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A SYNTHETIC ROUTE TO THIONOLACTONES[1]

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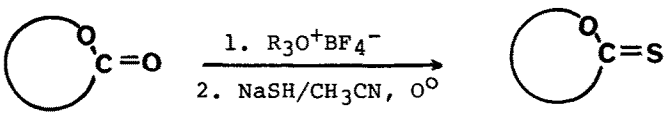
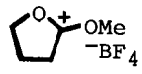
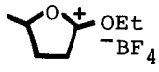
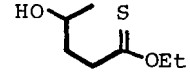
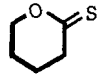
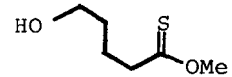
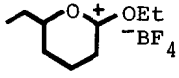
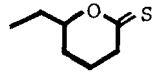
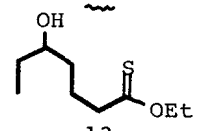
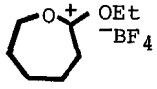
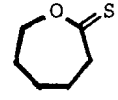
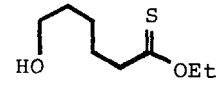
ABSTRACT: The treatment of O-alkyllactonium tetrafluoroborate salts with anh. NaSH in CH_3CN at 0^oC led to five-, six-, and seven-membered thionolactones (44-90% yield).

We recently described a synthetic route to five-, six-, and seven-membered thionolactones by a two-step, low temperature (-78°C) sulfhydrolysis-acetylation of N,N-dimethyliminolactonium salts.[2] We herein report a new, shorter and more convenient route from lactones to thionolactones. The method is also of wider scope than that effected by the thionation of lactones with P_2S_5,[3] or the dimer of p-methoxyphenylthionophosphine sulfide.[4] The novel procedure involves O-alkylation of a lactone with Meerwein's salts $R_3O^+ BF_4^-$ (R = Me, Et),[5] followed by sulfhydrolysis of the intermediate lactonium salt with anhydrous sodium hydrosulfide in acetonitrile at 0^oC:



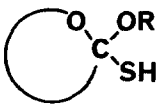
The following Table summarizes our experimental results:

Lactonium Salt	Reaction Time(h)	Thionolactone	Isolated Yield(%) of Thionolactone	By-product	Isolated Yield(%) of By-product
 1	2½	 6	90	-	-
 2	1½	 7	78	 11	10
 3	2	 8	54	 12	40
 4	2½	 9	43	 13	49
 5	2	 10	44	 14	17

In a typical procedure, anhydrous sodium hydrosulfide[6] (0.13 g, 2.32 meq) was gradually added, under nitrogen, over a period of 3 min to a cold (0°C) stirring solution of O-ethyl-γ-valerolactonium tetrafluoroborate (0.50 g, 2.31 meq) in dry acetonitrile (3 mL). The solution was stirred at 0°C for 2 h, diluted with anh. diethyl ether (7 mL) and the solution was filtered through Celite, and concentrated by distillation under nitrogen at atmospheric pressure. The residue was chromatographed on two 20x20 cm silica gel plates eluting with $CHCl_3$-CH_3CN (5:1 v/v). The thionolactone (R_f = 0.69 on TLC plates using $CHCl_3$-CH_3CN 5:1 v/v) was extracted with CH_2Cl_2 and the solvent was removed by careful distillation through a 20-cm Vigreux column to give 0.21 g (78%) of thionolactone 7; NMR($CDCl_3$): δ 1.50 (3H, d, J = 7 Hz, CH_3-), 1.75-2.60 (2H, m, CCH_2C), 3.10 (2H, m, $CH_2C(=S)$), 5.00 (1H, m, HCO) ppm; IR(neat): 1450, 1345, 1310, 1235, 1150, 1030, 860 cm^{-1}; UV(hexane): λ_{max} 384(ε 9.5), 248 (ε 10,7000) nm. Anal. Calcd for C_5H_8OS: C, 51.69; H, 6.94. Found: C, 51.98; H, 7.10.

Various attempts at cyclizing the hydroxythionesters listed in the Table to the corresponding thionolactones resulted in the decomposition of the acid- and water-sensitive thionolactones. These attempts involved (i) azeotropic removal of the alcohol as a binary azeotrope with acetonitrile, cyclohexane, methylcyclohexane or xylene with or without Amberlyst-15 as catalyst and (ii) acid-catalyzed cyclization utilizing Amberlyst-15, oxalic acid, p-toluenesulfonic acid or ethereal HBF_4 in acetonitrile. With the exception of 14, all hydroxythionoesters (11-13; Table) underwent some degree of lactonization (decreasing rate: 5-> 6-> 7-membered ring) on contact with Amberlyst-15, p-toluenesulfonic acid or ethereal HBF_4 after which rapid decomposition ensued within 10 min. The reluctance of 14 to cyclize to thionolactone 10 strongly suggests that 10 and portions of 6-9 are primary products resulting directly from the breakdown of hemiorthothiol ester inter-

mediate [15]. Hence, the method is adaptable to the conversion of macrocyclic lactones to the corresponding thionolactones.



[15]

Temperature studies of the sulfhydrolysis of 4 revealed that the cleavage products (13:9) were formed in the ratio of 100:0 (-78°C), 80:20 (-42°C) and 53:47(0°C). These results clearly indicate that the kinetic breakdown of [15] is subject to stereoelectronic control (Deslongchamps effect) and involves the preferential cleavage of the endocyclic C-O bond.[1b]

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