

DIPHOSPHORUS TETRAIODIDE (P_2I_4) A VALUABLE REAGENT FOR REGIOSELECTIVE
SYNTHESIS OF IODOALKANES FROM ALCOHOLS.^{1,13,14}

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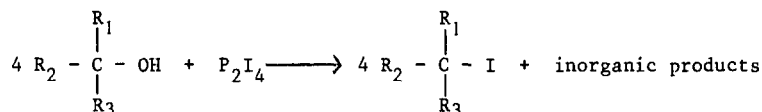
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Summary : Primary, secondary and tertiary alcohols are transformed regioselectively and in high yield to alkyl iodides by P_2I_4 in CS_2 and at 20°C.

The synthesis of alkyl iodides has attracted, for a long time, wide interest in organic synthesis. Among the different routes to such derivatives, are the ones using alcohols as readily available starting materials and a substitution reaction for the introduction of the iodine atom². Substitution reactions have been conducted under neutral or acidic conditions. The former and generally unsatisfactory for the synthesis of tertiary alkyl iodides while acidic reaction conditions sometimes lead to substantial amounts of rearranged products³.

We would like to reintroduce diphosphorus tetraiodide (P_2I_4) a well characterized, stable, orange gold, crystalline solid (mp : 125°)^{4,5} as a powerful reagent in organic synthesis, especially for the synthesis of alkyl halides from alcohols. (Scheme I).

SCHEME I



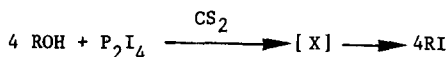
P_2I_4 has been used only scarcely as a reagent since Berthelot's⁶ report disclosing the P_2I_4 mediated 1-iodo-2-propene synthesis from glycerol. It has been introduced by Kuhn⁷ for the deoxygenation of glycols to olefins in the polyene field and has been since then mainly used for this purpose⁸.

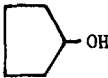
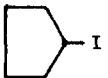
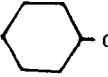
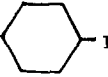


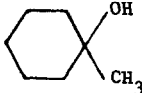

Aliphatic alcohols have already been reacted with P_2I_4 : instead of the desired diphosphorus tetraalkoxides diphosphate esters $(RO)_2P-P(OR)_2$, the authors⁹ found an orange polymeric amorphous material as the sole product.

We have reinvestigated this reaction and found that primary, secondary and tertiary alkyl iodides and diiodoalkanes are formed from the corresponding alcohol in high yield together with the amorphous material already described⁹.

In a typical experiment the alcohol (10^{-3} mole) is added to a stirred P_2I_4 ($0.26 \cdot 10^{-3}$ mole) solution^{7,10,11} in CS_2 (10ml) maintained at 0°C under argon. The orange solution turns brown, then an orange precipitate is formed. At this stage solid potassium carbonate is added, followed by saturated aqueous carbonate solution. The aqueous layer is carefully extracted with ether (30ml x 6 times). The extracts are filtered on cellite before drying over $MgSO_4$. Removal of the solvents leads to a crude product from which the pure alkyl iodide is obtained by distillation or chromatography (PLC).

TABLE I



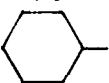
entry	ROH	RI	Yield % (time hr)	bp _{mm Hg} °C
a	$\text{nC}_6\text{H}_{13}\text{CH}_2\text{OH}$	$\text{nC}_6\text{H}_{13}\text{CH}_2\text{I}$	69 (24)	bp ₁₅ : 83
b	$\text{nC}_7\text{H}_{15}\text{CH}_2\text{OH}$	$\text{nC}_7\text{H}_{15}\text{CH}_2\text{I}$	80 (24)	bp ₁₅ : 99
c	$\text{C}_6\text{H}_5\text{-CH}_2\text{CH}_2\text{OH}$	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{I}$	80 (24)	bp ₁₅ : 114
d	$\text{C}_2\text{H}_5\underset{\text{CH}_3}{\text{CH}}\text{-CH}_2\text{OH}$	$\text{C}_2\text{H}_5\underset{\text{CH}_3}{\text{CH}}\text{-CH}_2\text{I}$	71 (144)	bp ₁₆ : 40
e	$\text{C}_2\text{H}_5\underset{\text{OH}}{\text{CH}}\text{-C}_2\text{H}_5$	$\text{C}_2\text{H}_5\underset{\text{I}}{\text{CH}}\text{-C}_2\text{H}_5$	81 (24)	bp ₇₆₀ : 145
f	$\text{C}_3\text{H}_7\underset{\text{OH}}{\text{CH}}\text{-CH}_3$	$\text{C}_3\text{H}_7\underset{\text{I}}{\text{CH}}\text{-CH}_3$	84 (24)	bp ₇₆₀ : 143
g	$\text{C}_6\text{H}_{13}\underset{\text{OH}}{\text{CH}}\text{-CH}_3$	$\text{C}_6\text{H}_{13}\underset{\text{I}}{\text{CH}}\text{-CH}_3$	70 (24)	bp ₁₅ : 91
h			88 (24)	bp ₁₃ : 50
i			88 (96)	bp ₁₅ : 72
j			45 (110)	PLC ¹²
k	$(\text{CH}_3)_3\text{COH}$	$(\text{CH}_3)_3\text{CI}$	73 (0.5)	bp ₇₆₀ : 99
l	$\text{C}_4\text{H}_9\underset{\text{OH}}{\text{C}}(\text{CH}_3)_2$	$\text{C}_4\text{H}_9\underset{\text{I}}{\text{C}}(\text{CH}_3)_2$	82 (0.5)	bp ₁₂ : 58
m			86 (1)	(PLC) ¹²
n	$\text{C}_6\text{H}_5\text{CH}_2\text{OH}$	$\text{C}_6\text{H}_5\text{CH}_2\text{I}$	89 (0.5)	bp ₁₅ : 102
o	$\text{C}_6\text{H}_5\underset{\text{OH}}{\text{CH}}\text{-CH}_3$	$\text{C}_6\text{H}_5\underset{\text{I}}{\text{CH}}\text{-CH}_3$	90 (1)	unstable
p	$\text{C}_6\text{H}_5\underset{\text{OH}}{\text{C}}\text{-(CH}_3)_2$	$\text{C}_6\text{H}_5\underset{\text{I}}{\text{C}}\text{(CH}_3)_2$	90 (1)	unstable
q	$\text{HOCH}_2\text{CH}_2\text{CH}_2\text{OH}$	$\text{ICH}_2\text{CH}_2\text{CH}_2\text{I}$	70 (96)	bp ₁₄ : 99
r	$\text{HOCH}_2(\text{CH}_2)_2\text{CH}_2\text{OH}$	$\text{ICH}_2(\text{CH}_2)_2\text{CH}_2\text{I}$	56 (24)	bp ₁₄ : 120
s	$\text{HOCH}_2(\text{CH}_2)_3\text{CH}_2\text{OH}$	$\text{ICH}_2(\text{CH}_2)_3\text{CH}_2\text{I}$	63 (24)	bp _{0.5} : 87

The reaction occurs in two distinct steps. In the first one, the alcohol is rapidly consumed (^1H NMR) producing transient intermediate(s) (brown solution) which decompose(s) in the second step to the alkyl iodide. The rate of this last step clearly differs depending on the structure of the alcohol used: it occurs rapidly (<1h) for methanol, tertiary and benzyl alcohols (Table I, entry k-p) but requires much longer time for primary (Table I, entry a-d) and secondary ones (Table, entry e-j), especially for those possessing a neopentyl structure (Table I, entry d).

For example when 1-octanol is reacted with P_2I_4 as described above and the reaction quenched ($\text{K}_2\text{CO}_3/\text{H}_2\text{O}$) after the time shown in brackets, 1-iodooctane is formed in the following amounts: 20%(0.1hr) ~50%(0.5hr); ~55%(1hr); ~64%(3hrs); 87%(8hrs); 90%(24hrs) and the reaction is complete after 48hrs at 20°C .

The first attempts to trap and isolate the transient intermediate(s) - by addition of anhydrous bases just after the disappearance of the alcohol - as pure product(s) failed. However quenching the brownish solution by hydrolysis after 0.1hr reaction leads to the destruction of the intermediate(s) and produces, in the case of primary and secondary alcohols, the corresponding dialkyl phosphites¹² in 55-60% yield as pure products along with the alkyl iodides (30-157).

TABLE II

ROH	+	P_2I_4	\longrightarrow	$[\text{X}]$	$\xrightarrow{\text{H}_2\text{O}}$	$(\text{RO})_2\overset{\text{O}}{\parallel}\text{P} - \text{H}$
R					Yield % (time hr)	$\text{bp}_{\text{mm Hg}}^\circ\text{C}$
$\text{C}_2\text{H}_5 -$					56 (0.1)	$\text{bp}_{12} : 70^\circ$
$\text{C}_4\text{H}_9 -$					55 ^a (0.1)	$\text{bp}_{14} : 121^\circ$
					57 ^b (0.1)	PLC
$(\text{CH}_3)_2\text{CH} -$					60 (0.1)	$\text{bp}_{14} : 85^\circ$
$(\text{CH}_3\text{CH}_2)_2\text{CH} -$					56 (0.1)	$\text{bp}_{12} : 125^\circ$
$\text{CH}_3\text{CH}_2\text{CH}_2\underset{\text{CH}_3}{\text{CH}} -$					56 (0.1)	$\text{bp}_{13} : 130^\circ$

a 1-iodobutane is also formed in 33% yield

b iodocyclohexane is also formed in 13% yield

In all the cases described the alkyl iodide synthesis occurs highly regioselectively. For example 2-iodopentane and 3-iodopentane are obtained uncontaminated by each other³ (GC analysis), respectively from 2-pentanol and 3-pentanol and 2-methyl 1-butanol is selectively transformed to 2-methyl 1-iodobutane free of other isomers [3-iodopentane or 2-methyl 2-iodobutane -(NMR analysis)].

The reaction occurs stereoselectively with inversion of configuration in the case of secondary alcohols. For instance (+)2-octanol produces (-)2-iodooctane^{2a,f} and trans 4-tbutyl-1-cyclohexanol leads to cis 4-tbutyl 1-iodocyclohexane (45% yield) free of trans isomer (^1H NMR)^{2g}. However when the cis 4-tbutyl 1-cyclohexanol is reacted under similar condition 4-tbutyl 1-cyclohexene is formed in large amount.

It is not clear if P_2I_4 or a mixture xPI_3/yP is the real reagent in these transformations. We in fact found that all the three products are present in equilibrium [in favor of P_2I_4 (>95%)] when P_2I_4 (mp 124°) is dissolved in CS_2 [^{31}P NMR: PI_3, P_2I_4, P : -178, -106, +460 ppm (TMS as standard) respectively]. Whatever the mechanism is, the reaction just described is a one pot, simple one, using a cheap, easily available, easily handled reagent and the by-products are all inorganic and water soluble.

Work is now in progress to determine the scope of this reaction, the reactivity of P_2I_4 toward other functional groups, and the nature of the intermediates observed in the reactions just disclosed, mainly by using ^{31}P NMR.

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- 11) P_2I_4 (mp 124°) can be readily prepared by addition of solid iodine (64.7g, 0.255 moles) at once to white phosphorous (7.85 g, 0.253 Atom g, washed with acetone) in CS_2 solution (170 ml) under argon and maintained at $0^\circ C$. Iodine dissolves after a few minutes producing a deep violet solution turning orange after stirring (20° , 2hrs) the solvent is partially evaporated (water pump) leaving orange gold crystals which are recrystallized once in CS_2 leading to orange gold needles (35g, 50% yield, mp 124°). P_2I_4 is stable for several month under argon. The desired amount of reagent can be removed rapidly and weighed without any special precaution.
- 12) Purified by distillation or chromatography over silicagel (PLC). The products have been identified by comparison with samples prepared by known procedures. They present in their 1H NMR typical absorption of hydrogen bonded to a phosphorus atom.
- 13) The authors are grateful to the FNRS for the funds for the purchase of a multinuclear NMR.
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