SYNTHESIS OF O,O-DIALKYL S-LUPINANE THIOPHOSPHATES, O,O-DIALKYL S-EPILUPINANE THIOPHOSPHATES, AND THEIR METHIODIDES

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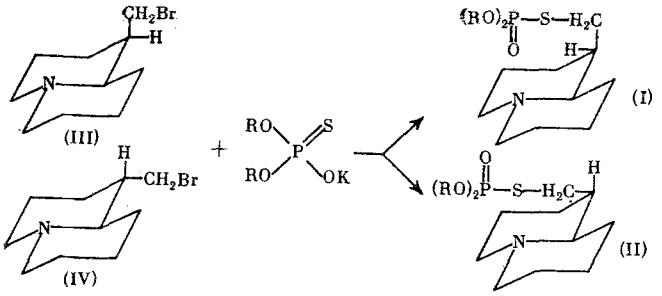
It is known that organophosphorus inhibitors of cholinesterase, which are derivatives of monothiophosphoric acids that contain a nitrogen atom in the thioester radical, exhibit a high anticholinesterase activity. Here compounds with large hydrophobic groupings, which facilitate manifestation of a selective activity toward butyrylcholinesterase, are of special interest [1, 2].

In view of this it seemed of interest to synthesize and study the anticholinesterase activity of organophosphorus compounds that contain the lupinine (I) moiety or its conformer, epilupinine (II), in the thioester radical. We obtained these compounds by reacting either bromolupinane (III) or bromoepilupinane (IV) with potassium dialkyl thiophosphates:



The starting bromolupinane (III) and bromoepilupinane (IV) were synthesized as described in [3]. The corresponding methiodides were obtained by the reaction of (I) and (II) with CH_3I. The data on the anticholinesterase activity will be published separately.

EXPERIMENTAL

O,O-Diethyl S-Epilupinane Thiophosphate. To 2.32 g (0.01 mole) of epibromolupinane in 50 ml of abs. alcohol was added in drops an alcohol solution of 1.86 g (0.01 mole) of potassium O,O-diethyl thiophosphate [4]. The mixture was refluxed for 2 h, the obtained precipitate was filtered, the solvent was distilled off, and the residue was mixed with an equal volume of water and extracted with ether. The ether extracts were dried over anhydrous Na_2SO_4, the ether was distilled off, and the residue was purified by chromatography on a column packed with Al_2O_3 (II activity), using ether as the eluant.

The other compounds were obtained in a similar manner (Tables 1 and 2).

TABLE 1. O,O-Dialkyl S-Lupinane Thiophosphates (I)

R	Yield, %	n_D^{20}	$[\alpha]_D$ (benzene) 20°	Found, %			Empirical formula	Calculated, %		
				C	H	P		C	H	P
n-C_5H_{11}	65	1,4902	−18,44°	59,62	10,01	7,95	$C_{20}H_{40}PO_3SN$	59,38	9,87	7,65
i-C_3H_7	63	1,4944	−9,25°	55,31	9,04	9,00	$C_{16}H_{32}PO_3SN$	55,0	9,00	8,88
i-C_4H_9	59	1,4911	−26,03°	57,40	9,62	8,44	$C_{18}H_{36}PO_3SN$	57,30	9,54	8,20
i-C_5H_{11}	71	1,4890	−14,49°	59,17	9,63	7,78	$C_{20}H_{40}PO_3SN$	59,38	9,54	7,65

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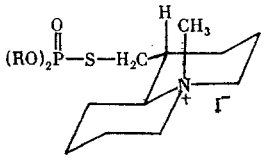
TABLE 2. O,O-Dialkyl S-Epilupinane Thiophosphates (II)

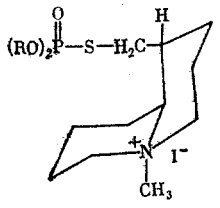
R	Yield, %	n_D^{20}	$[\alpha]_D^{20}$ (benzene)	Found, %			Empirical formula	Calculated, %		
				C	H	P		C	H	P
C_2H_5	59	1,4950	+94,53°	52,47	8,93	9,81	$C_{14}H_{28}PO_3SN$	52,30	8,72	9,65
n-C_3H_7	64	1,4981	+66,06°	55,27	9,11	8,61	$C_{16}H_{32}PO_3SN$	55,0	9,00	8,88
n-C_4H_9	73	1,5005	+29,64°	57,35	9,54	8,45	$C_{18}H_{36}PO_3SN$	57,30	9,54	9,20
n-C_5H_{11}	75	1,4863	+54,65°	59,27	9,70	7,45	$C_{20}H_{40}PO_3SN$	59,38	9,87	7,65
i-C_3H_7	73	1,4943	+75,34°	55,10	8,95	9,00	$C_{16}H_{32}PO_3SN$	55,0	9,00	8,88
i-C_4H_9	81	1,4901	+78,06°	57,47	9,64	8,21	$C_{18}H_{36}PO_3SN$	57,30	9,54	8,20
i-C_5H_{11}	67	1,4920	+70,40°	59,71	9,90	7,80	$C_{20}H_{40}PO_3SN$	59,38	9,87	7,65

TABLE 3. Methiodides of O,O-Dialkyl S-Epilupinane Thiophosphates



R	Yield, %	mp, °C	Found, N, %	Empirical formula	Calculated, N, %
C_2H_5	83	131	3,15	$C_{15}H_{31}PO_3SNI$	3,00
n-C_3H_7	67	103	2,88	$C_{17}H_{35}PO_3SNI$	2,85
n-C_4H_9	78	133	2,63	$C_{19}H_{39}PO_3SNI$	2,69
n-C_5H_{11}	59	96	2,47	$C_{21}H_{43}PO_3SNI$	2,55
i-C_3H_7	64	137	3,00	$C_{17}H_{35}PO_3SNI$	2,85
i-C_4H_9	58	119	2,79	$C_{19}H_{39}PO_3SNI$	2,69
i-C_5H_{11}	70	105	2,45	$C_{21}H_{43}PO_3SNI$	2,55

TABLE 4. Methiodides of O,O-Dialkyl S-Lupinane Thiophosphates



R	Yield, %	mp, °C	Found, N, %	Empirical formula	Calculated, N, %
n-C_5H_{11}	69	114	2,36 2,59	$C_{21}H_{43}PO_3SNI$	2,55
i-C_3H_7	84	120	3,12 2,84	$C_{17}H_{35}PO_3SNI$	2,85
i-C_4H_9	75	110	2,76 2,44	$C_{19}H_{39}PO_3SNI$	2,69
i-C_5H_{11}	62	107	2,40	$C_{21}H_{43}PO_3SNI$	2,55

Methiodide of O,O-Diethyl S-Epilupinane Thiophosphate. To 0.5 g (0.0015 mole) of O,O-diethyl S-epilupinane thiophosphate in 5 ml of abs. ether was added 1 g (0.0075 mole) of CH_3I. The obtained precipitate was filtered and washed with abs. acetone.

The other methiodides were obtained in a similar manner (Tables 3 and 4).

CONCLUSIONS

We synthesized a number of O,O-dialkyl S-epilupinane thiophosphates, O,O-dialkyl S-lupinane thiophosphates, and their methiodides.

LITERATURE CITED

1. A. P. Brestkin, I. L. Brik, L. I. Ginetsinskaya, N. N. Godovikov, M. I. Kabachnik, and N. E. Teplov, Izv. Akad. Nauk SSSR, Ser. Khim., 1968, 2161.
2. A. P. Brestkin, I. L. Brik, L. I. Ginetsinskaya, N. N. Godovikov, M. I. Kabachnik, E. G. Kireeva, and S. A. Trifonova, Izv. Akad. Nauk SSSR, Ser. Khim., 1976, 883.
3. Kh. A. Aslanov, T. K. Kasymov, A. S. Sadykov, and A. I. Ishbaev, Khim. Geterotsikl. Soedin., 1970, 492.
4. V. G. Pesin and A. M. Khaletskii, Zh. Obshch. Khim., 31, 2508 (1961).

TETRAKIS(TRIFLUOROMETHYL)ETHYLENE ANION-RADICAL

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Within the framework of the simple MO theory, the formation of the anion-radical (AR) of π-conjugated systems in solution can be depicted by the transfer of the spare electron to a lower vacant MO of the starting molecule and the subsequent solvation of the AR. It could be expected that the hypothetical polarographic reduction of molecules with the same Hückel energies of the boundary π-MO, and specifically of the six-membered ring (benzene) and the double bond (ethylene), should proceed at close half-wave potentials. This hypothesis is valid for the corresponding analogs, in which the hydrogen atoms are completely replaced by CF_3 groups: hexakis(trifluoromethyl)benzene (I) and tetrakis(trifluoromethyl)ethylene (II).

The temperature dependence of the EPR spectrum in the range 299-185°K was studied for the AR of (I), which was obtained by the reduction of (I) with K metal in THF. The polarographic reduction of (I) and (II) at a dropping mercury electrode in DMF at 20°C was studied in the present paper. Tetra-n-butylammonium perchlorate was used as the supporting electrolyte. Both compounds give two reduction waves. The half-wave potentials, measured relative to the saturated calomel electrode, were respectively equal to $E_{1/2}'(I) = -0.525$ and $E_{1/2}''(I) = -1.305$ V, and also $E_{1/2}'(II) = -0.445$ and $E_{1/2}''(II) = -1.475$ V. The first waves are reversible and correspond to one-electron processes for the formation of the AR of (I) and (II). It is easily seen that the quantities $E_{1/2}'(I)$ and $E_{1/2}'(II)$ are actually close. A shift of $E_{1/2}'(II)$ by 0.08 V to the positive side when compared with $E_{1/2}'$ (I) is in order due to the smaller size of AR (II) and, consequently, the more negative ΔH value of solvation.

The AR of (I) and (II) were obtained by the electrolysis of solutions that respectively contained $1.5 \cdot 10^{-3}$ and $5.0 \cdot 10^{-3}$ M of the starting compounds. The EPR spectra were recorded on a JES-3BX radiospectrometer at the frequency of the X band (λ 3.2 cm). The hyperfine structure (HFS) of the EPR spectrum of AR (I) (Fig. 1) was caused by the splitting from 18 equivalent ^{19}F nuclei. Due to the low intensity, the extreme components of the HFS ($M_I = \pm 9; \pm 8$) do not appear in the spectrum. The lines $M_I = \pm 7$ are observed at a greater amplification of the

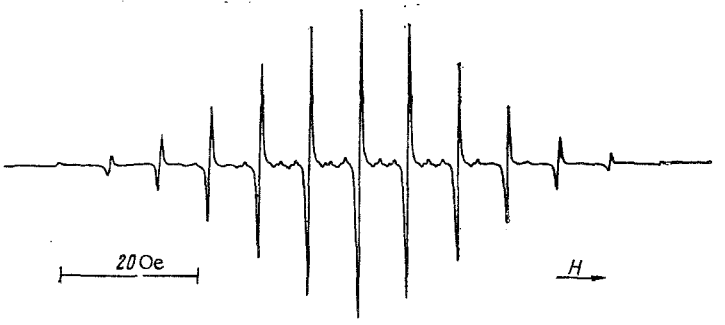

Fig. 1. EPR spectrum of $C_6(CF_3)_6^-$ anion-radical

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