. Kumar, N. Sharma, R. Gupta, R. R. Gupta, *Heterocycl. Commun.*, **4**, 187 (1992).
45. D. D. Bhatnagar, K. K. Gupta, V. Gupta, R. R. Gupta, *Pharmazie*, **43(12H)**, 863 (1988).
46. V. Carelli, F. M. Moracci, M. Cardellini, F. Liveratore, M. G.  
Lucarelli, P. Machini, G. Liso, A. Reho, *Int. J. Sulph. Chem.*, **8**,  
267 (1973).
47. D. D. Bhatnagar, K. K. Gupta, V. Gupta, R. R. Gupta, *Curr. Sci.*, **58**, 1091 (1989).
48. G. Trapani, A. Latrofa, A. Reho, M. Franco, G. Liso, *J. Heterocycl. Chem.*, **29**, 1155 (1992).
49. S. Miyano, N. Abe, K. Sumoto, *J. Chem. Soc. Chem. Commun.*, 760 (1975).
50. B. J. Evans, J. T. Doi, W. K. Musker, *J. Org. Chem.*, **55**, 2337  
(1990).
51. W. E. Fristad, J. R. Peterson, *Synth. Commun.*, **15**, 1 (1985).



52. S. Uemura, S. Tanaka, M. Okana, Bull. Chem. Soc. (Japan), **50**, 220 (1977).
53. A. McKillop, D. Koyuncu, Tetrahedron Lett., **31**, 5007 (1990).
54. W. A. Pryor, D. F. Church, C. K. Govindan, G. Crank, J. Org. Chem., **47**, 156 (1982).
55. T. J. Wallace, A. Schriesheim, W. Bartok, J. Org. Chem., **28**, 1311 (1963).
56. S. Rajaram, G. S. Reddy, D. S. Iyengar, Ind. J. Chem., **38B**, 639 (1999).
57. R. R. Gupta, G. S. Kalwania, R. Kumar, Bull. Chem. Soc. (Japan), **57**, 2343 (1984).
58. R. R. Gupta, K. G. Ojha, G. S. Kalwania, M. Kumar, Heterocycles, **14**, 1145 (1980).

