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STEREOSELECTIVE SYNTHESIS OF 2-ALKYLIDENE-3,4-DIHYDRO-3-OXO-2H-1,4-BENZOTHIAZINES

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Abstract—Metallation of 4-methyl-3,4-dihydro-3-oxo-2H-1,4-benzothiazine with LDA and subsequent reaction with aldehydes leads to diastereomeric aldols **4** and **5**. Acetylation followed by acetic acid elimination of the aldols provides a stereoselective and high yield route to 2-alkylidene-3,4-dihydro-3-oxo-2H-1,4-benzothiazines.

Synthesis of various 2 - alkylidene - 3,4 - dihydro - 3 - oxo - 2H - 1,4 - benzothiazines[1] of interest in the pharmaceuticals area due to their activity as anti-inflammatory agents, has been described but only Worley[3] has examined the stereochemistry in this system. Moreover, the stereochemistry of the condensation reaction between the precursor 3,4 - dihydro - 3 - oxo - 2H - 1,4 - benzothiazine and carbonyl compounds has not been investigated at all.

We wish to report on the aldol-type condensation of metallated 4 - methyl - 3,4 - dihydro - 3 - oxo - 2H - 1,4 - benzothiazine **2** and on the utility of the corresponding aldols in a new and stereoselective route to alkylidene benzothiazinones.

The present paper was based on the concept that 2-substituted benzothiazinones **3** might be available directly from **1** through metallated derivative **2**. Subsequent reactions of **2** with electrophilic reagents could then lead to the introduction of 2-substituents without requiring costruction of the benzothiazinone ring from acyclic precursors each time a different substituent was desired.

As far as we know, there are no previous reports on the generation of metallated intermediate **2** and its application in synthesis.

RESULTS AND DISCUSSION

Metallation of 4-methyl-3,4-dihydro-3-oxo-2H-1,4-benzothiazine **1**.

Treatment of 1 equiv of **1** with 1.1 equiv of lithium diisopropylamide (LDA) in THF-hexane at −78° leads to stable organolithium **2**, as proved by trapping it either with deuterium oxide or methyl iodide to give **3a** and **3b** respectively.[4]

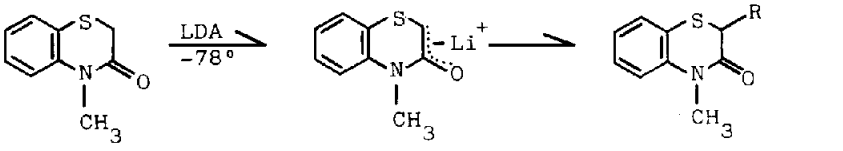
Reactions of **2** *with aldehydes.*

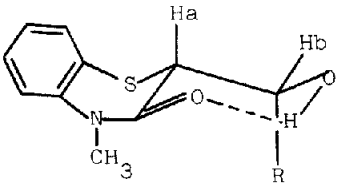
Aldol condensation reaction of **2** (1 equiv) in THF at −78° resulted in the ready formation of a mixture of the diastereomeric aldols **4** and **5**, which where separated by chromatography and characterized by elemental analysis and IR and NMR spectroscopy (see Table 1).

Aldols **4** and **5** were assigned the threo and erythro configuration respectively on the basis of the ^{1}H NMR coupling constants between Ha and Hb protons of the preferred chair-like conformations in which an intramolecular hydrogen bridge sets up between C=O and OH groups.

Aldol condensation of **2** with bulky aliphatic aldehydes proceeded with high stereoselectivity and the erythro product (higher J_{Ha-Hb}) was favored in each case. In order to check whether the aldol product ratios we observed are kinetic or thermodynamic in nature, we examined the equilibration of some erythro/threo pairs. The erythro aldolate **7a**, generated either by adding the erythro-aldol **5b** to LDA or to **2** at −78°, was allowed to stand at this temperature for 30 min and for much longer time at room temperature, whereupon a very slow equilibration to the threo-counterpart **8a** occurred.

In the same conditions the threo lithium aldolate **8b** equilibrated to its erythro isomer **7b** but still very slowly, notwithstanding the fact that the erythro-aldolate is expected to be considerably more stable (as suggested by Dreiding models). These results seem to indicate that the aldol condensation reaction of **2** with aldehydes is under kinetic rather than thermodynamic control and the erythro stereoselectivity observed with branched aliphatic aldehydes can be explained in terms of a six-centre chair-like transition state. The transition state B that leads to the threo aldol is energetically less stable than A,





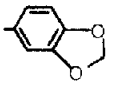
threo

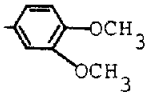
4a : R = CH_3

4b : R = Ph

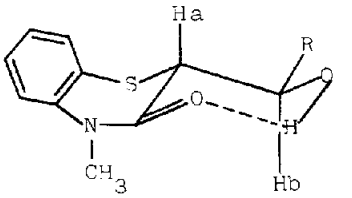
4c : R = p-ClPh

4d : R = $CH(C_2H_5)_2$

4e : R = 

4g : R = 

4h : R = CH_2Ph



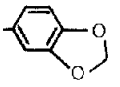
erythro

5a : R = CH_3

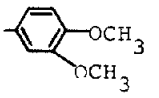
5b : R = Ph

5c : R = p-ClPh

5d : R = $CH(C_2H_5)_2$

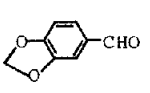
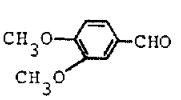
5e : R = 

5f : R = $CH(CH_3)_2$

5g : R = 

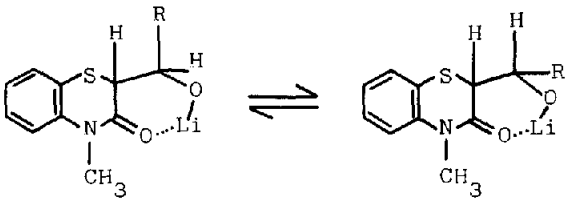
5h : R = CH_2Ph

Table 1. Aldols 4 and 5 from the reaction between 2 and aldehydes at −78°C in THF

Substrate	Aldehyde	Reaction time	Aldols: Overall yield %	Aldols: Relative percentages[a] %	
2	CH_3CHO	30 min	78	4a(52)	5a(48)
"	PhCHO	30 min	82	4b(50)	5b(50)
"	p-Cl-PhCHO	30 min	86	4c(48)	5c(52)
"	$(C_2H_5)_2CHCHO$	30 min	77	4d(17)	5d(83)
"		30 min	91	4e(50)	5e(50)
"	$(CH_3)_2CHCHO$	20 min	69		5f(100)
"		30 min	86	4g[b](50)	5g[b](50)
"	$PhCH_2CHO$	30 min	86	4h(47)	5h(53)

[a] Percentages determined from isolated and purified aldols.

[b] Aldols were not isolated and relative percentages measured by ^{1}HNMR of the reaction mixture.



7a : R = Ph 8a : R = Ph

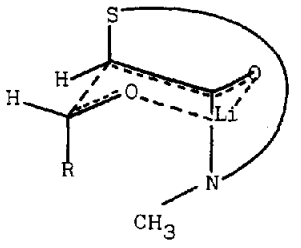
7b : R = $CH(C_2H_5)_2$ 8b : R = $CH(C_2H_5)_2$

in which the more bulky –R and –S– groups are far away.

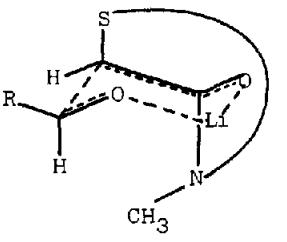
On the other hand, it is interesting to note that the erythro adduct is favored while benzothiazine enolate **2** is fixed in the E-geometry. Indeed, it is well known that under kinetic control Z-enolates generally favor erythro adducts and E-enolates the threo-isomers.[5]

The reaction of metallated intermediate **2** with ketones has not been thoroughly investigated, but we have found that **2** reacts readily with acetone giving the related aldol **3c**, even though the conversion was not complete, possibly due to the competing enolization of the acetone by the anion **2**. No reaction was observed with acetophenone and benzophenone.

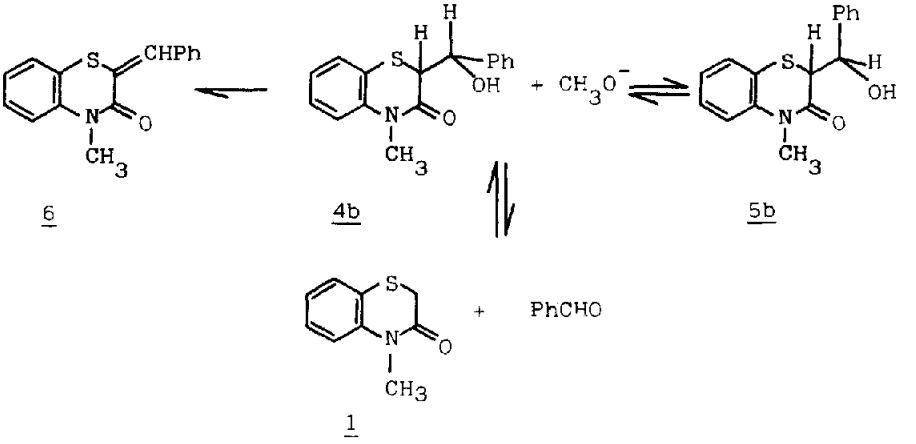
All attempts to dehydrate aldols **4** and **5** directly to the corresponding 2-alkylidene benzothiazinones were unsuccessful because of the competitive reactions of equilibration of the diastereomeric aldols and retro-aldol condensation. Indeed, reactions of **4b** (or **5b**) with bases such as CH_3O^- in CH_3OH, CH_3O^- in DMF or with diluted HCl or H_2SO_4 at room temperature gave a mixture of the diastereomeric aldols **4b** and **5b**, benzothiazinone, and only traces of desired alkylidene **6**. In order to circumvent this inconvenient aldols **4** and **5** were converted into the acetyl derivatives **9** and **10** respectively by means of acetic acid anhydride in pyridine; subsequent acetic acid elimination promoted by sodium methoxide in dimethylformamide (DMF) at room temperature afforded the expected alkylidenes cleanly and in high yield (see Table 3). The reaction turned out to be very highly stereoselective, the alkylidenes **11** of Z-configuration being in all cases by far the main product of the reaction, whatever the starting acetylated aldol (threo or erythro).[6] TLC and ^1H NMR revealed the presence of only traces of the E-isomers **12**. Since only Z-isomers generally form, more advantageously alk-



A



B



6 4b 5b 1

ylidenes were alternatively obtained directly from enolate **2** and the appropriate aldehyde without isolating any of abovementioned intermediates (aldols and their acetyl derivatives; Method B, see Experimental).

Acetic acid elimination from **9b** with methanolic sodium methoxide gave the corresponding alkylidene together with aldols **4b** and **5b** and benzothiazinone **1** arising from the competive transesterification of **9b**, subsequent isomerization of the aldols (**4b**→**5b**) and retro-aldol condensation.

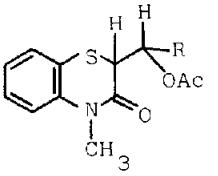
The alkylidenes were assigned the configuration on the basis of the chemical shift of the vinyl proton. The experimentally observed values matched quite well those calculated by application of the substituent shielding constants for vinyl proton absorption to compound **13**.[3,7]

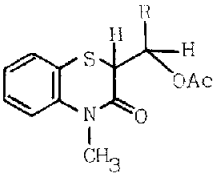
The mechanism of the elimination reaction to the alkylidenes is not clear. E_2 and/or E_1cB mechanisms[8] might be here operating. Indeed, a E_2 mechanism might account for the observed Z-stereoselectivity if one assumes that both the isomers form upon treatment of the acetylated aldol with CH_3O^-, but the less stable E-alkylidene promptly converts into the more stable Z-isomer. On the other hand, a E_1cB-like mechanism is to be taken into consideration in view of the considerable acidity of the β-hydrogen of the acetylated aldol and the stabilizing effect of both the thioether and the carbamoyl groups upon the related carbanion. Nevertheless, no deuterium exchange in the recovered starting material was found in a reaction between **9a** (1 mole) and CH_3ONa (0.5 mole) in CH_3OD/DMF, but this might be due to the irreversibility of the carbanion formation step. More studies will be performed by us on the mechanism of the above elimination reaction.

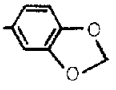
EXPERIMENTAL

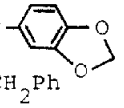
MPS taken on an Electrothermal apparatus were uncorrected. ^1H NMR spectra were recorded on a Varian EM 360A spectrometer and chemical shifts are reported in parts per million (δ) from internal Me_4Si. IR spectra were recorded on a Perkin Elmer 681 spectrometer. Thin-layer chromatography (TLC) was performed on silica gel sheets with fluorescent indicator (stratocrom SIF, Carlo Erba). Column chromatography was carried out by using 70–230 mesh silica gel from Merck. All new compounds had satisfactory microanalytical data (C, H, N; ± 0.3%).

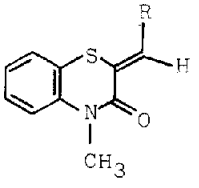
Materials. Tetrahydrofuran (THF) from commercial source (RS, Carlo Erba) was purified by distillation (twice) from sodium wire in a N_2 atmosphere. Diisopropylamine (Carlo Erba) was freshly distilled and stored under N_2. Standardized (1.3 M) *n*-



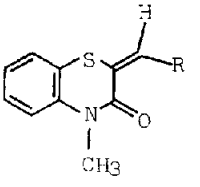


9a:R=CH_3; 9b:R=Ph;
9c:R=p-ClPh; 9e:R= 
9g:R=CH_2Ph

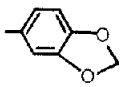
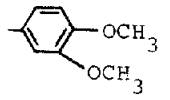
10a:R=CH_3; 10b:R=Ph; 10c:R=p-ClPh
10d:R=$CH(C_2H_5)_2$; 10e:R= 
10f:R=$CH(CH_3)_2$; 10g:R=CH_2Ph

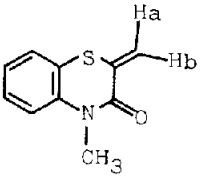


11



12

11a : R = Ph
11b : R = p-ClPh
11c : R = $CH(CH_3)_2$
11d : R = $CH(C_2H_5)_2$
11e : R = 
11f : R = 
11g : R = m-NO_2Ph



13

butyllithium in hexane was from Aldrich Chemical Co. All other chemicals, were commercial grade and were purified by distillation or crystallization prior to use. 4-methyl-3,4-dihydro-3-oxo-2H-1,4-benzothiazine **1** was obtained by methylation of the commercial 3,4-dihydro-3-oxo-2H-1,4-benzothiazine according to the reported procedure.[3]

Procedure for generation of anion **2**. To a nitrogen-flushed, 100-ml, three necked flask, equipped with a magnetic stirrer and a nitrogen inlet and containing 20 ml of anhydrous THF, was added 0.9 g (9 mmole) of diisopropylamine. The solution was cooled at −78° and 7.8 ml (9 mmole) of 1.3 M n-butyllithium solution in hexane was added via a dropping funnel. The mixture was stirred for 30 min and then a 15-ml THF solution of **1** (1 g, 8.2 mmole) was added. The resulting yellow solution of **2** was used in specific reactions described below.

General procedure for reactions of anion **2** *with aldehydes.* To a stirred solution of anion **2** (1 mmole) prepared as above, a 10 ml THF solution of the aldehyde (1 mmole) was added at −78°. The mixture was kept at this temperature for 30 min, then allowed to warm to room temp. and stirred there for 3 h. Quenching with sat NH_4Cl, extraction with ether, drying over Na_2SO_4 and removal of the solvent under reduced pressure gave a mixture of the diastereomeric aldols **4** and **5**, separated by column chromatography on silica gel, using ether–petrol 8:2 as eluent. Overall yields and relative percentages are summarized in Table 1.

General procedure for acetylation of aldols. To 0.78 mmole of the aldol were added 5 ml of pyridine and 5 ml of acetic anhydride and the resulting solution kept at room temp. overnight with stirring. The mixture was then poured into water and extracted with CH_2Cl_2. The CH_2Cl_2 extracts were washed several times with dil HCl and dried over Na_2SO_4. Removal of the solvent *in vacuo* gave the acetylated aldol. By this procedure were synthetized compounds **9** and **10**. Relevant properties are summarized in Table 2.

2 - *Alkylidene* - 4 - *methyl* - 3,4 - *dihydro* - 3 - *oxo* - 2*H* - 1,4 - *benzothiazines* **11a–g**. *General procedure. Method A.* To a 10-ml DMF solution of the acetylated aldol (2.4 mmole), 1.2 ml of 1.8 N (2.6 mmole) methanolic sodium methoxide was added at room temp. and the reaction followed by TLC until the disappearance of the starting material was complete (~ 1 h). The yellow mixture was then poured into water (100 ml), extracted with CH_2Cl_2 and dried over Na_2SO_4. Removal of the solvent under reduced pressure left the alkylidene which was purified by crystallization or by column chromatography on silica gel, using ether–petrol 1:1 as eluent. The yields and properties of the products are summarized in Table 3.

Method B. This procedure has been followed for the synthesis of the alkylidenes **11f** and **11g**. The diastereomeric mixture (10 mmole) of the aldols, obtained from **2** and the appropriate aldehyde as above, was treated with 40 ml of acetic anhydride and 40 ml of pyridine. The solution was allowed to stand at room temp. overnight, then poured into water and extracted with CH_2Cl_2. The CH_2Cl_2 extracts were washed many times with 10% HCl, dried over Na_2SO_4 and evaporated under reduced pressure. The residue was dissolved in 20 ml of DMF and treated with 1.8N methanolic sodium methoxide (11 mmole). The mixture was poured into water after 1 h. Usual work-up gave the alkylidene compound.

2 - (1 - *Hydroxyethyl*) - 4 - *methyl* - 3,4 - *dihydro* - 3 - *oxo* - 2*H* - 1,4 - *benzothiazine* **4a**, **5a**. Threo-form **4a**, m.p. 81–82° (ethanol); IR (CH_2Cl_2): $\nu_{O-H} = 3560\ cm^{-1}$; $\nu_{C=O} = 1650\ cm^{-1}$; ^1H NMR ($CDCl_3$, δ): 1.3(d, 3H), 3.2(d, 1H, $J = 7Hz$), 3.4(s, 3H), 3.8–4.4(cm, 1H), 6.7–7.6(cm, 4H). Erythro-form **5a**: m.p. 126–127° (methanol); IR (CH_2Cl_2): $\nu_{O-H} = 3500\ cm^{-1}$; $\nu_{C=O} = 1650\ cm^{-1}$.

Table 2. Acetylated aldols **9** and **10** from aldols **4** and **5** and acetic anhydride

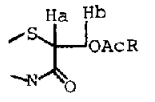
			^{1}HNMR ($CDCl_3$), δ		
					
Compound	mp°C	Yield%	Ha	Hb	J_{Ha-Hb} Hz
9a	95–96	88	3.30	4.90	6
10a	84–85	87	3.30	4.90	7
9b	133–135	88	3.80	5.85	8
10b	79–81	80	3.75	5.80	10
9c	oil	>95	3.65	5.80	6
10c	oil	78	3.55	5.60	10
10d	97–98	74	3.50	4.80	10
9e	115–116	74	3.80	5.80	7
10e	205–206	79	3.65	5.55	10
10f	94–95	81	3.40	4.60	9
9g	oil	>95	3.55	5.40	6
10g	98–100	>95	3.55	5.15	8

Table 3. 2-Alkylidene-3,4-dihydro-3-oxo-2H-1,4-benzothiazines 11

Compound	yield%	method
11a	>95	A[a]
11b	62	A
11c	81	A
11d	89	A
11e	>95	A
11f	90	B[b]
11g	90	B

[a] average of the yields from the acetylated erythro and threo aldols.

[b] Yield based on the starting benzothiazinone 1.

^{1}H NMR[9] ($CDCl_3$, δ): 1.35 (d, 3H), 3.25 (d, 1H, J = 10 Hz), 3.45 (s, 3H), 3.7–4.3 (cm, 1H), 6.7–7.5 (c, m 4H).

2-(*α-Hydroxybenzyl*)-4-*methyl*-3,4-*dihydro*-3-*oxo*-2*H*-*benzothiazine* **4b,5b**. Threo-form **4b**, mp 118–119° (ethanol); IR (CH_2Cl_2): ν_{O-H} = 3500 cm^{-1}; $\nu_{C=O}$ = 1670 cm^{-1}. ^{1}H NMR ($CDCl_3$, δ): 3.3 (s, 3H), 3.55 (d, 1H, J = 5 Hz), 5.15 (d, 1H), 6.7–7.4 (cm, 9H). Erythro form **5b**: mp 146–147° (ethanol); IR (CH_2Cl_2): ν_{O-H} = 3500 cm^{-1}; $\nu_{C=O}$ = 1650 cm^{-1}. ^{1}H NMR ($CDCl_3$, δ): 3.4 (s, 3H), 3.5 (d, 1H, J = 10 Hz), 4.7 (d, 1H), 6.6–7.4 (cm, 9H).

2-(*α-Hydroxy-p-chlorobenzyl*)-4-*methyl*-3,4-*dihydro*-3-*oxo*-2*H*-*benzothiazine* **4c,5c**. Threo-form **4c**, mp 138–139° (methanol); IR (CH_2Cl_2): ν_{O-H} = 3560 cm^{-1}; $\nu_{C=O}$ = 1650 cm^{-1}. ^{1}H NMR ($CDCl_3$, δ): 3.4 (s, 3H), 3.5 (d, 1H, J = 5 Hz), 5.2 (d, 1H), 6.7–7.6 (cm, 8H). Erythro form **5c**: mp 169–170° (methanol); IR (CH_2Cl_2): ν_{O-H} = 3500 cm^{-1}; $\nu_{C=O}$ = 1650 cm^{-1}. ^{1}H NMR ($CDCl_3$, δ): 3.4 s, 3H), 3.5 (d, 1H, J = 9Hz), 4.8 (d, 1H), 6.7–7.6 (cm, 8H).

2-(1-*Hydroxy*-2-*ethylbutyl*)-4-*methyl*-3,4-*dihydro*-3-*oxo*-2*H*-1,4-*benzothiazine* **4d,5d**. Threo-form **4d**, mp 93–94° (ethanol); IR (CH_2Cl_2): ν_{O-H} = 3560 cm^{-1}; $\nu_{C=O}$ = 1660 cm^{-1}. ^{1}H NMR (CCl_4, δ): 0.7–1.1 (cm, 6H), 1.2–1.8 (cm, 5H), 3.3–3.6 (bs, 4H), 3.9–4.2 (bs, 1H), 6.8–7.6 (cm, 4H). Erythro-form **5d**, mp 118–119° (ethanol); IR (CH_2Cl_2): ν_{O-H} = 3500 cm^{-1}; $\nu_{C=O}$ = 1650 cm^{-1}. ^{1}H NMR (CCl_4, δ): 0.5–0.9 (cm, 6H), 0.9–1.4 (cm, 5H), 3.1 (d, 1H, J = 10 Hz), 3.2 (s_1, 3H), 3.8 (bd, 1H), 6.7–7.3 (cm, 4H).

2-(*α-Hydroxy*-3,4-*methylenedioxybenzyl*)-4-*methyl*-3,4-*dihydro*-3-*oxo*-2*H*-1,4-*benzothiazine* **4e,5e**. Threo-form **4e**, mp 149–150° (ethanol); ^{1}H NMR ($CDCl_3$, δ): 3.4 (s, 3H), 3.6 (d, 1H, J = 6Hz), 5.1 (d, 1H), 5.9 (s, 2H), 6.7–7.5 (cm, 7H). Erythro-form **5e**, mp 147–148° (ethanol); ^{1}H NMR ($CDCl_3$, δ): 3.4 (s, 3H), 3.5 (d, 1H, J = 10 Hz), 4.8 (d, 1H, J = 10 Hz), 5.9 (s, 2H), 6.7–7.4 (m, 7H).

2-(1-*Hydroxy*-2-*methylpropyl*)-4-*methyl*-3,4-*dihydro*-3-*oxo*-2*H*-1,4-*benzothiazine* **5f**. mp 84–85° (methanol). IR (CH_2Cl_2): ν_{O-H} = 3500 cm^{-1}; $\nu_{C=O}$ = 1650 cm^{-1}. ^{1}H NMR ($CDCl_3$, δ): 0.95 (dd, 6H), 1.65–2.30 (cm, 1H), 3.25 (d, 1H, J = 10 Hz), 3.4 (s, 3H), 3.7–3.9 (dd, 1H), 6.7–7.6 (m, 4H).

2-(*α-Hydroxy*-3, 4-*dimethoxybenzyl*)-4-*methyl*-3, 4-*dihydro*-3-*oxo*-2*H*-1,4-*benzothiazine* **4g,5g**. Aldols **4g** and **5g** were not isolated and relative percentages were determined by ^{1}H NMR ($CDCl_3$, δ) of the diastereomeric mixture. Threo-form, 3.30 (s, 3H), 3.45 (d, 1H), 3.75 (s, 6H), 4.95 (d, 1H, J = 5 Hz), 6.60–7.30 (m, 7H). Erythro-form, 3.40 (s, 3H), 3.60 (d, 1H), 3.75 (s, 6H), 4.70 (d, 1H, J = 11 Hz), 6.60–7.30 (m, 7H).

2-(1-*Hydroxy*-2-*phenylethyl*)-4-*methyl*-3, 4-*dihydro*-3-*oxo*-2*H*-1,4-*benzothiazine* **4h,5h**.[10] Threo-form **4h**, oil. ^{1}H NMR ($CDCl_3$, δ): 2.83–3.10 (cm, 2H), 3.4 (s, 3H), 3.42 (d, 1H), 4.50 (m, 1H), 7.0–7.50 (cm, 9H). Erythro form **5h**, mp 113–114° (methanol). ^{1}H NMR ($CDCl_3$, δ): 2.9–3.30 (cm, 2H), 3.4 (bs, 4H), 4.20 (m, 1H), 7.0–7.50 (cm, 9H).

2-(2-*Hydroxyisopropyl*)-4-*methyl*-3,4-*dihydro*-3-*oxo*-2*H*-1,4-*benzothiazine* **3c**. To a stirred solution of **2** (4.46 mmole) was added an excess of acetone (1 ml) at −78°. After 30 min the solution was warmed at room temp. and stirred there for 3 h. The mixture was then diluted with sat NH_4Cl. Usual work-up gave a mixture of the starting benzothiazinone **1** and a new product. Column chromatography on silical gel using ether–petrol 6:4 as eluent gave 0.27 g of **1** and 0.62 g of a thick oil, n_{20}^D = 1.584. ^{1}H NMR ($CDCl_3$, δ): 1.4 (s, 6H), 3.4 (s, 3H), 4.4 (s, 1H), 6.9–7.4 (m, 4H).

2-*Benzylidene*-4-*methyl*-3,4-*dihydro*-3-*oxo*-2*H*-1,4-*benzothiazine* **11a**. mp 87–88° (lit[3] 86–87.5°) (CH_2Cl_2-petrol). ^{1}H NMR ($CDCl_3$, δ): 3.5 (s, 3H), 6.7–7.6 (m, 9H), 7.9 (s, 1H).

2-*p-Chlorobenzylidene*-4-*methyl*-3,4-*dihydro*-3-*oxo*-2*H*-1,4-*benzothiazine* **11b**, mp 126–127° (CH_2Cl_2-petrol). ^{1}H NMR ($CDCl_3$, δ): 3.3 (s, 3H), 6.7–7.6 (m, 8H), 7.8 (s, 1H).

2-*Isobutylindene*-4-*methyl*-3,4-*dihydro*-3-*oxo*-2*H*-1,4-*benzothiazine* **11c**, oil. ^{1}H NMR (CCl_4, δ): 1.1 (d, 6H), 2.4–3.3 (cm, 1H), 3.4 (s, 3H), 6.6 (d, 1H), 6.7–7.4 (m, 4H).

2-(2-*ethylbutylidene*)-4-*methyl*-3,4-*dihydro*-3-*oxo*-2*H*-1,4-*benzothiazine* **11d**, mp 43–44°. ^{1}H NMR ($CDCl_4$, δ): 0.9 (d, 6H), 1.0–1.8 (cm, 4H), 2.0–2.7 (cm, 1H), 3.4 (s, 3H), 6.6 (d, 1H), 6.8–7.4 (m, 4H).

2 - (3,4 - *methylenedioxybenzylidene*) - 4 - *methyl* - 3,4 - *dihydro* - 3 - *oxo* - 2*H* - 1,4 - *benzothiazine* **11e**, mp 152–153° (lit[3] 151–152°) (CH_2Cl_2–petrol). ^{1}H NMR ($CDCl_3$, δ): 3,5 (*s*, 3H), 5.95 (s, 2H), 6.7–7.6 (m, 7H), 7.8 (s, 1H).

2 - (3,4 - *dimethoxybenzylidene*) - 4 - *methyl* - 3,4 - *dihydro* - 3 - *oxo* - 2*H* - 1,4 - *benzothiazine* **11f**, mp 114–115° (CH_2Cl_2–ether). ^{1}H NMR ($CDCl_3$, δ): 3.5 (*s*, 3H), 3.9 (s, 6H), 6.7–7.5 (m, 7H), 7.8 (s, 1H).

2 - *m* - *Nitrobenzylidene* - 4 - *methyl* - 3,4 - *dihydro* - 3 - *oxo* - 2*H* - 1,4 - *benzothiazine* **11g**, mp (127–128° (ethanol). ^{1}H NMR ($CDCl_3$, δ): 3.60 (s, 3H), 7.0–7.30 (cm, 4H), 7.60 (t, 1H), 7.90 (s, 2H), 8.20 (d, 1H), 8.55 (s, 1H, vinyl proton).

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[6]Both acetyl derivatives **9g** and **10g** underwent β'-elimination leading to 2-(trans-β-styryl)-4-methyl-3,4-dihydro-3-oxo-2H-1,4-benzothiazine [mp 110–111° (ethanol). ^{1}H NMR ($CDCl_3$, δ): 3.50 (s, 3H), 4.25 (d, 1H, J = 6Hz), 6.15 (dd., 1H, J = 6Hz, J' = 16 Hz), 6.55 (d, 1H, J = 16 Hz), 6.95–7.45 (cm, 9H)].

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[9]^{1}H NMR spectra of aldols were recorded in $CDCl_3$ (CCl_4) in the presence of a few drops of D_2O.

[10]Isomers **4h** and **5h** were assigned the threo-and erythro-configuration respectively on the basis of the configuration of the corresponding acetylated aldols **9g** and **10g**.