# A CONVENIENT METHOD FOR THE SYNTHESIS OF DIIODO COMPOUNDS. FACILE CLEAVAGE OF CYCLIC ETHERS BY PHENYL DICHLOROPHOSPHATE AND SODIUM IODIDE

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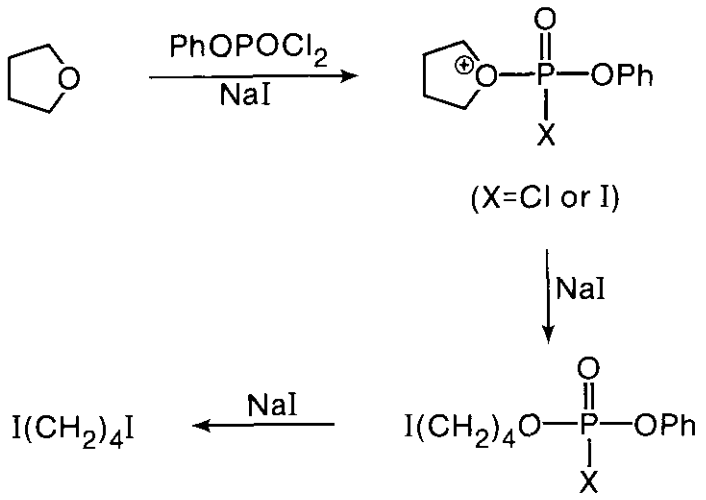
Abstract — Cyclic ethers were found to react readily with phenyl dichlorophosphate and sodium iodide to give diiodo compounds under mild reaction conditions.

Recently, we observed that β-diketones gave rise to β-chloro-α,β-unsaturated ketones, when subjected to treatment with lithium hydride, phenyl dichlorophosphate and lithium chloride.[1,2] The method can, in principle, be extended to the preparation of the β-iodo analogs using sodium iodide - in place of lithium chloride. This expectation was experimentally shown to be valid.[3] Several diketones were readily converted to the corresponding β-iodo enones when exposed to these reagents. Interestingly, when tetrahydrofuran was used as a solvent, 1,4-diiodobutane, resulting apparently from the cleavage of tetrahydrofuran, was also isolated. We have undertaken a study of this unexpected and potentially useful finding and now wish to report a facile cleavage, under remarkably mild conditions, of cyclic ethers leading directly to diiodo compounds[4] which are of broad synthetic utility.

As one would anticipate from the hypothetical mechanism outlined in Scheme 1, both phenyl dichlorophosphate and sodium iodide were found to be essential to induce the cleavage of the tetrahydrofuran ring, whereas lithium hydride was not required as a reagent. Treatment of an excess of tetrahydrofuran with phenyl dichlorophosphate (yield-limiting agent) and sodium iodide (5 equiv.) at reflux for 24 h resulted in an 85% yield of 1,4-diiodobutane.

The generality of the reaction is apparent from the results summarized in Table 1 for the seven ethers examined. Apart from operational simplicity, uniformly

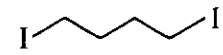
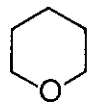
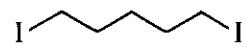
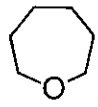
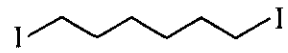
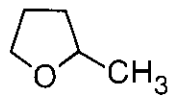
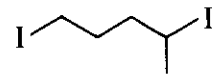
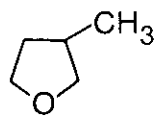
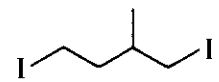
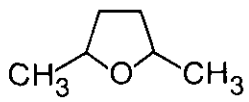
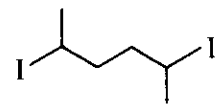
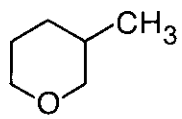
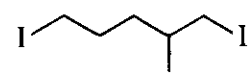
## Scheme 1




high yields of products, and virtually neutral conditions, a further salient feature of the reaction lies in its applicability to rings of various sizes. Tetrahydropyran (Entry 2) and oxepane (Entry 3) were converted smoothly to 1,5-diiodopentane and 1,6-diiodohexane respectively under similar reaction conditions. Equally effective was the cleavage of substituted cyclic ethers. Excellent results were obtained for a number of selected examples (Entries 4-7), regardless of the substitution pattern.

Although the mechanism of the reaction remains to be ascertained, it is clear that hydriodic acid[8] is not responsible for the ether ring cleavage. This is evident from the observation that the reaction of tetrahydrofuran with phenyl dichlorophosphate and sodium iodide in the presence of 1 equimolar calcium hydride also gave rise to a high yield (88%) of 1,4-diiodobutane. Experimental results also suggested that either phenyl chloroiodophosphate (PhOPOClI) or the corresponding diiodo compound ($PhOPOI_2$) generated in situ served as the activating agent, since neither phenyl dichlorophosphate alone nor its combination with lithium chloride/bromide was found to be effective. Moreover, when the reaction of 2-methyltetrahydrofuran was worked up prior to completion (4 h), three products, 1,4-diiodopentane, 5-iodo-2-pentanol and the corresponding phenyl halophosphate [$I(CH_2)_3CH(CH_3)OPO(OPh)X$ (X = Cl or I)], were isolated in nearly equal amount. This observation is consistent with the hypothetical pathway

Table 1. Transformation of cyclic ethers to diiodo compounds with phenyl dichlorophosphate and sodium iodide.

| Entry | Ether | Time (h)[a] | Product | % Yield[b] |
|---|---|---|---|---|
| 1 |  | 24 |  | 85 |
| 2 |  | 24 |  | 83 |
| 3 |  | 36 |  | 99 |
| 4 |  | 24 |  | 98 |
| 5 |  | 40 |  | 85 |
| 6 |  | 48 |  | 96 |
| 7 |  | 35 |  | 84 |

[a]All reactions were carried out at refluxing temperature.

[b]Yields are based on phenyl dichlorophosphate.

depicted in Scheme 1 and further indicates that the ether ring opening process is $S_N2$ in nature.

The general experimental procedure is illustrated below with tetrahydrofuran. To a solution of phenyl dichlorophosphate (706 mg, 3.35 mmol) in tetrahydrofuran (5 ml) under an atmosphere of argon, was added sodium iodide (2.509 g, 16.73 mmol). The reaction mixture was heated to reflux in dark for 24 h. It was then cooled to room temperature and filtered. The residue was thoroughly washed with petroleum ether. Concentration of the filtrate gave a yellow liquid which was subjected to column chromatography on silica gel. Elution with petroleum ether gave 1,4-diiodobutane (878 mg; 85% yield).

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