Reaction of a Phosphorothioate Ester with Ethylene Oxide. Evidence for a Five-covalent Intermediate

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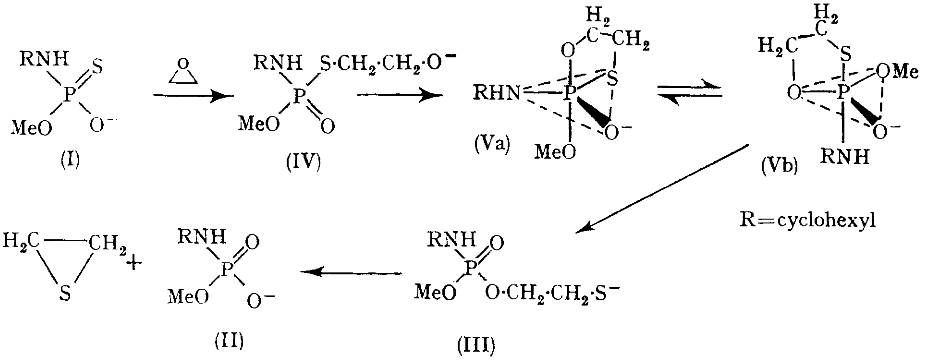
RECENT work on nucleophilic attack on fully esterified phosphates and phosphonates has shown that several reactions, particularly those involving the opening or closing of a five-membered ring containing phosphorus, can be satisfactorily rationalised on the assumption of a five-covalent intermediate, with the phosphorus at the centre of a trigonal bi-pyramid, in which pseudorotation is permitted subject to certain restrictions.[1] One consequence of this assumption is that, in favourable cases, it should be possible to observe the migration of the phosphoryl group intact to a vicinal nucleophile.[2] Previous attempts to observe such a process have been uniformly unsuccessful and in some cases it has been specifically excluded.[3] We report a system in which it seems essential to postulate its occurrence.

Aqueous solutions of sodium methyl *N*-cyclohexylphosphoramidothioate[4] (I) (0·5M) on treatment with excess of ethylene oxide (2 equiv.) at 0—5°, gave ethylene sulphide, which was identical (g.l.c. and ^{1}H n.m.r. spectrum) with an authentic sample. With CCl_4 present to extract, and hence reduce, the amount of polymerisation of ethylene sulphide, the yield was 70% which must be an absolute minium. Chromatography showed that the major product (85%) was sodium methyl *N*-cyclohexylphosphoramidate (II)[4] accompanied by small amounts 12—15% of slow-running products. The reaction thus shows a striking similarity to the reaction of thiocyanate ion with epoxides the mechanism of which is well established.[5]



While almost all *O*-phosphorylated derivatives of 2-mercaptoethanol could eliminate ethylene sulphide under the reaction conditions (pH 9—10), the concomitant high yield of (II) requires that at least 55% of the reaction must proceed *via* the ester (III). Since initial attack of (I) on the epoxide will give the *S*-phosphoryl ester (IV), it is clear that a ready conversion of (IV) → (III) must occur. This can be accommodated on the basis of the reaction scheme involving five covalent intermediates, if the rate of pseudorotation (Va) → (Vb) is faster than the rate of elimination of methoxide ion from (Va).

An alternative explanation involving initial expulsion of cyclohexylamine from (IV) by the vicinal alkoxide ion giving a cyclic triester (VI), which is then opened by the liberated amine with expulsion of thiolate ion, is extremely unlikely since phosphoramidate esters invariably lose alkoxide ion rather than amine under nucleophilic attack in basic conditions.

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