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Direct Preparation of Vinyl Halides from the corresponding Ketones and Acetyl Halides

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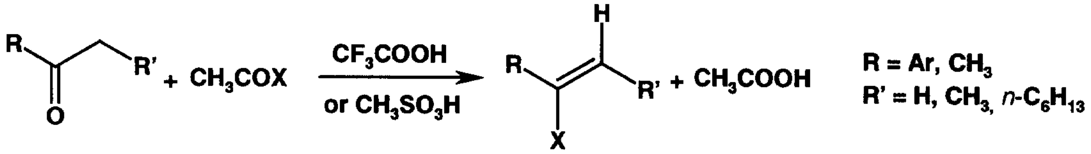
Abstract : Vinyl chlorides and bromides are obtained in good yield from the corresponding ketones and acetyl halides in the presence of trifluoroacetic or trifluoromethanesulfonic acid. The Z isomer is selectively formed.

Vinyl halides can be synthesized using various ways, mainly from alkynes.[1] Direct formation of vinyl chlorides from the corresponding ketones has long been known to occur using phosphorus pentachloride as reagent, but this reaction also leads to *gem*-dichloro compounds and various other products.[2] Reagents used more recently to perform this transformation include dichloromethyl methyl ether with zinc chloride,[3] thionyl chloride,[4] the Vilsmeier reagent,[5] catechylphosphorus trichloride[6] and phosphorus trihalides[7].

This work reports the direct formation of vinyl chlorides or bromides from ketones using the appropriate acetyl halide in a strongly acidic solvent (trifluoroacetic acid or methanesulfonic acid) :



The results are displayed in Table 1. The most stable (Z) vinyl halide was selectively obtained, and contained less than 1% (E) isomer.

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Table 1. Preparation of vinyl halides RCX=CHR' from ketones R-CO-CH_2R' and acetyl halide CH_3COX in trifluoroacetic or methanesulfonic acid.[a]

R	R'	X	Solvent	(Z) RCX=CHR' isolated yield (%)	Product reference
Ph	H	Cl	CF_3COOH	83	8 [b]
		Br	CF_3COOH	79	9
4-Me-Ph	H	Cl	CF_3COOH	63	10 [c]
Ph	CH_3	Cl	CF_3COOH	96	11, 12
		Cl	CH_3SO_3H	91	
		Br	CF_3COOH	94	9, 12
CH_3	*n*-Hexyl	Cl	CH_3SO_3H	91 [d]	13
		Br	CH_3SO_3H	97	14

a - A solution of ketone (10 mmol) in the acidic solvent (20 mL) was cooled to 0°C and acetyl chloride or bromide (8 equiv.) was added dropwise. After 36 h stirring at room temperature the mixture was poured in water and extracted with pentane. After several washings with $NaHCO_3$ solution, drying and solvent evaporation, the product was purified by chromatography on silica gel eluted with 90/10 pentane/ethyl acetate.

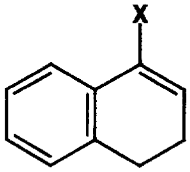
b - Reported yields from the ketone : 64% using catechylphosphorus trichloride[6a], 73% using dichloromethyl methyl ether with zinc chloride[3].

c - Prepared from the ketone using phosphorus pentachloride, reported yield 69%.

d - In addition to this product, the regioisomer $CH_3(CH_2)_6CHCl=CH_2$ was obtained in 9% yield.

While 4-methylacetophenone reacted with acetyl chloride satisfactorily, with acetyl bromide it led only to polymers under the same conditions. Polymers were also obtained from 4-methoxyacetophenone and either acetyl chloride or acetyl bromide. On the other hand, 4-nitroacetophenone remained unchanged when treated with acetyl chloride or bromide under these conditions, either in trifluoroacetic or in methanesulfonic acid. Attempts to decrease the temperature in the case of 4-methoxyacetophenone or to increase it in the case of 4-nitroacetophenone were unsuccessful.

The aliphatic ketone nonan-2-one did not react in the presence of trifluoroacetic acid, but methanesulfonic acid proved to be a suitable solvent for vinylic halide formation. The reaction remained stereoselective and was fairly regioselective since only a small amount of primary alkene was formed.



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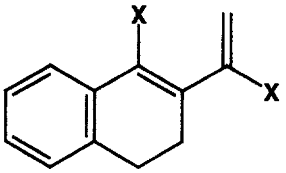

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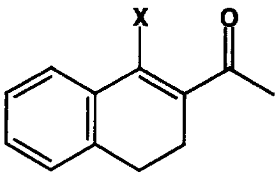

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a : X = Cl
b : X = Br

Conversion of α-tetralone to halides **1** has been efficiently performed using trichloroacetyl halides as reagents.[15] However, α-tetralone did not react satisfactorily under our reaction conditions and the conversion yield remained low (20-50%). Beside the expected vinyl halide **1**,[16] obtained in approximate yields of 7% for **1a** and 6% for **1b**, several products were formed, in particular **2** according to spectroscopic data,[17] which could not be separated from **1**. A likely intermediate in the formation of **2** is ketone **3**, since **3** was also detected in the reaction mixture,[18] and conversion of **3** to **2** corresponds to the reaction described in this work. Ketone **3** is probably formed through addition of acetyl halide to the halide **1**, which is a known reaction.[19]

The formation of a vinyl halide observed as the main reaction in the general case (Table 1) probably proceeds through a preliminary equilibrium corresponding to overall addition of acetyl halide to the carbonyl, leading to an α-haloacetate,[20] followed by elimination of acetic acid. The first step likely involves acid-catalyzed enolization. Conversion of β-diketones to β-chloro-α,β-unsaturated ketones is effected by acetyl[21] or better oxalyl[22] chloride, no acidic solvent being necessary for these partly enolized substrates, in agreement with an enol involvement in the reaction mechanism. The fact that aliphatic ketones, which contain less enol form than aromatic ketones,[23] require the use of a stronger acid (methanesulfonic versus trifluoroacetic acid), is also consistent with this mechanism.

The reaction of acetyl halide with ketones in a strongly acidic solvent as described above is efficient although not for all substrates, stereoselective, and uses easily available reagents. Therefore it may constitute a useful way for preparing vinyl chlorides and bromides.

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17. For **2a** : ^1H NMR (250 MHz, $CDCl_3$) δ 2.52 (2H, dist.t, J = 8 Hz), 2,80 (2H, dist.t, J = 8 Hz), 5.47 (1H, d, J = 1.5 Hz), 5.56 (1H, d, J = 1.5 Hz), 7.1-7.3 (2H, m), 7.6-7.8 (2H, m); MS (EI) m/z (%) 228 (7), 226 (44), 224 (67) (M^+), 191 (30), 189 (89) (M^+ - Cl), 153 (100), 152 (75). For **2b** : ^1H NMR (250 MHz, $CDCl_3$) δ 2.52 (2H, dist.t, J = 8 Hz), 2,81 (2H, dist.t, J = 8 Hz), 5.71 (1H, d, J = 2 Hz), 5.76 (1H, d, J = 2 Hz), 7.1-7.3 (2H, m), 7.6-7.8 (2H, m); MS (EI) m/z (%) 316 (28), 314 (56), 312 (29) (M^+), 235 (99), 233 (100) (M^+ - Br), 154 (85), 153 (69), 152 (58).

18. For **3a** : ^1H NMR (250 MHz, $CDCl_3$) δ 2.16 (3H, s), 2.59 (2H, dist.t, J = 8 Hz), 2.78 (2H, dist.t, J = 8 Hz), 7.1-7.35 (5H, m), 7.9 (1H, m); MS (EI) m/z (%) 208 (27), 206 (81) (M^+), 193 (33), 191 (100) (M^+ - CH_3), 165 (13), 163 (40) (M^+ - $COCH_3$), 171 (25) (M^+ - Cl), 128 (50). For **3b** : ^1H NMR (250 MHz, $CDCl_3$) δ 2.17 (3H, s), 2.53 (2H, dist.t, J = 8 Hz), 2.81 (2H, dist.t, J = 8 Hz), 7.1-7.35 (5H, m), 7.9 (1H, m); MS (EI) m/z (%) 252 (54), 250 (55) (M^+), 237 (64), 235 (64) (M^+ - CH_3), 209 (26), 207 (27) (M^+ - $COCH_3$), 171 (46) (M^+ - Br), 128 (100), 127 (33).

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