

AN IMPROVED PREPARATION OF VINYL IODIDES

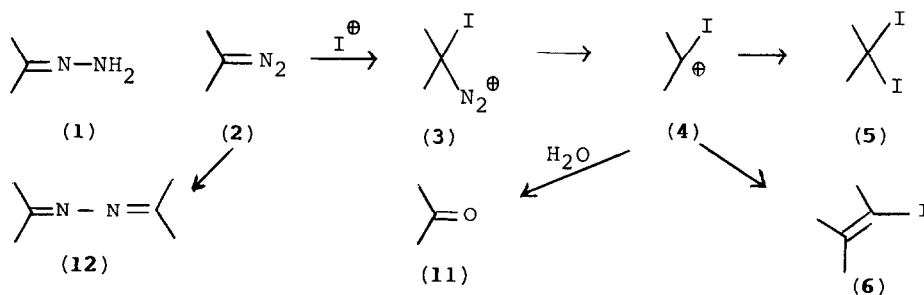
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The oxidation of ketone hydrazones by iodine in the presence of a base to furnish vinyl iodides has been considerably improved. The three factors responsible are (1) absence of water, (2) the use of strong guanidine bases and (3) inverse addition.

During the determination of the structure of limonin¹, we had need to design a reaction for the conversion of the neopentyl aldehyde function into the neopentane function under mild conditions. We showed² that the hydrazones of aldehydes on oxidation with iodine in the presence of triethylamine gave good yields of diiodides easily reduced to hydrocarbons. The same reaction when applied to hindered ketone hydrazones afforded vinyl iodides in useful yields, but unhindered ketone hydrazones afforded mixtures of vinyl iodides and geminal diiodides. The scope of this reaction was more extensively studied by Sternhell and his colleagues³.

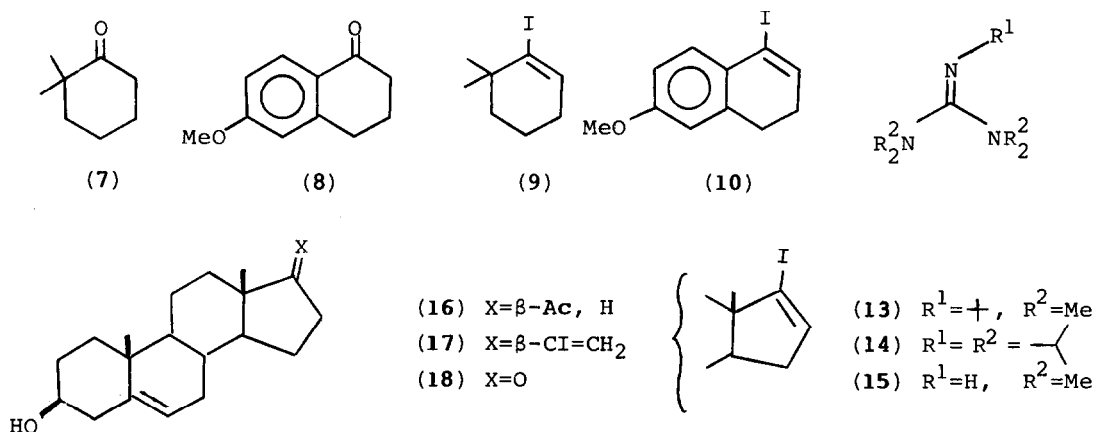
The mechanism originally proposed for this reaction² indicated in Scheme I proposes that the hydrazone (1) is oxidised by iodine to the diazo-compound (2) which reacts further to give the iodo-derivative (3) which by loss of nitrogen



Scheme I

affords the key iodicarbonium ion (4). Addition of iodide ion (less hindered (4)) gives gem-diiiodides (5) whilst loss of a proton [more hindered (4)] gives vinyl iodides (6). Considerable mechanistic support (cationic rearrangements) for the existence of (4) has been accumulated^{3,4}.

This reaction has been used for synthetic purposes a number of times⁵. Recently Professor M.E. Jung (U.C.L.A.) kindly drew our attention to two ketones (7) and (8) which gave only 40% and 30% respectively of vinyl iodides (9) and (10) under standard conditions. Stimulated by these observations we have reinvestigated the reaction and have improved the yields that can be obtained. The principal by-products in the synthesis of vinyl iodides are (Scheme I) the ketone (11), the azine (12) and the diiodide (5). The ketone is formed by attack of water on the cation (4). Thoroughly dried solvents prevent the formation of this by-product. The azine (12) is formed by a bimolecular reaction of (2) with (1). Inverse addition (addition of hydrazone to the iodine) in presence of the base greatly reduces azine formation⁶.



Finally, the use of strong fully substituted guanidine bases (13) or (14)⁷ in slight excess proved greatly superior to the traditional triethylamine. Commercially available tetramethylguanidine (15) also gives improved yields. Data for normal addition to the hydrazone from (8), or (last two results) from (16), are given in Table I. The best solvents are ether, tetrahydrofuran and toluene.

With the inverse addition procedure (Table II) increasing the concentration of base favours slightly the formation of vinyl iodide. The gem-diiodides are stable at room temperature in the reaction medium and are not the precursors of the vinyl iodides. However, when excess of base is used, and the solvent is removed at the end of the reaction prior to heating at 80-90°, good yields of vinyl iodides can be obtained at the expense of the gem-diiodides (Table II)

Table Ia

Base	Solvent	Yield (%)		
		Vinyl Iodide	Azine ^b	Ketone ^b
Triethylamine	ether	38 (10)	20	-
Base (13)	ether	78 (10)	8	-
Base (14)	ether	78 (10)	8	-
Base (13)	tetrahydrofuran	70 (10)	15	10
Base (13)	toluene	68 (10)	15	12
Base (13)	toluene	78 (17)	-	-
Base (15)	toluene	80 (17)	-	-

- a. Normal addition. Iodine (3.2 mmols) in dry solvent (20 ml) was added dropwise to a stirred solution of base (5.3 mmols) and hydrazone (1.5 mmols) in the same solvent (25 ml) at room temperature. The reaction is instantaneous, but stirring was continued for a further 15 mins. The reaction mixture was washed with 2N HCl, aqueous Na₂SO₃, aqueous NaHCO₃ and dried (Na₂SO₄). Removal of solvent and column chromatography over silica gel (grade 60 Merck) gave the products listed.
- b. When the yield of azine or ketone is not given it was not determined.

Table II (Inverse addition)^a

Parent ketone or aldehyde	Base (equiv.)	Solvent	Yield (%)	
			Vinyl iodide ^b	gem-Diiodide ^b
(8)	(13) (3.5)	ether	89 (10)	-
(8)	(15) (3.5)	ether	87 (10)	-
(7)	(13) (3.5)	ether	49 (9)	29
(7)	(15) (11)	ether	54 (9)	33
(7)	(13) (9)	ether	91 ^c (9)	0
cyclohexanone	(13) (3.5)	ether	50	25
cyclohexanone	(13) (9)	ether	92 ^c	0
(18)	(13) (3.5)	THF ^d	68 (19)	23
(18)	(13) (6)	THF	70 (19)	23
(18)	(15) (15)	THF	75 (19)	16
(18)	(13) (30)	THF	80 (19)	11
(18)	(13) (7)	THF	95 ^e (19)	0
Isobutyraldehyde	(13) (3.5)	ether	0	70

- a. Inverse addition. The base (see Table) in ether (30 ml) was mixed slowly (30 mins) with iodine (3.2 mmols) in ether (20 ml) at room temperature. The hydrazone (1.5 mmols) in ether (10 ml) was added dropwise (10 mins) at room temperature. The work up procedure was as in Table I.
- b. Mixtures of vinyl iodides and gem-diiodides eluted together and were not separated. The yields were determined by NMR.
- c. After completion of the reaction the solvent was removed and the residue heated at 90° for 1.5 hrs.
- d. Tetrahydrofuran.
- e. As for c, but heating at 80° for 5 hrs.

Camphor hydrazone under normal addition with base (13) or base (15) afforded 65% of unrearranged vinyl iodide and only 10% of 1-iodocamphene. The guanidine bases, therefore, reduce the lifetime of the key iodocarbonium ion (4) and hence its rearrangement.

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