SYNTHESIS OF S-β-ARYL(BENZYL)MERCAPTOETHYL ESTERS OF PHOSPHORUS THIOACIDS

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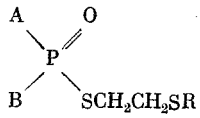
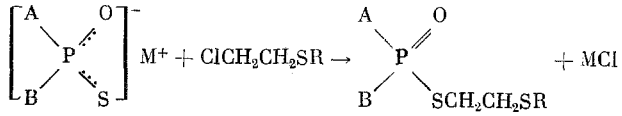
The S-β-arylmercaptoethyl esters of phosphorus acids exhibit a substantially greater anticholinesterase activity than the corresponding compounds, containing a β-alkylmercaptoethyl group. It was also found that the character of the aromatic substituent substantially affects the type of cholinesterase inhibition [1, 2]. Consequently, it seemed of interest to study in more detail the effect of the aromatic group in the thioester radical on the anticholinesterase activity. For this purpose we synthesized a number of S-β-aryl(benzyl)-mercaptoethyl esters of phosphorus thioacids.

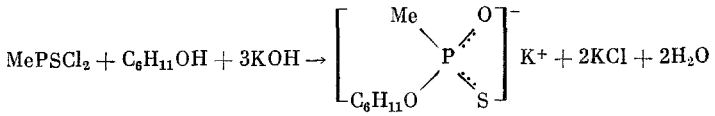


A = Me, Ph, EtO, $C_6H_{13}O$; B = EtO, BuO, $C_6H_{13}O$, $C_6H_{11}O$; R = Ph, $PhCH_2$, *p*-MeC_6H_4, *p*-$MeOC_6H_4$.

These compounds were obtained by reacting β-chloroethyl aryl(benzyl) sulfides [3-5] with either the Na or K salts of the corresponding phosphorus thioacids.



O-Cyclohexylmethylthiophosphonic acid was obtained by reacting methyldichlorothiophosphonic acid with KOH solution in cyclohexanol.



The products were purified by vacuum-distillation and preparative TLC. The yields, constants, and elemental analysis data are given in Table 1.

The data on the anticholinesterase activity will be published separately.

EXPERIMENTAL

S-β-Alkylmercaptoethyl Esters of Phosphorus Thioacids. To 0.05 mole of either the Na or K salt of the appropriate phosphorus thioacid in 50 ml of EtOH was added 0.05 of the β-chloroethyl aryl(benzyl) sulfide and the mixture was refluxed for 5 h, the precipitate was filtered, the alcohol was distilled from the filtrate, the residue was dissolved in ether, washed with water and dried over Na_2SO_4, the ether was distilled off, and the residue was

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TABLE 1. S-β-Aryl(benzyl)mercaptoethyl Esters of Phosphorus Thioacids ABP(O)SCH_2CH_2SR*

A	B	R	Yield, %	bp, °C ($p \cdot 10^2$, mm of Hg)	d_4^{20}	n_D^{20}	Found, %			Empirical formula	Calculated, %		
							C	H	P		C	H	P
EtO	EtO	Ph	62	140–142 (1,6)	1,1966	1,5804	47,2	6,2	10,1	$C_{12}H_{19}O_3PS_2$	47,1	6,2	10,1
$C_6H_{13}O$	$C_6H_{13}O$	Ph	84	†	1,0688	1,5188	57,3	8,5	7,6	$C_{26}H_{35}O_3PS_2$	57,4	8,4	7,4
Me	$C_6H_{11}O$	Ph	58	†	1,1722	1,5670	54,1	6,9	9,2	$C_{15}H_{23}O_2PS_2$	54,5	7,0	9,4
Me	EtO	*p*-MeC_6H_4	20	163–166 (1,9)	–	1,5474	46,7	6,0	9,8	$C_{12}H_{19}O_3PS_2$	47,1	6,2	10,1
EtO	EtO	*p*-$MeOC_6H_4$	21	160–162 (2,0)	–	1,5502	46,0	6,1	9,2	$C_{13}O_{21}O_4PS_2$	46,4	6,3	9,2
Me	BuO	*p*-$MeOC_6H_4$	34	166–169 (4,0)	–	1,5567	49,8	6,6	9,1	$C_{14}H_{23}O_3PS_2$	50,3	6,9	9,3
Me	$C_6H_{11}O$	*p*-$MeOC_6H_4$	22	†	1,1928	1,5690	52,8	6,7	8,6	$C_{16}H_{25}O_3PS_2$	53,3	6,9	8,6
$C_6H_{13}O$	$C_6H_{13}O$	*p*-$MeOC_6H_4$	30	†	1,0942	1,5230	56,0	8,1	6,7	$C_{21}H_{37}O_4PS_2$	56,3	8,3	6,9
$C_6H_{13}O$	$C_6H_{13}O$	$PhCH_2$	84	†	1,0706	1,5194	58,0	8,5	7,1	$C_{21}H_{37}O_3PS_2$	58,3	8,6	7,2
Me	$C_6H_{11}O$	$PhCH_2$	38	†	1,1518	1,5672	56,3	7,5	8,8	$C_{16}H_{25}O_2PS_2$	55,8	7,3	9,0
Ph	EtO	*p*-MeC_6H_4	38	†	1,1861	1,5916	58,1	6,0	8,6	$C_{17}H_{21}O_2PS_2$	58,0	6,0	8,8
$C_6H_{13}O$	$C_6H_{13}O$	*p*-MeC_6H_4	44	†	1,0609	1,5200	58,7	8,8	6,9	$C_{21}H_{37}O_3PS_2$	58,3	8,6	7,2

*Cf. [6].

†Purified by preparative TLC without prior distillation.

distilled and purified by preparative TLC on Silica Gel L 100/160 μm (eluant= 10:1 benzene—acetone).

CONCLUSIONS

The S-β-aryl(benzyl)mercaptoethyl esters of the diethyl- and dihexylthiophosphoric acids, and of the O-ethyl-, O-butyl-, O-cyclohexylmethyl-, and O-ethylphenylthiophosphonic acids, were synthesized.

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1,1-BIS(TRIFLUOROMETHYL)HYDRAZINE

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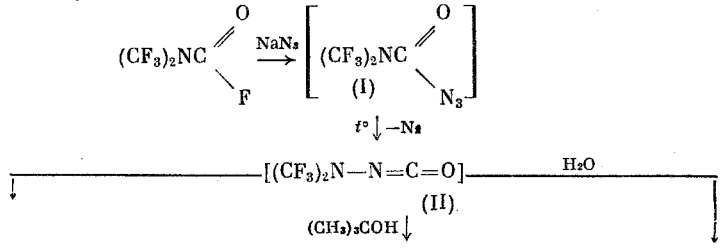
Previously it was reported that bis(trifluoromethyl)carbamic acid azide (I) (obtained by reacting bis(trifluoromethyl)carbamoyl fluoride with a suspension of NaN_3 in xylene) decomposes to give the unstable bis(trifluoromethyl)amino isocyanate (II), which spontaneously trimerizes to (III) [1].

In order to synthesize 1,1-bis(trifluoromethyl)hydrazine* the decomposition of azide (I) was run in the presence of either tert-butanol or water. In the first case tert-butyl bis(trifluoromethyl)-carbamate (IV) is formed, whose pyrolysis at 270-300°C gave 1,1-bis(trifluoromethyl)hydrazine (V). However, it is more convenient to obtain hydrazine (V) by the decomposition of azide (I) in the presence of water.



*We were unable to obtain 1,1-bis(trifluoromethyl)hydrazine either by the reduction of bis(trifluoromethyl)nitrosamine or by the reaction of bis(trifluoromethyl)chloramine with ammonia.

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