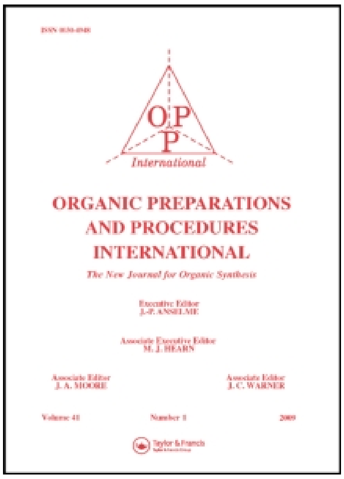

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SYNTHESIS OF α-CHLORO-α,β-UNSATURATED ALDIMINES AND OF α-CHLORO-α,β-UNSATURATED ALDEHYDES

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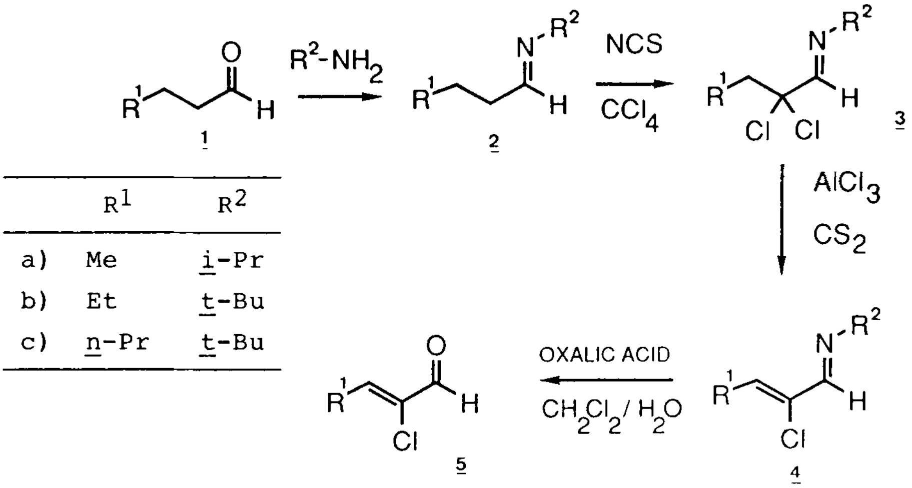
α-Chloro-α,β-unsaturated aldehydes constitute a class of compounds known since the end of the previous century.[1] Many syntheses are published in the literature but few methods produce these aldehydes in high purity. These problems arise from the lability of the α-chloro-α,β-unsaturated aldehydes which are not only moisture- and light-sensitive but also are prone to polymerization. The original methods did not lead to successful isolation of pure compounds.[1] α-Chlorocrotonaldehyde was first isolated in the pure state by heating α,β-dichlorobutyraldehyde with aqueous sodium acetate, according to the method used for the synthesis of monobromoacrolein.[2] Other methods describe the chlorination of unsaturated aldehydes with t-butyl hypochlorite,[3] addition of dichlorocarbene to enamines followed by hydrolysis,[4] ring opening of dichlorocyclopropanes or chlorofluorocyclopropanes with alkoxides[5] and addition of lithium difluoroethene to aldehydes followed by hydrolysis.[6] Other convenient methods describe the reaction of α,β-unsaturated aldehydes with phenylselenyl chloride which gives the α-chloro-α,β-unsaturated aldehydes after dehydrochlorination with pyridine[7] or the chlorination of aldehydes followed by dehydrochlorination with N,N-dimethylaniline.[8]

The present paper describes an alternative entry into α-chloro-α,β-unsaturated aldimines and α-chloro-α,β-unsaturated aldehydes. Aliphatic aldehydes 1 were transformed into the corresponding aldimines 2, which were chlorinated with two molar equivalents of N-chlorosuccinimide to afford α,α-dichloroaldimines 3.[9]



	R^1	R^2
a)	Me	i-Pr
b)	Et	t-Bu
c)	n-Pr	t-Bu

α,α-Dichloroaldimines 3 were then dehydrochlorinated with aluminium chloride in carbon disulfide. The use of aluminium chloride in dichloromethane has already proved its utility for the dehydrochlorination of α,α-dichloroamides and α,α-dichloroamidines to the corresponding α-chloro-α,β-unsaturated amides and α-chloro-α,β-unsaturated amidines.[10] This step constitutes the bottle neck of the reaction sequence due to the extreme lability of the α-chloro-α,β-unsaturated aldimines 4. The reaction was first performed using dry benzene as solvent with two molar equivalents of aluminium chloride, leading to high yields of the α,β-unsaturated aldimines 4 (70-85%). Unfortunately, the reaction mixture contained unidentified impurities (upto 20%) which were not removable by column chromatography. Distillation of the unsaturated imines 4 is not recommended because they polymerize upon heating. The impurities probably result from a Friedel-Crafts reaction with benzene, catalyzed by aluminium chloride.

In order to avoid this problem, different solvent systems were examined. The best solvent seems to be carbon disulfide (Caution : Poisoning occurs from inhalation but may also be caused by ingestion and skin absorption) using three molar equivalents of aluminium chloride. The quality of aluminium chloride is very important to obtain good results. Fresh, free-flowing, finely powdered aluminium chloride was used throughout all experiments, but even then, the reproducibility of the reactions was problematic. Sometimes, the reaction mixture contains little of the desired products using the described conditions. The reasons for these reproducibility problems are not known. A problem with carbon disulfide arose during the alkaline work-up of the reaction mixture with formation of xanthate-type contaminants. Therefore, the carbon disulfide was evaporated after the reaction and replaced by dichloromethane before the alkaline workup.

TABLE 1. Synthesis of α-Chloro-α,β-unsaturated Imines and α-Chloro-α,β-unsaturated Aldehydes

Starting material	R^1	R^2	Reaction Conditions[a]		Purity (%)	Yield (%)	bp (°C/mmHg)
3a	Me	i-Pr	2E $AlCl_3/CS_2$ Δ, 15 hrs	4a	75	43	57-60/14
3b	Et	t-Bu	2E $AlCl_3/CS_2$ Δ, 16 hrs	4b	80	41	<20/0.05
3c	n-Pr	t-Bu	2E $AlCl_3/CS_2$ Δ, 15 hrs	4c	50	50	32-34/0.05
4a	Me	i-Pr	1E$(COOH)_2.2H_2O/H_2O/$ CH_2Cl_2, Δ, 1 hr	5a	80-90	78	-
4b	Et	t-Bu	1E$(COOH)_2.2H_2O/H_2O/$ CH_2Cl_2, Δ, 1 hr	5b	85-90	65	40-41/13
4c	n-Pr	t-Bu	1E$(COOH)_2.2H_2O/H_2O/$ CH_2Cl_2, Δ, 1 hr	5c	65-70	80	47-50/13

[a] E = molar equivalent.

α-Chloro-α,β-unsaturated aldimines 4 were hydrolyzed to α-chloro-α,β-unsaturated aldehydes 5 by using oxalic acid in a two-phase-system (water/dichloromethane : 1/1). This procedure yielded α-chloro-α,β-unsaturated aldehydes 5 in moderate yields with a purity of 65-90%. α-Chloro-α,β-unsaturated aldehydes are vesicants and should therefore be handled with care. The aldehydes are best stored at -20° but even then the purity decreased after a few days, so that α-chloro-α,β-unsaturated aldehydes should preferably be used, immediately after synthesis.

Although most of the known procedures describe only the synthesis of α-chlorocrotonaldehyde, the present synthesis is also applicable for the synthesis of 2-chloro-2-pentenal 5b (R^1 = Et) and 2-chloro-2-hexenal 5c (R^1 = *n*-Pr).

EXPERIMENTAL SECTION

Infrared spectra were recorded on a Perkin Elmer model 1310 spectrophotometer. ^1H NMR spectra were measured in $CDCl_3$ on a Varian T-60 NMR spectrometer while ^{13}C spectra were recorded on a Varian FT-80 NMR spectrometer (20 MHz). Mass spectra were obtained on a Varian-MAT 112 mass spectrometer (70 eV) using a direct inlet or by using a GC-MS coupling (20 m capillary column). α,α-Dichloroaldimines 3 were synthesized from aldehydes 1 *via* aldimines 2 according to a previously described method.[9] The instability of the products precluded the obtention of combustion analyses.

General Procedure for the Synthesis of α-Chloro-α,β-unsaturated Imines (4) from α,α-Dichloroaldimines (3). - To a solution of 0.04 mole of α,α-dichloroaldimines 3 in 100 ml dry carbon disulfide was added 0.12 mole of pure aluminium chloride at 0°. The reaction mixture was stirred and heated under reflux for 16 hrs under nitrogen atmosphere. The solvent was evaporated *in vacuo* and replaced by 100 ml of dichloromethane, and poured into 50 ml of ice-cold sodium hydroxide (6N). The reaction mixture was extracted with dichloromethane, dried ($MgSO_4$) and evaporated *in vacuo*. It is counterproductive to attempt distillation of compounds 4 since this leads to extensive tar formation, affording only about 5-10% of distilled material. The compounds were partially purified using column chromatography (silica gel) using dry ether as eluent.

N-(2-Chloro-2-buten-1-ylidene)isopropylamine (4a) : ^1H NMR : δ 1.21 (6H, d, J = 6Hz, $CH(Me_2)$); 1.95 (6H, d, J = 7Hz, $C\underline{H}_3CH=$); 3.46 (1H, sept, J = 6Hz, $C\underline{H}Me_2$); 6.26 (1H, q, J =

7Hz, MeC$\underline{H}$=); 7.81 (1H, s, C$\underline{H}$=N). ^{13}C NMR ($CDCl_3$) : 14.56 (q, $\underline{C}H_3C$=); 24.00 (q, $(\underline{C}H_3)_2$); 60.85 (d, $\underline{C}HMe_2$); 133.82 (d, C=); 134.01 (d, C=); 155.32 (d, $\underline{C}$=N). IR (NaCl) : $\nu_{C=N}$: 1642 cm^{-1}. Mass Spectrum m/z(%) : 145/47 (M^+, 36); 130/32 (100); 110 (11); 104(9); 103(11); 102(11); 94(18); 91(9); 89 (27); 68(25); 67(11); 53(16); 43(50); 42(30); 41(32)

<u>N-(2-Chloro-2-penten-1-ylidene)t-butylamine</u> ($\underline{4b}$) : ^{1}H NMR : δ 1.10 (3H, t, J = 7Hz, C$\underline{H}_3$); 1.26 (9H, s, C(C$\underline{H}_3$)$_3$); 2.45 (2H, quint, J = 7Hz, $CH_3C\underline{H}_2$); 6.25 and 6.96 (1H, t, J = 7Hz, C$\underline{H}$=CCl); 7.66 and 7.83 (1H, s, 28% Z and 72% E). ^{13}C ($CDCl_3$) : 12.59 (q, Me); 22.42 (t, $\underline{C}H_2CH_3$); 29.74 (q, C($\underline{C}H_3)_3$); 57.36 (s, $\underline{C}$(Me)$_3$); 133.21 (s, $\underline{C}$Cl); 140.21 (d, $\underline{C}$H = CCl); 152.64 (d, $\underline{C}$ = N). IR (NaCl) : $\nu_{C=N}$: 1640 cm^{-1}. Mass spectrum m/z(%) : 173/75 (M^+, 11), 158/60 (25); 118 (14); 117(7); 82(14); 57(100); 56(11); 41(34); 39 (11).

<u>N-(2-Chloro-2-hexen-1-ylidene)t-butylamine</u> ($\underline{4c}$) : ^{1}H NMR : δ 0.93 (3H, t, J = 7Hz, C$\underline{H}_3CH_2$); 1.20 (9H, s, C(C$\underline{H}_3$)$_3$); 1.3-1.7 (2H, m, $CH_3C\underline{H}_2$); 2.38 (2H, q, J = 7Hz, C$\underline{H}_2$CH=C); 6.20 (1H, t, J = 7Hz, C$\underline{H}$ = CCl); 7.77 (1H, s, C$\underline{H}$ = N). ^{13}C ($CDCl_3$) : 13.81 (t, $CH_3\underline{C}H_2$); 21.53 (t, $\underline{C}H_2$CH=); 29.69 (q, $(\underline{C}H_3)_3$); 30.99 (q, $\underline{C}H_3$); 57.18 (s, $\underline{C}$(Me)$_3$); 133.99 (s, =$\underline{C}$Cl); 138.35 (d, $\underline{C}$H = CCl); 152.31 (d, $\underline{C}$H = N). IR (NaCl) : $\nu_{C=N}$: 1642 cm^{-1}. Mass Spectrum m/z(%) : 187/89 (M^+, 34); 172/74(100); 144 (13); 132(35); 130(24); 116(16); 90(22); 58(42); 57 (85); 56(29); 51(16).

<u>General Procedure for the Synthesis of α-Chloro-α,β-unsaturated Aldehydes $\underline{5}$ from α-Chloro-α,β-unsaturated Aldimines</u> ($\underline{4}$). A solution of 0.025 mole of α-chloro-α,β-unsaturated aldimine $\underline{4}$ in 50 ml dry dichloromethane was added to a solution of 0.025 mole of oxalic acid in 50 ml water. After 1 hr of reflux, the organic layer was separated and the water layer extracted with dichloromethane. The dichloromethane extracts were dried ($MgSO_4$), filtered and the solvent evaporated <u>in vacuo</u>. The crude reaction mixture was partially purified by column chromatography (silica gel, eluent :

ether).

<u>2-Chloro-2-butenal</u> (<u>5a</u>) : ^{1}H NMR : δ 2.11 (3H, d, J = 6.8Hz, $C\underline{H}_3CH$); 7.06 (1H, q, J = 6.8Hz, CH_3-$C\underline{H}$=); 9.39 (1H, s, $C\underline{H}O$). ^{13}C ($CDCl_3$) : 15.26 (q, $\underline{C}H_3CH$=); 136.81 (s, =$\underline{C}Cl$); 147.23 (d, $\underline{C}H$=); 185.63 (d, $\underline{C}HO$). IR (NaCl) : $\nu_{C=O}$: 1702 cm^{-1}; $\nu_{C=C}$: 1632 cm^{-1}. Mass Spectrum m/z (%) : 104/6 (M^+, 100); 103/5(17); 86(9); 84(12); 77(10); 75(26); 69(17); 58 (12); 51(9); 49 (28); 43(23); 41(60).

<u>2-Chloro-2-pentenal</u> (<u>5b</u>) : ^{1}H NMR : δ 1.16 (3H, t, J = 7Hz, $C\underline{H}_3$); 2.50 (2H, quint, J = 7Hz, $C\underline{H}_2$-CH=); 6.85 (1H, t, J = 7Hz, $C\underline{H}$ = CCl); 9.30 (1H, s, $C\underline{H}O$). ^{13}C ($CDCl_3$) : 11.98 (q, $\underline{C}H_3$); 22.94 (t, $\underline{C}H_2$); 135.23 (s, $\underline{C}Cl$); 152.82 (d, $\underline{C}H$=); 185.65 (d, $\underline{C}HO$). IR (NaCl) : ν_{CHO} : 1702 cm^{-1}; $\nu_{C=C}$: 1625 cm^{-1}. Mass Spectrum m/z (%) : 118/20 (M^+, 100); 89 (30); 83(65); 75 (17); 55(52); 53(70); 51(17); 43(30).

<u>2-Chloro-2-hexenal</u> (<u>5c</u>) : ^{1}H NMR : δ 1.00 (3H, t, J = 7Hz, $C\underline{H}_3CH_2$); 1.60 (2H, sext, J = 7Hz, $CH_2C\underline{H}_2CH_3$); 2.58 (2H, q, J = 7Hz, $C\underline{H}_2CH$=); 6.95 (1H, t, J = 7.5Hz, $C\underline{H}$=). 9.41 (1H,s, $C\underline{H}O$). ^{13}C ($CDCl_3$) : 13.77 (q, Me); 21.11 (t, $CH_3\underline{C}H_2$); 31.46 (t, $CH_3CH_2\underline{C}H_2$); 135.87 (s, =CCl); 151.54 (d, $\underline{C}H$ = CCl); 185.66 (d, $\underline{C}HO$). IR (NaCl) : $\nu_{C=O}$: 1700 cm^{-1}; $\nu_{C=C}$: 1625 cm^{-1}. Mass Spectrum m/z (%) : 132/34 (M^+, 46); 117/19(25); 104/6 (17); 103/5(21); 97(92); 93(29); 91(92); 81(29); 79 (17); 77(13); 75(29); 69(21); 67(50); 53(33); 43 (46); 41(100); 39(100).

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