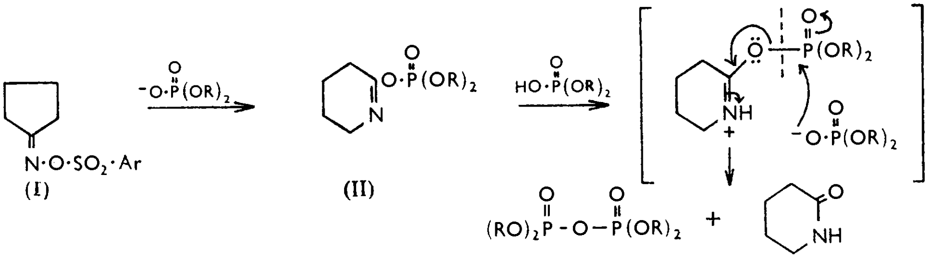
319. *Reactions between O-Benzenesulphonyl-lactims and Phosphates.*

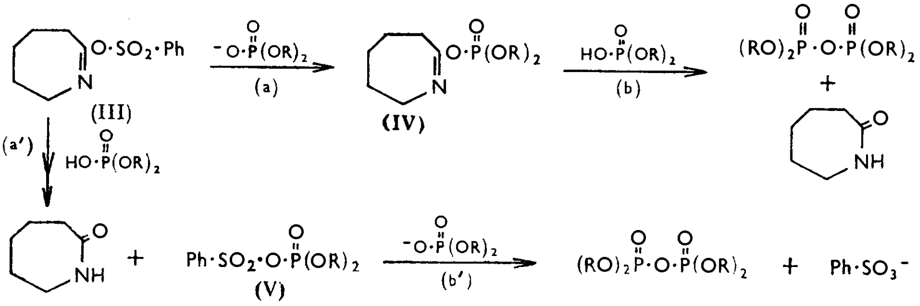
By R. J. W. Cremlyn.

Several *O*-benzenesulphonyl-lactims have been treated with diesters of phosphoric acid and an excess of a tertiary base in nitromethane solution. The hexanolactam derivative gave the highest yields of pyrophosphates. Yields from similar reactions employing tetra-alkylammonium phosphates without an excess of base were smaller.

One method[1] for the preparation of pyrophosphates utilises spontaneous Beckmann rearrangement of a ketoxime benzenesulphonate, preferably cyclopentanone oxime *p*-nitrobenzenesulphonate[2] (I; Ar = *p*-NO_2·C_6H_4) in a polar solvent at room temperature. The reaction probably proceeds in stages, as shown, although the intermediate imidoyl phosphate (II) has not been isolated.



The optimum preparative conditions were found to require the use of 2 mol. of the phosphate and 1 mol. of triethylamine in anhydrous nitromethane. This procedure has also been extended to the production of unsymmetrical *P*¹*P*²-pyrophosphates, though in considerably lower yields.[1] A modification of this scheme has now been investigated: the lactams, prepared by Beckmann rearrangement of cyclic oximes, were converted into imidoyl benzenesulphonates (*e.g.*, III) by reaction with benzenesulphonyl chloride as described by Oxley, Peak, and Short.[3] Subsequent treatment with 2 mol. of a secondary phosphate in the presence of an excess of a tertiary base and in a polar solvent yielded pyrophosphates. Two routes for phosphorolysis of *O*-benzenesulphonylhexanolactim can be envisaged. Neither of the intermediates (IV) and (V) has been isolated, and therefore in both cases the speeds of stages a and b (or a′ and b′) are probably comparable.



The presence of an excess of a tertiary base increases the yield of pyrophosphate, so the phosphorolysis of benzenesulphonyl-lactims is base-catalysed, in contrast to the phosphorolysis of ketoxime benzenesulphonates. As the latter reaction is generally

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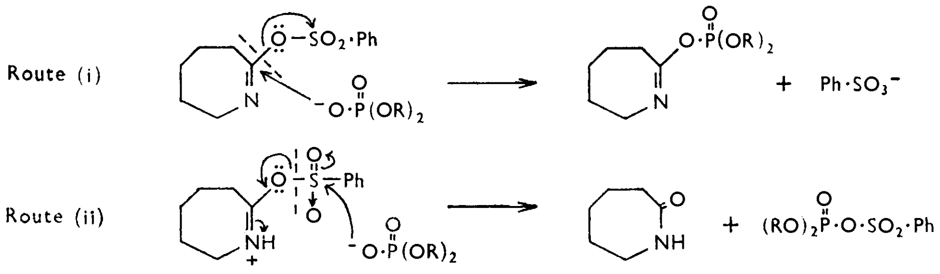
[1] Kenner, Todd, and Webb, *J.*, 1956, 1231.

[2] Oxley and Short, *J.*, 1948, 1514.

[3] Oxley, Peak, and Short, *J.*, 1948, 1618.

regarded as proceeding by way of the imidoyl phosphate (IV) it is likely that the pyrophosphate arises from the benzenesulphonyl-lactim through the alternative route (ii) or by a combination of both routes. In either case, the function of excess of base is presumably to increase the degree of ionisation of the phosphoric acid, and consequently the ease of anion-exchange (route i; a, b) or anion attack (route ii; a′, b′):



6-Hexanolactam, valerolactam, and butyrolactam have been studied. The progress of the reaction with 1 mole of benzenesulphonyl chloride and slightly more than 1 mole of triethylamine in benzene was followed by the separation of the triethylamine hydrochloride. When reaction was complete, the mixture was treated with 2 mol. of the phosphate and an excess of a tertiary base in nitromethane and then left at room temperature. The yield of pyrophosphate was estimated by fission with cyclohexylamine.[4] Care was taken that all the sulphonyl chloride had been consumed before addition of the phosphate, in order to exclude the alternative production of pyrophosphates from arylsulphonyl halides.[5]

TABLE 1.

	Hexanolactam	Valerolactam	Butyrolactam
Lactam taken (mmoles)	4·4	5·0	4·3
* $(Ph{\cdot}CH_2{\cdot}O)_2PO_2H$ (mmoles)	8·8	10·0	8·6
Pyrophosphate yield (%)	90	80	55

* In similar experiments with $(PhO)_2PO_2H$ the pyrophosphate yields were 29, 16, and 0 respectively.

The results, summarised in the Table, show that the yield of pyrophosphate decreases sharply with decreasing ring-size of the lactam. An increasing proportion of *N*-benzenesulphonylation may be responsible; this side-reaction would be favoured as the ring-size decreases from 7 to 5 according to the concepts of Brown, Brewster, and Schechter.[6] *O* → *N*-Migration of the sulphonyl or phosphoryl group cannot be responsible because, by analogy with work of Huisgen and Reinertshofer,[7] on the isomerisation of *N*-nitrosolactams to the corresponding cyclic diazo-esters, this migration should be facilitated by increasing ring-size.

In further experiments benzenesulphonylhexanolactim was treated with a tetra-alkylammonium phosphate, followed by a secondary phosphate in nitromethane; and excess of base was not employed. The yield of pyrophosphate fell to approximately 25% and reversal of the order of addition of the reactants to the benzenesulphonyl-lactim did not appreciably alter the result. The low yields were almost certainly due to the absence of the excess of base, because when the reaction of benzenesulphonylhexanolactim with 2 mol. of dibenzyl hydrogen phosphate was repeated, in the presence of only one mol. of triethylamine, the yield of tetrabenzyl pyrophosphate was only 30% (cf. Table).

The benzenesulphonyl-lactims were brown oils incapable of purification and therefore the action of various sulphonyl chlorides on hexanolactam was studied. The relative

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[4] Corby, Kenner, and Todd, *J.*, 1952, 1234.
[5] Corby, Ph.D. Thesis, Cambridge, 1952.
[6] Brown, Brewster, and Schechter, *J. Amer. Chem. Soc.*, 1954, **76**, 467.
[7] Huisgen and Reinertshofer, *Annalen*, 1952, **575**, 197.

times required for 90% completion of reaction (estimated from the precipitation of triethylamine hydrochloride) were: methanesulphonyl chloride, 5 min.; *p*-acetamidobenzenesulphonyl chloride, 20 min.; *p*-nitrobenzenesulphonyl chloride, 2½ hr.; benzenesulphonyl chloride, 12 hr.; toluene-*p*-sulphonyl chloride, 50% after 46 hr. (this reaction did not go to completion). The products were not solid, and only from the benzenesulphonyl derivatives were appreciable quantities of pyrophosphates produced under standard conditions of phosphorolysis.

EXPERIMENTAL

Tetrabenzyl Pyrophosphate.—Benzenesulphonyl chloride (0·58 c.c., 4·4 mmoles) was added to a solution of hexanolactam [8] (0·50 g., 4·4 mmoles) in dry benzene (2 c.c.) and triethylamine (0·80 c.c., 5·0 mmoles) with external cooling. After 12 hr. at room temperature filtration yielded triethylamine hydrochloride (0·520 g., 93%). The brown liquor was diluted with nitromethane (6 c.c.), treated with dibenzyl hydrogen phosphate (2·4 g., 8·8 mmoles) and triethylamine (1·9 c.c., 3 mmoles), and left for 19 hr. at room temperature, then extracted with chloroform (200 c.c.). The extract was washed with 50% aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated *in vacuo*. Treatment with cyclohexylamine (2 c.c.) in benzene (8 c.c.) gave, after 12 hr., crystalline cyclohexylammonium dibenzyl phosphate (1·36 g., 90%). The filtrate therefrom, when worked up as usual,[4] gave a brown oil (0·213 g.).

Tetraphenyl Pyrophosphate.—Anhydrous tetraethylammonium diphenyl phosphate (0·880 g., 2·2 mmoles) in nitromethane (4 c.c.) was added to a benzene solution of *O*-benzenesulphonylhexanolactim (prepared from 0·250 g. of the lactam). After 2 days at room temperature, anhydrous diphenyl hydrogen phosphate (0·550 g., 2·2 mmoles) was added, and the mixture left for a further 3 days at room temperature. After the usual working-up, the neutral fraction was treated overnight with cyclohexylamine (1 c.c.) in benzene (4 c.c.); this gave cyclohexylammonium diphenyl phosphate (0·430 g., 56%) and diphenyl cyclohexylphosphoramidate (0·134 g., 19%).

These examples illustrate the general procedure for the experiments summarised in the Table.

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[8] Eck and Marvel, *Org. Synth.*, Coll. Vol. II, 1st edn. 1943, p. 371.