SOME AZOLE DERIVATIVE PHOSPHORIC AND THIOPHOSPHORIC ESTERS

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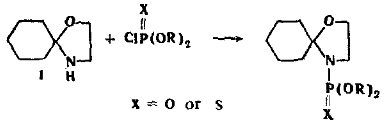
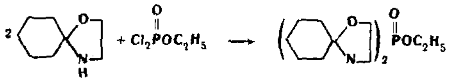
Reaction of spiro[cyclohexane-1, 2'-oxazolidine] (I) with phosphorochloridic and phosphorochloridothionic acids gave the corresponding ethers. It did not prove possible to prepare derivatives containing dispiro[cyclohexane-1, 2'-oxazolidine] radicals. Reaction of 2-thio-5, 5-dimethyloxazolid-4-one with diethylphosphorochloridate led to isolation of an alkylation product. 5, 5-Dimethylhydrantoin did not react with chlorides of phosphoric acid under the reaction conditions of these particular experiments.

Continuing work on the synthesis of esters of phosphoric and thiophosphoric acids containing heterocyclic radicals [1], we have prepared some spiro[cyclohexane-1, 2'-oxazolidine] (I) esters. It is known [2–4] that cyclohexanone and amino alcohols give a pure oxazolidine of spiran structure. Hence, one would expect reaction with the acid halides derived from phosphoric and thiophosphoric acids to give derivatives formed according to the equation:



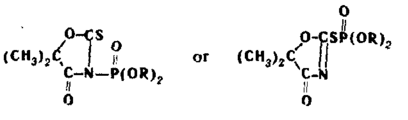
Reaction of I, dissolved in benzene or ether, with the appropriate acid chloride derived from phosphoric and thiophosphoric acids, in the presence of triethylamine or pyridine, leads to synthesis of the following esters: spiro[cyclohexane-1,2'-oxazolidyl]diethyl phosphate (II), spiro[cyclohexane-1, 2'-oxazolidyl] di-isobutyl phosphate (III), spiro[cyclohexane-1, 2'-oxazolidyl]diethyl phosphate (IV), and spiro[cyclohexane-1,2'-oxazolidyl]diphenylamidophosphate (V). The table gives analytical data and physical constants found for these compounds.

Reaction of ethyl phosphorodichloridate with I was assumed to give dispiro[cyclohexane-1, 2'-oxazolidyl] ethyl phosphate according to the equation



However, the product isolated did not analyze correctly, and a more detailed investigation was not made.

Treatment of 2-thio-5, 5'-dimethyloxazolid-4-one (VII) with an acid chloride derived from a phosphoric acid would be expected to give a number of compounds of the type



Repeated runs, under various conditions, for the reaction between diethyl phosphorochloridate (VIII) and compound VII gave complex mixtures from which all that could be isolated purely were crystals that did not contain phosphorus. Analysis corresponded to an alkylation product, demonstrated by the undepressed mixed melting point with 2-thio-5, 5-dimethyl-3-ethyloxazol-4-one, prepared by ethylating VII with diethyl sulfate [5].

The action of phosphorodiphenylamidic chloride (IX) on VII is found to give phosphorodiphenylamidic acid $(C_6H_5NH)_2PO(OH)$.

A study was also made of the effect of the acid chlorides derived from phosphoric acid on 5, 5-dimethylhydantoin (XII). Under ordinary conditions, when the reactants are heated together in a solvent, compound XII does not react with these acid chlorides, and the starting materials are isolated unchanged. When, as has been pointed out [6], the reaction is run in the presence of sodium methoxide, as alkylation product is isolated along with the starting materials.

EXPERIMENTAL

I was prepared by condensing cyclohexanone with ethanolamine in the known way [7]. 54° C (2 mm); d_4^{20} 1.0181; n_D^{23} 1.4805.

Spiro[cyclohexane 1, 2'-oxazolidyl]-N-diethyl phosphate (II). A solution of 12.2 g (0.07 mole) diethyl phosphorochloridate (VI) in 30 ml ether was added gradually to a solution of 10 g I (0.07 mole) and 10.9 g Et_3N in 50 ml ether. The mixture was heated for 3 hr on a water bath, the amine hydrochloride washed out with water, the ether solution dried over Na_2SO_4, the ether distilled off, and the residue distilled twice. 10.5 g II was obtained, as a colorless oily liquid.

Spiro[cyclohexane-1, 2'-oxazolidyl]-N-di-isobutyl phosphate (III). Prepared similarly to II by heating for 9 hr: 7.9 g I (0.05 mole), 7.8 g Et_3N in 50 ml ether, and 12.5 g (0.05 mole) di-isobutyl phosphorochloridate added over a period of 30 min. 13.8 g III was obtained by working up the products in the way described above. It formed a rather viscous colorless oil.

Spiro[cyclohexane-1, 2'-oxazolidyl]-N-diethyl phosphate (IV). A solution of 6.5 g (0.03 mole) diethyl phosphorochloridothionate was added to a solution of 5.2 g I (0.03 mole) and 6 g pyridine in 50 ml benzene. The whole was heated for 4 hr at 60° C, and for 1 hr at 80° C. The resinous looking reaction product was, after removing solvent and pyridine hydrochloride, distilled with decomposition. Yield 2.3 g of a yellowish liquid with an unpleasant odor.

Spiro[cyclohexane-1, 2'-oxazolidyl]-N-diphenylamidophosphate (V). 3 g (0.002 mole) I and 3 g (0.001 mole) phosphorodiphenylamidic chloride were dissolved in 20 ml pyridine. The transiently yellow reaction mixture was heated for 4 hr at 100° C, then poured into water. A solid resinous mass separated. One recrystallization from acetone and two from MeOH gave 2.7 g white product in the form of minute crystals.

2-Thio-5, 5-dimethyloxazolid-4-one (VII) was prepared from acetone cyanohydrin and ammonium thiocyanate [8], mp 152° C.

Reaction of VII with VIII. 11 g (0.06 mole) VIII was added to 8 g (0.05 mole) VII 7.9 g Et_3N, and 100 ml benzene, and the whole was heated for 2 hr at 70°–80° C. The product was worked up similarly to II, to give colorless crystals (3.5 g) mp 61°–62° (ex MeOH). Found: 18.55; 18.73%, calculated for $C_7H_{11}NO_2S$: S 18.51%.

Spiro[cyclohexane-1,2'-oxazolidine] Derivatives

Compound	Bp, °C (pressure, mm)	n_D^{20}	d_4^{20}	Formula	MR		P, %		Yield, %
					Found	Calculated	Found	Calculated	
II	121—123 (1.5)	1.4650	1.1214	$C_{12}H_{24}NO_4P$	68.35	69.14	10.95 10.85	11.17	53.6
III	122—123 (0.07)	1.4610	1.0480	$C_{16}H_{32}NO_4P$	87.06	87.61	9.47 9.31	9.29	74.1
IV	146—147 (3)	1.5000	1.1450	$C_{12}H_{24}NO_3PS$*	75.36	75.00	10.52 10.98	10.56	21.1
V	212—213**	—	—	$C_{20}H_{26}N_3O_2P$	—	—	8.47 8.22	8.34	64.5

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*Found: S 11.04; 11.68%. Calculated: S 10.94%.

**Mp.

Reaction of VII with IX. 1.8 g (0.01 mole) VII, 3.15 g (0.01 mole) IX, 40 ml pyridine, and 200 ml benzene were heated together under reflux for two days. The product was isolated as the finest of small hairs, mp 222° C. Found: P 13.24; 13.34%, calculated for $C_{12}H_{13}NO_2P$: P 13.22%.

REFERENCES

1. B. A. Arbuzov, A. R. Bil'chinskaya, and V. A. Frinovskaya, ZhOKh, **33**, 3076, 1963.
2. E. D. Bergmann, E. Limkin, and S. Pinchas, Rec. tray. chim., **71**, 168, 1952.
3. E. M. Hancock and A. C. Cope, J. Am. Chem. Soc., **66**, 1738, 1944.
4. E. M. Hancock, E. M. Hardy, D. Heyl, M. E. Wright, and A. C. Cope, J. Am. Chem. Soc., **66**, 1747, 1944.
5. J. S. H. Davies, W. H. Hook, and F. Long, J. Chem. Soc., 39, 1950.
6. S. P. Lingo and H. R. Henze, J. Am. Chem. Soc., **61**, 2030, 1939.
7. A. C. Cope and E. M. Hancock, J. Am. Chem. Soc., **64**, 1505, 1942.
8. K. Iwaya and S. Mitsuhashi, Jap. pat. no. 179886, 1949; C. A., **46**, 1593, 1952.

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