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The Reaction of Vinyl Phosphates with Iodotrimethylsilane: Synthesis of Vinyl Iodides from Ketones

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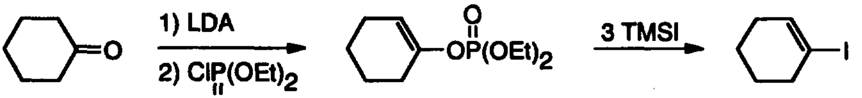
Abstract: A new method for preparation of vinyl iodides from ketones is described, based on the reaction of vinyl phosphates with iodotrimethylsilane.

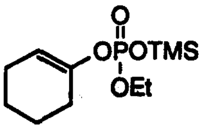
In recent years vinyl iodides have become important intermediates in organic synthesis. For example, reactions of vinyl iodides with organometallic compounds are often used for carbon-carbon bond formation through Pd-catalyzed cross coupling reactions,[1] and vinyl iodides also serve as precursors for the vinyl radicals used in vinyl radical cyclizations.[2] Although there are several methods for the preparation of vinyl iodides from acetylenes[3] and aldehydes,[4] few approaches to vinyl iodides from ketones[3,5] are known. Since the first reports of vinyl iodides synthesis through reaction of ketone hydrazones with iodine,[5a,b] this method has been widely used despite its generally modest yields. An improved procedure was recently developed by Barton et al.,[3] but this method still suffers from harsh reaction conditions (both strong base and high temperature) and a limited number of examples have been described. In this paper, we present an efficient and mild alternative for the preparation of vinyl iodides from ketones via readily available vinyl phosphate intermediates (Eq. 1).



1 2 3 Eq. 1

Iodotrimethylsilane (TMSI), used directly or prepared in situ from chlorotrimethylsilane (TMSCl) and NaI, is known to react with dialkyl phosphonates to provide the corresponding alkyl iodide along with the bis(trimethylsilyl) phosphonates.[6] This prompted our investigation of the reactions of TMSI with the vinyl phosphate derivatives of ketones, with an emphasis on cyclic ketones. Preliminary experiments with two equivalents of TMSI and the diethyl phosphate derivative of cyclohexanone (2) produced a complex mixture including vinyl iodide 3, vinyl phosphates 4 and 5, and the trimethylsilyl phosphates 6 and 7, as evidenced by GC-MS analysis of the reaction mixture. These results indicate that alkyl cleavage of the vinyl phosphate is competitive with vinyl iodide formation. When three equivalents of TMSI are used, complete reaction to the vinyl iodide can be attained.

The fundamental reaction sequence is shown in Eq. 1. Vinyl phosphates can be prepared easily from the corresponding ketones according to known procedures,[7] and directly used in the subsequent reactions



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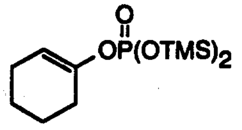


5

$EtOP(O)(OTMS)_2$

6

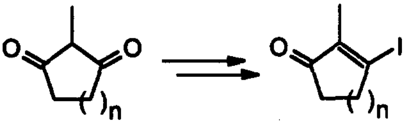
$P(O)(OTMS)_3$

7

without further purification. Treatment of the vinyl phosphates (e.g. 2) with three equivalents of TMSI in dichloromethane, or with TMSCl-NaI in acetonitrile, afforded the corresponding vinyl iodides (e.g. 3) within 10 minutes at room temperature.[8,9] We chose to use the more readily available TMSCl-NaI except in some cases where the volatile vinyl iodides are difficult to separate from the reaction solvent, acetonitrile. With either procedure, the phosphate by-products are easily removed as phosphoric acid salts by standard workup with $NaHCO_3$.

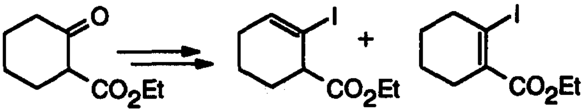
As shown in Table 1, the results are generally attractive. Five-, six-, and seven-membered ring ketones (Entries 1 - 7) were converted to vinyl iodides with high overall yields. In the case of 2-methylcyclohexanone, the enolate prepared under conditions of kinetic control gave a mixture of two regioisomeric vinyl iodides with fair selectivity for the more substituted olefin. Changing the reaction temperature from -78 °C to 40 °C did not affect the regioisomer ratio. This procedure also can be applied to acyclic ketones. Under typical reaction conditions the acyclic ketones pinacolone and acetophenone gave the desired vinyl iodides in very good yields, while 5-nonanone gave a 6.6:1 mixture of E- and Z-isomers.

Vinyl iodides have been prepared from ß-diketones through Piers' method[10a,b] involving reaction with $(C_6H_5)_3PI_2$, and by Kowalski's approach[10c] based on preparation of enone mesylates. Treatment of ß-diketones **8** and **9** with Et_3N and $(EtO)_2POCl$, and subsequent reaction with TMSI, gave excellent yields of the desired ß-iodo enones **10** and **11**, and a single regioisomer was obtained in each case. On the other hand, similar treatment of ß-keto ester **12** gave a mixture of regioisomeric iodides **13** and **14** with little selectivity. However, this appears to be the first preparation of a vinyl iodide from a ß-keto ester.



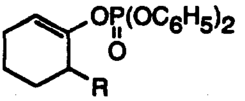
8 n = 1
9 n = 2

10 n = 1 (88%)
11 n = 2 (90%)



12 13 14

We also have examined the reaction of TMSI with the diphenyl vinyl phosphates **15** and the vinyl phosphonamide **16**, to determine if the vinyl iodide could be obtained with fewer equivalents of TMSI. However, in these cases, reactions with 1-2 equivalents of TMSI gave inferior results due to recovery of unreacted vinyl phosphates, formation of considerable amounts of diiodides, and difficulty in removing reaction by-products in the normal workup.



15 (R = H or CH_3)

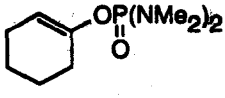


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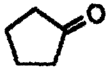
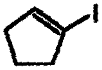
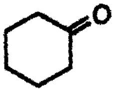
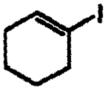
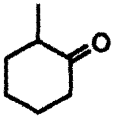
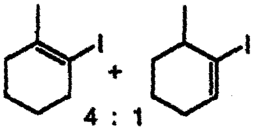
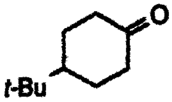
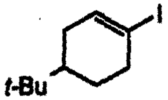
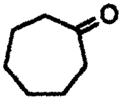
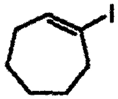
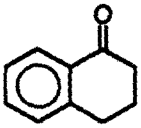
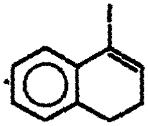
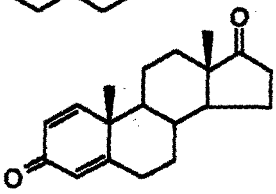
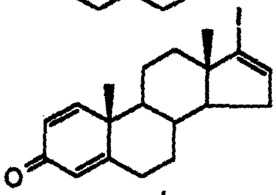
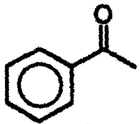
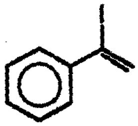
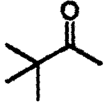
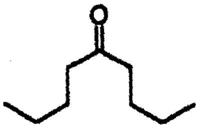
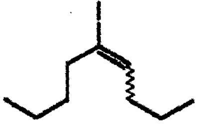
Table 1. Conversion of Ketones to Vinyl Iodides

Entry	Ketone	Method	Product	% Yield[a]	Ref.
1		TMSI		83 (93)	5b
2		TMSI TMSCl-NaI		86 (99) 83	5b
3		TMSI	 4 : 1	70 (87)	5d
4		TMSCl-NaI		88	5b
5		TMSCl-NaI		79	11
6		TMSCl-NaI		85	-
7		TMSI		62^b	-
8		TMSCl-NaI		87	5b
9		TMSI		71 (92)	5b
10		TMSI		68^c	-

[a] Isolated yield after purification by flash chromatography. Values in parentheses represent yields after standard workup but without further purification. [b] In addition, 25% of the ketone was recovered. [c] Isolated as a 6.6 to 1 mixture of E- and Z-isomers.

In summary, high yields of vinyl iodides can be obtained from various ketones, as well as some ß-keto carbonyl compounds, via vinyl phosphate intermediates. The mechanism(s) of this process, strategies for obtaining better regioselectivity, and applications to more complex substrates are currently under investigation.

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References and Notes.

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(8) General procedures. To a solution of vinyl phosphate (1 mmol) in anhydrous CH_2Cl_2 (2 mL) was added TMSI (3 mmol) dropwise via gas-tight syringe. After stirring for 10 min at room temperature, the reaction mixture was quenched by addition of saturated $NaHCO_3$ and saturated Na_2SO_3 solution. The organic layer was separated and the aqueous layer was extracted twice with CH_2Cl_2. The combined organic fractions were dried ($MgSO_4$) and concentrated. The vinyl iodide was purified by flash chromatography using *n*-pentane as an eluent. In the alternative procedure, TMSCl (3 mmol) was added dropwise to a solution of the vinyl phosphate (1 mmol) and NaI (3 mmol) at rt. After 10 min, the NaCl ppt was removed by filtration and solution was concentrated in vacuo. The yellow residue was dissolved in CH_2Cl_2, and workup and purification was conducted as described above.

(9) In some cases, the vinyl iodides were accompanied by ketones and diiodides.[5b]

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