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VERSATILE SYNTHESIS OF α,β-UNSATURATED ALDEHYDES AND NITRILES FROM KETONES VIA VILSMEIER FORMYLATION.

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Because of their easy preparation and wide applicability, the chemistry of β-chloro-α,β-unsaturated carbonyl compounds, especially β-chloro-α,β-unsaturated ketones has evoked a great deal of interest[1-3]. Little or no attention has been paid to the reductive dehalogenation of these compounds to α,β-unsaturated ketones (aldehydes).

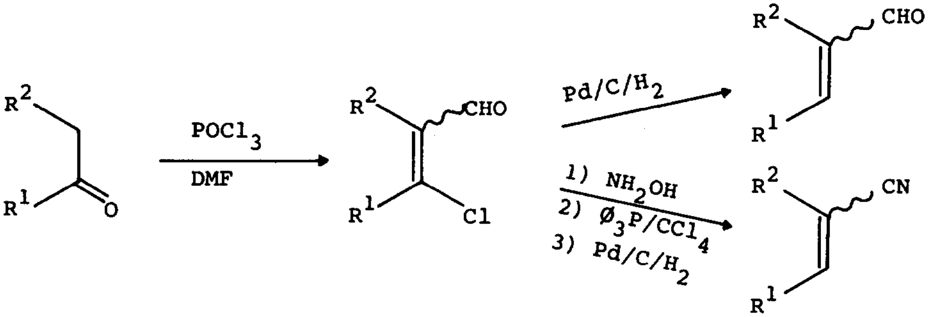
Crossly and Renouf[4] have reported the reduction of 3-chloro-5,5-dimethyl 2-cyclohexene-1-one to 5,5-dimethyl-2-cyclohexene-1-one by applying a zinc/copper couple. This method has recently been modified and strongly improved by Heathcock and coworkers[2,5], who replaced the zinc/copper couple by a zinc/silver couple. Moreover β-chloro-α,β-unsaturated ketones have been reduced with zinc in alcoholic solution[6,7].It is our experience that these processes, although very useful on a small scale, give rise to problems in large scale operations i.e. formation of side products, low yields and extreme reaction times in large scale operations. We therefore investigated catalytic hydrogenation as an alternative for dehalogenation despite discouraging reports in the literature.

When phenyl and vinylhalides are hydrogenated over a palladium catalyst saturation of the double bond and vinyl-halogen hydrogenolysis occur simultaneously[8a,b].

In previous communications[9a,b] we reported on the synthesis of 3,3-dimethylcyclohexylidene acetaldehyde, an important component of the sex-pheromone complex of the male Boll Weevil. A key step in this synthesis involved the selective catalytic hydrogenation of only one double bond in a conjugated unsaturated chloro-aldehyde including simultaneous removal of halogen ($RC(Cl){=}CH{-}CR'{=}CH{-}CHO \longrightarrow RCH_2{-}CH_2{-}CR'{=}CH{-}CHO$).

This work has triggered the present study of selective dehalogenation of the simple β-chloro(bromo)-α,β-unsaturated aldehydes without saturation of the double bond. Because the starting materials are readily accessible by Vilsmeier formylation, this comprises a versatile route to α,β-unsaturated aldehydes starting with ketones.

Vilsmeier formylation of the appropriate ketones was performed with phosphoryl chloride or bromide and dimethylformamide with or without benzene as a co-solvent. After alkaline work up (aqueous Na_2CO_3) the β-halo-α,β-unsaturated aldehydes were obtained by distillation over a small amount of solid sodium acetate in yields up to 85%.



Initially reduction experiments were carried out with a palladium catalyst on charcoal treated with quinoline and sulfur[10]. Although this catalyst gave satisfactory results (yields up to 80%), an improved palladium catalyst on charcoal[10], was applied for selective reductions in the present study. Reductive dehalogenations of the β-chloro-α,β-unsaturated carbaldehydes over palladium on charcoal[10] in methanol using triethylamine as hydrogen chloride scavenger proceeds quantitatively. The unsaturated carbaldehydes obtained in this way are contaminated with the corresponding saturated analogues in amounts (5-37%) varying with the nature of the starting material. Yields of selective hydrogenations are collected in table I.

2-Chlorocyclooctene carbaldehyde as well as 2-chlorocycloheptene carbaldehyde can be reduced to a mixture of the corresponding α,β-unsaturated and saturated aldehydes in a ratio of 19:1 (selectivity 95%) at 100% conversion.

A somewhat lower selectivity is found for the C_6 homologue (85%) and in the case of 2-chlorocyclopentene carbaldehyde the selectivity depends strongly on the degree of conversion (cf table I).

The reduction of 3-chloro-3-cyclopropyl acrolein is of special interest, because it features an example of a class of 3-cyclopropyl acrolein derivatives, which is difficult to synthesize. Vinylcyclopropanes without a (cyclo) alkyl substituent at the cyclopropylcarbinyl centre lack reactivity and give with few exceptions low yields of the corresponding 3-cyclopropyl acroleins in the Vilsmeier reaction[9c].

The reduction of 2-chlorocyclopentene carbaldehyde and of the acyclic β-chloro-α,β-unsaturated aldehydes proceeds less selectively than the cyclic analogues (Table I). This somewhat different behaviour is not so surprising, considering the findings of Maurel[11], who observed relatively high hydrogenation rates and large adsorption coefficients (indicating the efficiency of adsorption to the catalyst) for cyclopentenes and alkenes structurally related to our acyclic α,β-unsaturated aldehydes and assuming that the rate of hydrogenolysis of the carbon-halogen double bond in all β-chloro-α,β-unsaturated aldehydes is of the same order of magnitude.

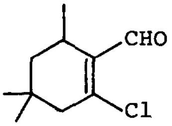
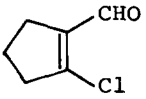
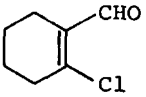
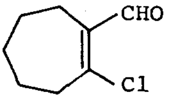
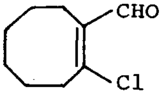
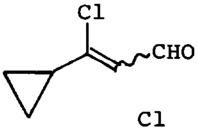
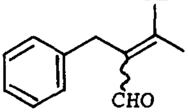
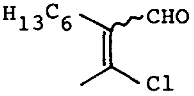
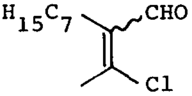
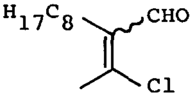
It should be noted, that these results with alkenes on a Platinum catalyst are not directly comparable with those obtained in the reduction of α,β-unsaturated aldehydes over a palladium catalyst, but at least the same tendency is observed. Conclusive evidence requires a more detailed kinetic study.

In order to improve the selectivity of the hydrogenation, the corresponding β-bromo-α,β-unsaturated aldehydes[12] was also investigated. It is well known that the rate of hydrogenolysis increases from F < Cl < Br < I. As a consequence the selectivity is highly increased and the corresponding α,β-unsaturated aldehydes are obtained in almost quantitative yield, especially in the alicyclic series. Even in the case of the aliphatic β-bromo-α,β-unsaturated aldehydes saturation of the double bond remains now below 5%.

We also observed that this method can be effectively applied for the preparation of α,β-unsaturated aldehydes from the corresponding conjugated dienals.

Table I Catalytic reduction of β-chloro-α,β-unsaturated aldehydes (100% conversion).

The figures between brackets refer to the bromo compounds.

Chloro aldehyde	Aldehyde	
	α,β-unsaturated	saturated
	90 (98)	10 (2)
	45*	55*
	85 (95)	15 (5)
	95	5
	95 (99)	5 (1)
	60	40
	70 (95)	30 (5)
	63 (94)	37 (6)
	66 (95)	34 (5)
	64 (95)	36 (5)

* At 85% conversion.

This method is also very useful for the synthesis of α,β-unsaturated nitriles. Reaction of the β-chloro-α,β-unsaturated aldehydes with hydroxylamine and subsequent oxime dehydration with triphenylphosphine in carbon tetrachloride affords the β-chloro-α,β-unsaturated nitriles in good yield (80-90%). In this case even the aliphatic β-chloro-α,β-unsaturated nitriles can be quantitatively dechlorinated to the corresponding α,β-unsaturated nitriles. Therefore this procedure is preferable to initial reduction of the β-chloro-α,β-unsaturated aldehydes followed by conversion of the aldehyde into the nitrile.

Acknowledgement

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References

1 . A.E.Pohland and W.R.Benson, Chem.Rev. 66, 161 (1966).

2 . R.D.Clark and C.H.Heathcock, J.Org.Chem. 41, 636 (1976).

3 . E. Piers and J.Nagakura, Syn.Commun 5, 193 (1975) and references cited therein.

4 . A. Crossley and N.Renouf, J.Chem.Soc. 91, 63 (1907).

5 . R.D. Clark and C.H.Heathcock, J.Org.Chem. 38, 3658 (1972).

6 . R.L.Frank and H.K.Hall, J.Amer.Chem.Soc. 72, 1645 (1950).

7 . A.Hara and M.Sekiya, Chem.Pharm.Bull.Japan 20, 309 (1972).

8a. H.Favre and H.Schinz, Helv.Chim.Acta 35, 2388 (1952).

8b. U.Ghatak, N.N.Shaka and P.C.Dutta, J.Amer.Chem.Soc. 79, 4487 (1957).

9a. P.C.Traas, H.Boelens and H.J.Takken, Recl.Trav.Chim.Pays Bas 95, 308 (1976).

9b. P.C.Traas, H.Boelens and H.J.Takken, Syn.Commun 1976, 489.

9c. P.C.Traas, H.Boelens and H.J.Takken, Recl.Trav.Chim.Pays Bas 95, 57 (1976).

10. Purchased from Johnson Matthey Chemicals.

11. R. Maurel, Catal.Lab.Ind.Rec.Trav.Sess. 2, 203 (1967).

12. β-Bromo-α,β-unsaturated carbaldehydes are rather unstable compounds, which must be distilled with care under sufficiently reduced pressure in order to avoid vigorous decomposition.