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# A CONVENIENT SYNTHESIS OF AROMATIC THIOLACTONES

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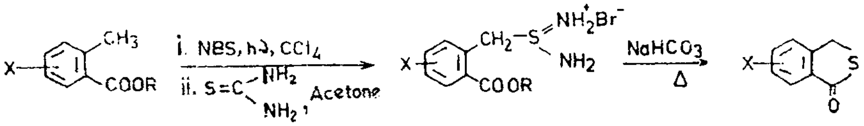
Abstract: Hydrolytic decomposition of thiouronium salts A with aqueous $NaHCO_3$ at 80° - 90°C directly furnished thiolactones 6 -10 in very good yields in one-flask operation.

The chemistry of thiophthalides[1] has begun to gain importance only in recent years despite their long existence[2] in literature. In a recent communication[3], we have reported their potential use as 1,4-dipolar phthaloyl synthons in constructing polycyclic carbon skeletons of polyketide-derived antibiotics, with a brief mention on their preparation. A closely related publication[4] in this journal prompted us to disclose full experimental details constituting a convenient one - flask preparation of thiolactones.

The route that has been executed in our laboratory and presented in the scheme 1

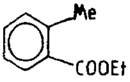
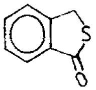
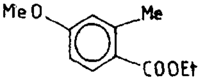
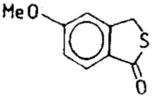
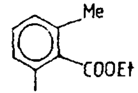
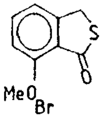
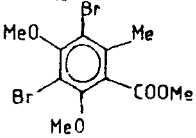
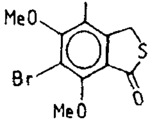
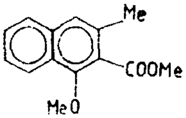
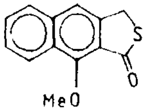


A

closely resemble that of Vegh et.al. However, our method is operationally much simpler and necessiates fewer steps to accomplish the transformation, ortho-methyl carboxylates to thiophthalides.

Although alkanethiols are traditionally prepared by alkaline hydrolysis[5] of the respective thiouronium salts, the preparation of thiouronium salts A from ortho-bromomethyl carboxylates in ethanol is often accompanied by phthalides as side products. After a few experimentations, we found that ethanol could be replaced by acetone to minimize the formation of by-products. The subsequent hydrolysis step deserves special mention; the use of sodium hydroxide was also found to have deleterious effect on product-yields. On the other hand, thiouronium salts A straight way transformed to thiolactones when heated with a saturated solution of $NaHCO_3$. The intermediate ortho-mercaptomethyl carboxylates could not be isolated. Thus, separate steps of the formation and the cyclisation of thiol esters in the presence of PPE (polyphosphate esters) as described by Vegh et.al are not required. In most of the cases examined (Table 1),

Table 1 : Thiolactones from O-methyl arenecarboxylates 1-5

| Ortho methyl-Carboxylates | No. | Thiolactones | No. | Overall % yield | mp (°C) |
|---|---|---|---|---|---|
|  | 1 |  | 6 | 64 | 58-60 |
|  | 2 |  | 7 | 45 | 105 |
|  | 3 |  | 8 | 61 | 70 |
|  | 4 |  | 9 | 65 | 142-143 |
|  | 5 |  | 10 | 52 | 129-130 |

the crude products were purified by recrystallization or filtration through a pad of silica gel. This method is also adaptable for a multigram scale. The new thiolactones 7,8,9 and 10 were fully characterised by IR, NMR and MS.

## Starting Materials

The compounds 1 [6], 2 [7], 3[8], 4[9] and 5[10] were prepared by following the reported procedures.

General Procedure:

To a solution of an ortho-methyl carboxylate 1-5 (50 mmol) in carbon tetrachloride (125 mL) containing benzoyl peroxide* (10 mg) was added of N-bromosuccinimide (50 mmol). The mixture was heated at reflux until the starting materials completely disappeared. The mixture was then cooled to 10° C and filtered. The filtrate was concentrated under reduced pressure. To the resulting residue was added dry acetone (50 mL) followed by thiourea (55 mmol). The mixture was then refluxed for 5-6 h. Evaporation of acetone yielded thiouronium salts A which was treated with an aqueous solution of $NaHCO_3$ (4.29g in 50 mL of water) under $N_2$-atmosphere at 80 - 90°C for 2 -3 h and then acidified with dil. HCl. The oil that precipitated at this point was separated and purified by passing it through a short column of silica gel.

*In the case of 2,AIBN was used as a catalyst instead of benzoyl peroxide.

Spectral Data

6 : IR (KBr) : $\nu_{max}$ 1686,1595,1237,908,766,701 $cm^{-1}$;
PMR ($CDCl_3$) : $\delta$ 7.97 - 7.38 (m,4H), 4.45 (s,2H).

7 : IR (KBr) : $\nu_{max}$ 1660,1592,1247,845 $cm^{-1}$;
PMR($CDCl_3$) : $\delta$ 7.76 - 7.68 (m,1H), 7.1 - 6.9 (m,2H), 4.40(s,2H), 3.96(s,3H).

8 : IR (KBr) : $\nu_{max}$ 1679,1590,1473,769 $cm^{-1}$;
PMR ($CDCl_3$) : $\delta$ 7.52 (t,1H, J = 8Hz), 7.08(d,1H,J=8.0Hz), 6.88(d 1H,J=8.0Hz),4.40(s,2H),3.96(s,3H)

9 : IR(KBr) : $\nu_{max}$ 1687,1561,1385,963,680 $cm^{-1}$;
PMR ($CDCl_3$) : $\delta$ 4.30 (s,2H), 3.95 (s,3H).

10: IR(KBr) : $\nu_{max}$ 1690,1054,960,754 $cm^{-1}$;
PMR ($CDCl_3$) : $\delta$ 8.40-8.20(m,1H), 7.84-7.42(m,4H), 4.50(s,2H), 4.10(s,3H).

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