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Photochemical Ring Contraction of Dihydro-1,4-benzothiazines

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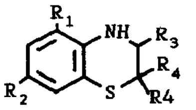
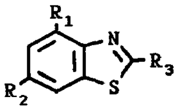
Abstract. The pheomelanin precursor **1a** and the related dihydro-1,4-benzothiazines **1b-f** undergo ring contraction upon irradiation with pyrex-filtered UV light to give 2-methylbenzothiazoles **2a-f** in good yields.

The chemistry of 1,4-benzothiazines has experienced a steady progress during the last two decades[1], following the discovery of structural units related to **1a** in pheomelanins and trichochromes, the characteristic pigments of red human hair[2]. Very little is known, however, on the photochemical behaviour of 1,4-benzothiazine compounds, though photolytic reactions targeted to pheomelanins and related metabolites have repeatedly been implicated to account for the abnormal susceptibility of fair-complexioned, red-haired individuals to sunburn and skin cancer[3]. We report now that irradiation with pyrex-filtered UV light (λ>320 nm) of the 5-hydroxydihydro-1,4-benzothiazine **1a**[4] in argon-saturated methanol-phosphate buffer pH 6.8 7:3 v/v promotes a decarboxylative ring-contraction to give the 2-methylbenzothiazole **2a**[5] in about 60% yield.


1

1a, R_1=OH, R_2=$CH_2CH(NH_2)COOH$, R_3=COOH, R_4=H
1b, R_1=OH, R_2=CH_3, R_3=COOH, R_4=H
1c, R_1=OH, R_2=CH_3, R_3=H, R_4=H
1d, R_1=H, R_2=OH, R_3=COOH, R_4=H
1e, R_1=OCH_3, R_2=CH_3, R_3=H, R_4=H
1f, R_1=OH, R_2=CH_3, R_3=COOH, R_4=CH_3

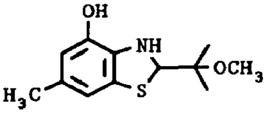

2

2a, R_1=OH, R_2=$CH_2CH(NH_2)COOH$, R_3=CH_3
2b, R_1=OH, R_2=CH_3, R_3=CH_3
2c, R_1=H, R_2=OH, R_3=CH_3
2d, R_1=OCH_3, R_2=CH_3, R_3=CH_3
2e, R_1=OH, R_2=CH_3, R_3= $C(CH_3)$=CH_2

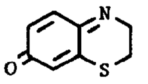
The structurally related 5-hydroxy- and 7-hydroxydihydro-1,4-benzothiazines **1b-d** afford likewise good yields (40-60%) of the corresponding 2-methylbenzothiazoles **2b-c**[5] when irradiated in argon-saturated methanol. The photochemical ring-contraction of **1a-d** is virtually unaffected under N_2O atmosphere, ruling out significant electron photoejection in the primary events[6], whereas photodecomposition of the benzothiazoles formed occurs in air. The reaction is not sensitised by acetophenone, under conditions where all the light is absorbed by the sensitiser, and is not inhibited by triplet quenchers, e.g. oxygen or 2-methyl-1,3-butadiene. These results suggest that ring contraction does not proceed *via* the triplet excited state of **1**.

Quinonimines are apparently not involved in the process, as compound **3**[7] failed to afford the benzothiazole **2c**. Moreover, the O-methyl derivative **1e**, in which quinonimine formation is precluded, undergoes efficient photochemical ring-contraction to the corresponding benzothiazole **2d**. Photolysis of compound **1f** furnishes **2e** in acetonitrile and **2f** in methanol, indicating that the exocyclic carbon in the benzothiazoles originates from the C-2 carbon of dihydrobenzothiazines.

On these grounds, a plausible mechanism would involve the initial generation of a 2*H*-benzothiazine intermediate, presumably *via* homolysis of the N-H bond, which would suffer intramolecular attack of the sulphur onto the C-3 carbon to produce an intermediate like **4**. This latter would then be converted to **5**, the tautomer of **2**, by fission of the S-C-2 bond and concomitant decarboxylation or deprotonation from C-3.



2f



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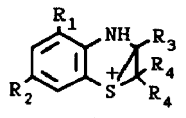

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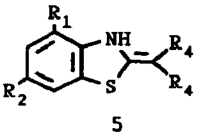

5

Besides providing the first example of a photochemically-induced ring contraction of 1,4-benzothiazines, the results of our study offer an attractive explanation to the suggested presence of 2-methylbenzothiazole units in natural pheomelanins[2].

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