CONCLUSIONS

We discovered a new thermal cationotropic isomerization of 1-trifluoroacetyl-4,6,8-trimethylazulene to the 2-isomer when it is heated in 95% sulfuric acid at 195°.

LITERATURE CITED

1. A. G. Anderson, R. G. Anderson, and G. T. Hollander, J. Org. Chem., 30, 131 (1965).
2. Yu. N. Porshnev and E. M. Tereshchenko, Zh. Organ. Khim., 11, 462 (1974).

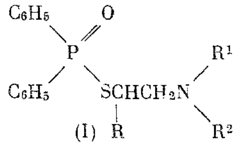
SYNTHESIS OF DIPHENYLPHOSPHINATES THAT HAVE ALIPHATIC NITROGEN-CONTAINING GROUPS IN THE β POSITION OF THE THIOALKYL RADICAL

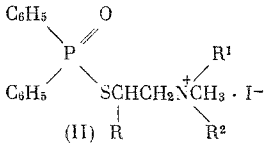
Kh. Kh. Gurdaliev, N. N. Godovikov,
M. I. Kabachnik, M. Kh. Berkhamov,
and N. A. Kardanov

UDC 542.91:547.1'118

We found that a combined type of inhibiting the enzymes butyrylcholinesterase (BuCE) and acetylcholinesterase (ACE) [1-3] is exerted by certain esters of diphenylthiophosphinic acid that have a nitrogen atom, attached to substituted aryl radicals, in the β position of the thioalkyl moiety [4] or a sulfur atom, attached to aliphatic radicals [5].

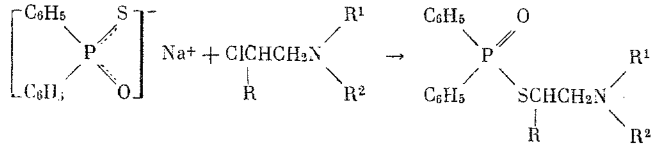
It seemed of interest to study the manifestation of the indicated inhibition effect for esters of diphenylthiophosphinic acid that have various aliphatic nitrogen-containing groupings in the β position of the alkthiol moiety. Methods for the synthesis of the S-(β-N,N-dialkylaminoalkyl) diphenylthiophosphinates (I) and their methiodides (II) are given in the present communication.


(I)


(II)

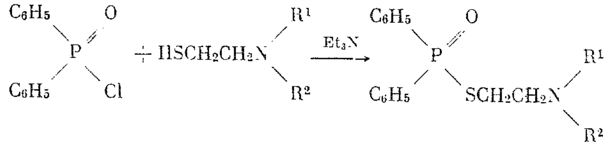
R=H, CH$_3$; R^1 = CH$_3$, C$_2$H$_5$: R^2=C$_2$H$_5$, cyclo-C$_6$H$_{11}$; R^1+R^2=CH$_2$(CH$_2$)$_3$CH$_2$, CH$_2$CH$_2$OCH$_2$CH$_2$

The (I) compounds were obtained by two different routes: by the reaction of sodium diphenylthiophosphinate with the appropriate (β-chloroalkyl)methylcyclohexylamines:



R = H, CH$_3$; R^1 = CH$_3$; R^2 = cyclo-C$_6$H$_{11}$

or by the reaction of the corresponding aminomercaptans with diphenylphosphinyl chloride in the presence of triethylamine:



R^1 = R^2 = C$_2$H$_5$; R^1 + R^2 = CH$_2$(CH$_2$)$_3$CH$_2$, CH$_2$CH$_2$OCH$_2$CH$_2$

Institute of Heteroorganic Compounds, Academy of Sciences of the USSR, Moscow. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 7, pp. 1644-1646, July, 1976. Original article submitted December 24, 1975.

TABLE 1. Diphenylthiophosphinates That Have Aliphatic Nitrogen-Containing Groups in the Thioalkyl Moiety $(C_6H_5)_2P(O)SCHRCH_2NR^1R^2$ (I)

R	R^1	R^2	Yield, %	n_D^{20}	Found, %			Empirical formula	Calculated, %		
					C	H	P		C	H	P
H	C_2H_5	C_2H_5	85	1,5877	—	—	9,2	$C_{18}H_{24}NOPS$	—	—	9,3
H	cyclo-C_6H_{11}	CH_3	80	1,5937	—	—	8,2	$C_{21}H_{28}NOPS$	—	—	8,2
CH_3	cyclo-C_6H_{11}	CH_3	72	1,5867	68,1	7,8	8,1	$C_{22}H_{30}NOPS$	68,2	7,8	8,0
H	$CH_2(CH_2)_3CH_2$		85	1,6007	66,0	6,7	9,0	$C_{19}H_{24}NOPS$	66,0	6,9	9,0
H	$CH_2CH_2OCH_2CH_2$		83	1,6042	62,1	6,5	8,3	$C_{18}H_{22}NO_2PS$	62,2	6,3	8,9

TABLE 2. Methiodides of Diphenylthiophosphinates That Have Aliphatic Nitrogen-Containing Groups in the Thioalkyl Moiety $[(C_6H_5)_2P(O)SCHRCH_2\overset{+}{N}CH_3R^1R^2]\cdot I^-$ (II)

R	R^1	R^2	Yield, %	mp, °C	Found, %			Empirical formula	Calculated, %		
					C	H	P		C	H	P
H	C_2H_5	C_2H_5	70	171—172	47,9	5,7	6,6	$C_{19}H_{27}INOPS$	48,0	5,7	6,5
H	cyclo-C_6H_{11}	CH_3	85	159—160	51,2	6,0	5,8	$C_{22}H_{31}INOPS$	51,3	6,0	6,0
CH_3	cyclo-C_6H_{11}	CH_3	89	*	—	—	5,5	$C_{23}H_{33}INOPS$	—	—	5,8
H	$CH_2(CH_2)_3CH_2$		86	181—182	—	—	6,3	$C_{20}H_{27}INOPS$	—	—	6,4
H	$CH_2CH_2OCH_2CH_2$		83	188—189 (dec.)	46,8	5,2	6,1	$C_{19}H_{25}INO_2PS$	46,9	5,2	6,3

*Thick glassy mass.

The purity of the obtained compounds was checked by TLC.

The (I) compounds by reaction with CH_3I in nitromethane were converted to the corresponding methiodides (II), which were recrystallized from a 2 : 1 ether–ethanol mixture.

EXPERIMENTAL

The TLC was run on KSK silica gel in various solvents, while iodine vapors were used for the development.

S-(β-N-Methyl-N-cyclohexylaminoethyl) Diphenylthiophosphinate. A suspension of 0.03 mole of diphenylthiophosphinic acid in 25 ml of abs. alcohol was neutralized with sodium ethylate to phenolphthalein. To the obtained solution was added 0.03 mole of N-methyl-N-β-chloroethylcyclohexylamine in 10 ml of alcohol and the stirred mixture was heated at 80° for 8 h. The obtained precipitate was filtered, the solvent was removed from the filtrate, and the residue was repeatedly reprecipitated from ether solution with hexane.

S-(α-Methyl-β-N-methyl-N-cyclohexylaminoethyl) diphenylthiophosphinate was obtained in a similar manner (Table 1).

S-(β-N,N-Diethylaminoethyl) Diphenylthiophosphinate. To a solution of 0.037 mole of diphenylphosphinyl chloride in 50 ml of abs. ether at ~20° was added in drops a mixture of 0.05 mole of β-N,N-diethylaminoethyl mercaptan and 0.042 mole of triethylamine, and the mixture was stirred for 1 h. The obtained precipitate was filtered and washed with 50 ml of ether, the filtrate was washed with 50 ml of water, and the ether extract was dried over Na_2SO_4. The solvent was removed, and the residue was repeatedly reprecipitated from ether solution with abs. hexane and then dried.

S-(β-N-piperidylethyl) diphenylthiophosphinate and S-(β-N-morpholylethyl) diphenylthiophosphinate were obtained in a similar manner (see Table 1).

S-(β-N,N-Diethylaminoethyl) Diphenylthiophosphinate Methiodide. To 2.9 g (0.01 mole) of S-(β-N,N-diethylaminoethyl) diphenylthiophosphinate in 10 ml of abs. nitromethane was added a solution of 2.8 g (0.02 mole) of CH_3I in 3 ml of nitromethane. The reaction mixture was let stand overnight, evaporated in vacuo, and the residue was purified by recrystallization from a 2 : 1 ether–ethanol mixture. The constants, yields, and analyses for the methiodides are given in Table 2.

CONCLUSIONS

We synthesized a number of diphenylthiophosphinates that have aliphatic nitrogen-containing groups in the thioalkyl radical, and also their methiodides.

LITERATURE CITED

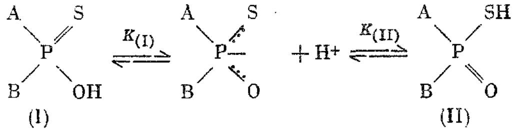
1. A. P. Brestkin, I. L. Brik, R. I. Volkova, N. N. Godovikov, Kh. Kh. Gurdaliev, M. I. Kabachnik, and N. A. Kardanov, Dokl. Akad. Nauk SSSR, 200, 103 (1971).
2. A. P. Brestkin, R. I. Volkova, N. N. Godovikov, M. I. Kabachnik, and N. A. Kardanov, Izv. Akad. Nauk SSSR, Ser. Khim., 622 (1973).
3. R. I. Volkova, N. A. Kardanov, A. P. Brestkin, N. N. Godovikov and M. I. Kabachnik, Izv. Akad. Nauk SSSR, Ser. Khim., 2114 (1973).
4. N. N. Godovikov, Kh. Kh. Gurdaliev, and M. I. Kabachnik, Zh. Obshch. Khim., 41, 1942 (1971).
5. N. N. Godovikov, N. A. Kardanov, and M. I. Kabachnik, Zh. Obshch. Khim., 42, 273 (1972).

DISSOCIATION CONSTANTS OF PHOSPHORUS MONOTHIOACIDS IN ABSOLUTE ETHANOL AND NITROMETHANE

A. G. Kozachenko, A. B. Uryupin,
L. L. Spivak,* A. A. Grigor'eva,
E. I. Matrosov, M. I. Kabachnik,
and T. A. Mastryukova

UDC 541.124.7:547.1'118

In connection with a study of the thione–thiol tautomeric equilibrium, the dissociation constants of some phosphorus monothioacids in aqueous alcohol media were measured [1-3], and also the protolysis constants in benzene and chlorobenzene [4].



(I) (II)

It was established that the position of the tautomeric equilibrium depends on the nature of the substituents on the P atom (A and B) and on the medium. Here in the nonpolar media C_6G_6 and C_6H_5Cl the equilibrium is shifted completely toward the thione forms (I), from which it follows that the measured protolysis constants belong specifically to these forms. In aqueous alcohol solutions the shift of the equilibrium toward the thiol forms (II) is greater the more electronegative the A and B substituents, and the higher the amount of water in the solution. In this case the measured dissociation constant is equal to the effective dissociation constant of the equilibrium mixture

$$K_{HA} = K_{(I)}K_{(II)}/(K_{(I)} + K_{(II)})$$

Here for the dialkylthiothiophosphinic acids $K_{(II)} \gg K_{(I)}$ and $K_{HA} \approx K_{(I)}$.

In the present paper we measured the dissociation constants and the position of the tautomeric equilibrium of some phosphorus monothioacids in solvents of medium ionizing and dissociating capacity, and specifically in abs. C_2H_5OH and CH_3NO_2. The phosphorus monothioacids were selected in such manner that the electron-acceptor properties of the substituents on the P atom could be varied as such as possible. The methods used to prepare and purify the employed acids were described previously [5-9], while their physicochemical constants

---

*Deceased.

Institute of Heteroorganic Compounds, Academy of Sciences of the USSR, Moscow. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 7, pp. 1646-1648, July, 1976. Original article submitted December 31, 1975.