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A NEW CONVENIENT METHOD FOR PREPARATION OF CONDENSED AROMATIC AND HETEROCYCLIC THIOLACTONES

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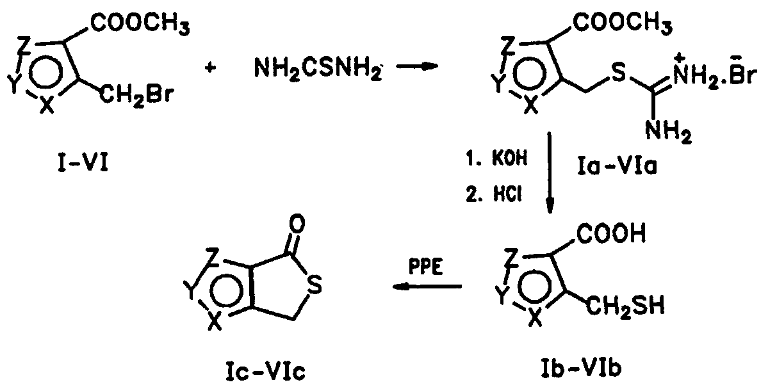
Cyclocondensation of the benzylic—type thiols (Ib–VIb) in ortho position on aromatic and heteroaromatic carboxylic acids to form the corresponding thiolactones (Ic–VIc) can be effected with polyphosphate esters (PPE) in organic solvents in 75-90% yields.

Growing interest in the synthetic utilization of aromatic and heteroaromatic thiolactones as intermediates for the synthesis of biologically active compounds[1] and novel materials[2] has promoted the search for new methods for the preparation of thiolactones.

We reported[3, 4] the formation, in 30–40% yield, of novel heterocyclic thiolactones as a by–product in the preparation of furothieno- and bis-furothiepinones.



Compd. a,b,c	X	Y	Z
I	CH	CH	CH=CH
II	S	CH	CH
III	CH	S	CH
IV	CH	CH	S
V	O	CH	CH
VI	CH	CH	O

We have found that various aromatic and heterocyclic 2-mercaptomethyl carboxylic acids (Ib–VIb), which are easily accessible from the corresponding 2-bromomethyl substituted esters of aromatic and heteroaromatic carboxylic acids (I–VI) treatment with thioureas, followed by a basic hydrolysis of the thiouronium salts (Ia–VIa) readily furnish thiolactones (Ic–VIc) upon treatment with polyphosphate esters (PPE). The PPE reagent itself is prepared from phosphorus pentoxide and ether[5,6]. Condensations with PPE proceed smoothly already at room temperature and give high yields of thiolactones.

Experimental

Melting points were determined with a Kofler hot-stage apparatus. ^{1}H NMR spectra were recorded with a 80 MHz Tesla spectrometer, model BS 487C Ia–VIa in DMSO-d_6, Ib,c–VIb,c in $CDCl_3$. Compounds I[7], II[8], III[9], IV[10], V[11], VI[12] were prepared by a NBSI bromination of the corresponding methyl derivatives.

Preparation of thiouronium salts Ia–VIa

0,01 mol of bromomethyl derivatives (I–VI) and 0,11 mol of thiourea in 20-40 ml of abs. acetone were refluxed 10 h, cooled with ice and the precipitated solid filtered off. The filtrate was reduced to half volume to recover further quantity of the product. The salts Ia–VIa were dried at room temperature. Yields 86–92%.

Preparation of thiols Ib–VIb

0,01 mol of thiouronium salts was refluxed 1 h in 40 ml 2N KOH (aqueous methanol 1:1), the methanol removed under reduced pressure, the aqueous solution cooled to room temperature, acidified with 1N HCl, and extracted with 3x25 ml ether. The combined ether layers, containing the crude thiol (Ib–VIb), were dried with anhydrous sodium sulphate and ether removed on a water bath. Yield 82-87% (Ib-VIb), see Table 2.

Preparation of thiolactones Ic-VIc

To the thiols (0.01 mol) Ib-VIb 20 ml PPE was added at room temperature and under Ar atmosphere. After stirring for 15 h at r.t. the mixture was poured into 100 ml of ice water and extracted with chloroform (3x25 ml). The combined extracts were washed once with 25 ml of 3% $NaHCO_3$, dried with sodium

Table 1 Physico-chemical data of compounds Ia–VIa

Comp	Formula	M.p. [°C]	Yield [%]	CH_x	CH_y	CH_z	J [Hz]	CH_2	CH_3
Ia	C10H13BrN2O2S2	171-173	90		7.57			4.75	3.81
IIa	C8H11BrN2O2S2	143-145	92	–	7.34	7.54	4.85	4.96	3.76
IIIa	C8H11BrN2O2S2	167-169	86	7.78	–	8.43	3.2	4.69	3.81
IVa	C8H11BrN2O2S2	160-162	90	7.30	7.90	–	4.8	4.76	3.79
Va	C8H11BrN2O3S	172-174	90	–	6.77	7.82	1.9	4.87	3.79
VIa	C8H11BrN2O3S	158-160	92	6.80	7.96	–	1.8	4.61	3.85

Table 2 Physico-chemical data of compounds Ib–VIb

Compd.	Formula	M.p. [°C]	Yield [%]	CH_x	CH_y	CH_z	J [Hz]	CH_2	SH
Ib	C8H8O2S	116-119	87	7.43	mult.	8.16		4.14	2.12
IIb	C6H6O2S2	130-132	85	–	7.09	7.45	5.5	4.28	2.31
IIIb	C6H6O2S2	134-136	83	7.25	–	8.29	3.5	4.03	2.08
IVb	C6H6O2S2	140-142	85	7.15	7.55	–	5.5	4.10	2.10
Vb	C6H6O3S	85-87	87	–	6.72	7.33	2.0	4.06	2.17
VIb	C6H6O3S	83-86	82	6.62	7.56	–	1.9	3.93	1.99

Table 3 Physico-chemical data of compounds Ic–VIc

Comp.	Formula	M.p. [°C]	Yield [%]	M^+. [m/e]	CH_x	CH_y	CH_z	J	CH_2
Ic	C8H6OS	57-60	90	150	7.55		7.75		4.45
IIc	C6H4OS2	114-117	87	156	–	7.19	7.48	5.4	4.45
IIIc	C6H4OS2	87-90	80	156	7.10	–	7.75	2.5	4.28
IVc	C6H4OS2	77-80	90	156	7.12	7.92	–	5.4	4.37
Vc	C6H4OS2	65-67	80	140	–	6.58	7.57	2.0	4.26
VIc	C6H4OS2	95-97	75	140	6.53	7.76	–	1.9	4.08

sulphate and passed through a short column packed with silica gel. The eluate was concentrated *in vacuo* and the residue purified by crystallization or sublimation. Yields 80-90% (Ic-VIc, see Table 3).

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