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NOTE

Synthesis of 5-Oxo-2-Arylamino Thiazol-[4,5-d]-Pyrans

A.P. RAJPUT
Department of Chemistry, Jai Hind College of Arts, Science & Comerce, Deopur, Dhule-424 802, India
e-mail : drapr@rediffmail.com Fax : +91-0256-220678

Initially (E)-5-(4-oxo-2-arylamino thiazolyl) acrylic acids (**3a–f**) were prepared from 4-oxo-2-arylamino thiazole-5-carboxaldehydes (**2a–f**) using Perkin's reaction. The acrylic acids (**3a–f**) on heating with polyphosphoric acid (PPA) at 245°C formed intermediates (**4a–f**) (not isolated) which on hydrolysis with cold alkali yielded pyrans, (**5a–f**). The structures of acrylic acids and pyrans were confirmed by physical as well as chemical methods.

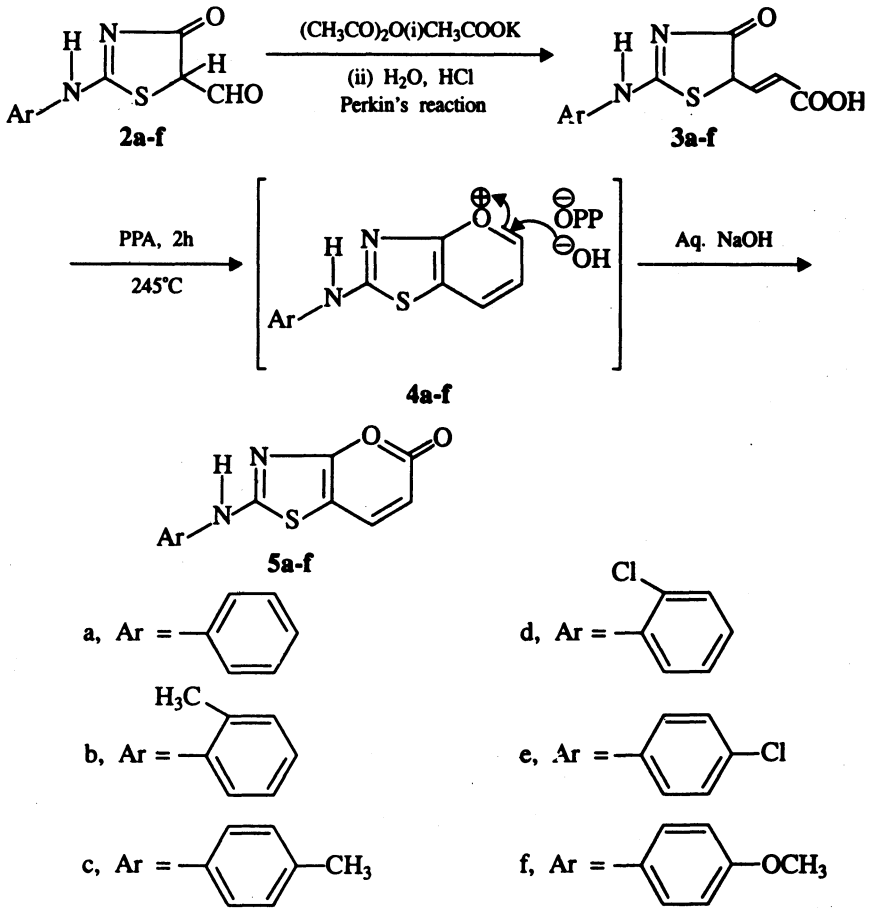
Key words: Pyrans, Arylamino thiazol pyrans.

Many compounds containing pyran and benzopyran moieties act as antibiotics and marketed an antibacterial and antimicrobial preparations under a variety of names[1]. Compounds possessing pyran moiety such as 5-hydroxy chromone and some of its derivatives show chelating properties and have been utilised in the determination of a number of metals[2, 3]. As a result of these useful properties a large number of groups are lured in the synthesis of new compounds of this type. In view of pharmacological[4–6], analytical and mechanistic [7, 8] utility of pyrans and benzopyrans, synthesis of 5-oxo-2-arylamino thiazol-[4,5–d]-pyrans (**5a–f**) have been attempted.

The first target for the synthesis was preparation of substituted (E)-5-(4-oxo-2-arylamino thiazole-5-carboxaldehydes (**2a–f**). The compounds (**3a–f**) showed IR bands at 1440 cm^{-1} (—OH deformation peak), 1680 cm^{-1} (carbonyl of α,β-unsaturated acid) and 3400 cm^{-1} broad (acid —O—H stretching bonded). An aldol type condensation mechanism involving the carbonyl group of the carboxaldehyde and an active methylene group of the acetic anhydride can be proposed for the formation of (**3a–f**). The basic catalyst, CH_3COO^- obtained from fused potassium acetate forms an anion from acetic anhydride by removing proton. It is followed by dehydration. Subsequent base catalysed hydrolysis yields (**3a–f**). The compounds (**2a–f**) were prepared by carrying out hydrolysis of 4-chloro-2-arylamino thiazole-5-carboxaldehydes (**1a–f**) using 6N HCl according to literature procedure[9].

The next requirement was to prepare 5-oxo-2-arylamino thiazol-[4,5-d]-pyrans (**5a–f**). These were prepared from corresponding acrylic acids, (**3a–f**), using the methods described by Cohn *et al.*[10], *via* intermediates (**4a–f**) (not isolated). These were being selectively converted into **5a–f** with cold alkali. The strategy visualised is shown in **Scheme-I.** In IR spectra of compounds (**5a–f**), —OH deformation peak at 1440 cm^{-1} and very broad band in the region 3500–3300 cm^{-1} for acid —OH group were found absent. Both the bands were present in the starting compounds, (**3a–f**). The observed IR bands in compounds (**5a–f**) at 1750 cm^{-1} can be assigned to carbonyl frequency of pyrans. This information indicates the cyclisation of acids

into pyrans. The structures assigned to compounds (**5a–f**) are also supported by elemental analysis.



Scheme-I

All m.p.'s were detemined in open capillaries and are uncorrected. IR spectra (nujol) were recorded on a Perkin-Elmer 337 spectrophotometer. The purity of the compounds was checked on TLC. The chlorocarboxaldehydes (**1a–f**) were prepared according to reported method[11]

Preparation of 4-oxo-5-formyl-2-arylamino thiazoles (2a–f)

4-Chloro-2-arylamino thiazole-5-carboxaldehydes, (**1a–f**) (0.02 mol) were heated on a water bath with 6 N HCl for 2 h. It was then poured into crushed ice with constant stirring. The resulting yellow solids were crystallised from acetic acid (70%) to afford the products: **2a** (82%), m.p. 148–150°C; **2b** (85%), 170°C, **2c** (81%), m.p. 195–196°C; **2d** (79%), m.p. 180°C; **2e** (83%), 209–211°C and **2f** (80%), m.p. 158°C.

Preparation of (E)-5-(4-oxo-2-arylamino thiazolyl) acrylic acids (3a–f)

A mixture of 4-oxo-2-arylamino thiazole-5-carboxaldehydes (**2a–f**) (0.02 mol), acetic anhydride (0.029 mol), freshly fused potassium acetate (0.012 mol) was mixed in a round bottom flask fitted with an air condenser carrying a $CaCl_2$ guard tube. The reaction mixture was heated in an oil bath initially at 160°C for 1 h and at 170–180°C for 3 h and then poured while still hot (80–100°C) into 10 mL of water contained in a round bottom flask which had previously been fitted for steam distillation. The steam distillation was carried out until all the distillate was clear. The residual solution was filtered after cooling and the filtrate was acidified with conc. HCl to get solid acids. The resulting crude acid product was crystallised from hot water to afford **3a** (67%), m.p. 201°C IR band (nujol) at 700, 1680, 3400; **3b** (62%), m.p. 180°C, IR 760, 1700, 3200; **3c** (63%), m.p. 165°C, IR 800, 1700, 3300; **3d** (57%), m.p. 195–200°C, IR 710, 1720, 3280; **3e** (59%), m.p. 203°C, IR 850, 1700, 1740, 3240 and **3f** (65%), m.p. 178°C, IR 840, 1690, 3200.

Preparation of 5-oxo-2-arylamino thiazol-[4,5–d]-pyrans (5a–f)

The acid (E)-5-(4-oxo-2-arylamino thiazolyl) acrylic acids (**3a–f**) (0.0035 mol) was stirred in polyphosphoric acid (10 g) for 2 h at 245°C. After cooling and diluting with ice water (100 mL), the clear solution was made alkaline with aqueous NaOH (4 M), allowed to stand and then filtered. The residue was washed with water and dried. The crude product was purified by sublimation to afford **5a**, (70%), m.p. 240°C; **5b** (55%), m.p. 280°C; **5c** (72%), m.p. 256°C; **5d** (62%), 260°C; **5e** (67%), m.p. 300°C; **5f** (73%), m.p. 221–222°C.

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