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REACTIVITY OF α-CHLORO-ALDIMINES[1]

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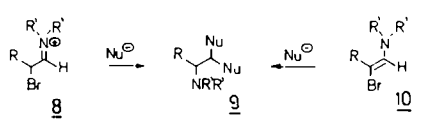
Abstract—A series of secondary N-1-(2-chloroalkylidene)amines has been prepared by condensation of disubstituted acetaldehydes with primary amines followed by chlorination with N-chlorosuccinimide in carbontetrachloride. A study of the reactivity of these N-homologues of α-chloroaldehydes is described. Treatment of the title compounds with sodium methoxide in methanol gave high yields of α,β-unsaturated aldimines. However, N-1-(2-chloro-2-methylpropylidene)amines afforded a mixture of elimination and rearrangement products, which proceeded via an aziridine intermediate. On the other hand, α-phenyl-substituted α-chloro aldimines on treatment with methoxide in methanol underwent α-substitution, consistent with an S_N1 mechanism. Powerful nucleophiles such as sodium thiophenolate in methanol and sodium azide in acetone caused α-substitution. Reaction of α-chloro aldimines with Grignard reagents produced coupling of two aldimine units or α-alkylation. Finally the reactivity of α-chloro aldimines was compared with the reactivity of the corresponding oxygen-analogues, i.e. α-chloro aldehydes.

The preparation and reactivity of α-halogenated imines has received only minor attention.[3] Although recently some synthetic methods for α-halo-aldimines[4] and α-halo-ketimines[5,6] came available, which pointed to an increasing interest in this class of compounds. Studies, dealing with the reactivity of α-halogenated imino compounds are desirable since these compounds are the corresponding N-homologues of α-halogenated carbonyl compounds, i.e. α-halo aldehydes and α-halo ketones. The reactivity of these α-halogenated aldehydes and ketones have been subject of considerable studies, especially in view of the Favorskii rearrangement[7-9] of the latter. A comparative study between α-halo carbonyl compounds and α-halo imines is of mechanistic importance since the N-analogues are the change-over from α-halogenated carbonylcompounds to allylhalogenides.

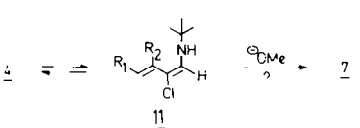
In order to compare the reactivity of these α-halogenated carbonyl compounds with the corresponding N-homologues, it was necessary to have a versatile synthetic method for the preparation of α-halo imines. We have recently reported on the chlorination of methylketimines[5,6] and primary aldimines.[10] The chlorination of imines with N-chlorosuccinimide was shown to be of synthetic value since reactions proceeded practically quantitatively. In this manner, N-2-(1,1-dichloroalkylidene)amines **1** and N-1-(2,2-dichloroalkylidene)amines **2** have been prepared and their reactivity was investigated: α,α-dichloroketimines **1** exhibited nucleophilic substitution and a new type of the

Favorskii rearrangement,[11] while α,α-dichloroaldimines were shown to give α-methoxy-α,β-unsaturated aldimines and rearrangement products.[12] The latter were explained by aziridine intermediates **6**.

The rearrangement of α,α-dichloroaldimines **2** was comparable with the rearrangement of α-bromo imonium bromides **8** and β-bromo enamines **10** with nucleophilic reagents ($Nu^{\ominus}$ = nucleophile).[13-15]

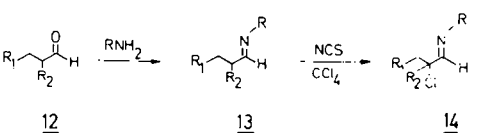


In order to elucidate whether the enaminic form **11** (derived from **4**) was the reactive intermediate in the rearrangement discussed above, we prepared secondary[16] α-chloro aldimines as in this case no tautomerism was possible.



Synthesis of N-1-(2-chloroalkylidene)amines

Secondary α-chloro aldimines **14** were prepared by condensation of disubstituted acetaldehydes **12** with primary amines, followed by chlorination of the resulting aldimines **13** with N-chlorosuccinimide in carbon tetrachloride.



According to this method it was impossible to obtain α-chloro aldimines derived from primary aldehydes (monosubstituted acetaldehydes: $R_2 = H$) because a mixture of monochloro- and dichloro aldimines was formed. Monochloro- and dichloro aldimines could not be separated by distillation, even when a spinning band column was used. Primary α-chloro aldimines ($R_2 = H$) can however be synthesized by condensation of an appropriate α-chloro aldehyde with a primary amine.[4] The results of the synthesis of N-1-(2-chloroalkylidene)amines **14** were given in Table 1.

N-1-(2-chloroalkylidene)amines **14** were characterized by NMR, IR and mass spectral data. The NMR spectrum (CCl_4) exhibited the typical aldimine singlet in the δ 7.5–7.7 ppm region. Only the diphenyl derivative **14l** showed a remarkable deshielding for the CH=N resonance (δ 8.05 ppm). As expected (based on accepted concepts of steric hindrance) all α-chloro aldimines **14** were found to exist in the *E*-configuration (NMR; CCl_4 solution). The position of the C=N stretching vibration in the IR spectrum was almost not influenced by α-chlorination, as shown by comparison with the value for

Table 1. Synthesis and spectroscopic properties of N-1-(2-chloroalkylidene)amines **14**

	Compound[a]			Yield	B.p.	N.M.R. (CCl_4) $\delta_{CH=N}$ (ppm)	I.R. (NaCl) $\nu_{C=N}$ (cm^{-1})	Mass spectrum m/e (%)
	R_1	R_2	R					
14a	H	CH_3	tBu	85 %	50 - 52°C/ 30 mmHg	7.58	1660-80	m/e 161/3(1% ; M^+) ; 146/8(8%) ; 126(3%) ; 125(1%) ; 106(2%) ; 96(1%) ; 89(2%) ; 84(19%) 77/9(2%) ; 70(13%) ; 69(1%) ; 68(1%) ; 57(100%) 56(7%) ; 55(3%) ; 53(1%) ; 41(13%).
14b	H	CH_3	cycloHex	70 %	90 - 93°C/ 12 mmHg	7.69	1670	m/e 187/9(0.2% ; M^+) ; 152(5%) ; 110(22%) ; 83(100%) ; 82(3%) ; 77/9(4%) ; 70(5%) ; 67(3%) 55(44%) ; 41(21%).
14c	H	CH_3	nBu	13 %[b]	69 - 75°C/ 17 mmHg	7.64	1672	m/e 161/3(0.2% ; M^+) ; 146/8(0.2%) ; 126(4%) ; 118/20(2%) ; 89/91(1%) ; 84(60%) ; 82(2%) ; 77/79(2%) ; 76(1%) ; 70(3%) ; 68(1%) ; 57(100%) 55(4%) ; 41(13%).
14d	H	CH_3	iPr	78 %	47 - 49°C/ 24 mmHg	7.62	1670	m/e 147/9(0.5% ; M^+) ; 146/8(0.3%) ; 132(2%) ; 112(7%) ; 96(8%) ; 89(2%) ; 79(4%) ; 77(11%) ; 71(5%) ; 70(100 %) ; 55(4%) ; 43(93%) ; 41(16%).
14e	H	CH_3	$CH_2C_6H_5$	77 %	130-136°C/ 12 mmHg	7.77	1671	m/e 195/7(2% ; M^+) ; 160(8%) ; 118(14%) ; 91(100%) ; 77(4%) ; 65(5%) ; 55(1%) ; 51(1%) ; 41(3%).
14f	CH_3	CH_3	tBu	73 %	63 - 67°C/ 12 mmHg	7.63	1660-78	m/e 160/2(4% ; M^+) ; 147/9(4%) ; 140(2%) ; 132/4(1%) ; 120(2%) ; 99(14%) ; 91(3%) ; 84(18%) ; 70(1%) ; 69(0.5%) ; 68(1%) ; 67(1%) ; 58(6%) ; 57(100%) ; 56(6%) ; 55(2%) ; 41(10%).
14g	CH_3	Et	tBu	79 %	74 - 76°C/ 12 mmHg	7.56	1660-72	no M^+ ; m/e 174/6 (4%) ; 161/3(6%) ; 105(5%) ; 99(23%) ; 98(12%) ; 84(13%) ; 69(4%) ; 58(12%) 57(100%) ; 56(13%) ; 55(7%).
14h	CH_3	Et	cycloHex	88 %	122-124°C/ 12 mmHg	7.57	1670	m/e 215/7(0.03% ; M^+) ; 187/9(10%) ; 180(9%) ; 172/4(2%) ; 164/6(1%) ; 144/6(1%) ; 125(26%) ; 110(16%) ; 98(6%) ; 83(100%) ; 82(7%) ; 69(4%) 67(4%) ; 55(36%) ; 54(4%) ; 53(4%) ; 44(12%) ; 41(19%).
14i	$(CH_2)_4$		tBu	80 %	94 - 97°C/ 12 mmHg	7.53	1672	m/e 201/03(0.01% ; M^+) ; 200/02(0.01%) ; 186/8 (4 %) ; 166(17%) ; 110(11%) ; 99(24%) ; 84(12%) 81(8%) ; 57(100%) ; 56(17%).
14j	$(CH_2)_4$		cycloHex	73 %	86 - 89°C/ 0.03 mmHg	7.59	1670	m/e 227/9(1% ; M^+) ; 192(90%) ; 184(5%) ; 172(9%) ; 162(3%) ; 125(53%) ; 110(42%) ; 93(5%) ; 83(100%) ; 82(12%) ; 81(16%) ; 67(9%) 55(30%) ; 41(18%).
14k	H	C_6H_5	tBu	90 %	125-130°C/ 12 mmHg	7.73	1660	m/e 223/5(0.03% ; M^+) ; 208/10(0.1%) ; 196/8 (0.03%) ; 188(1%) ; 187/9(2%) ; 172/4(3%) ; 139(4%) ; 133(1%) ; 132(6%) ; 131(5%) ; 130(9%) 117(2%) ; 115(3%) ; 105(4%) ; 103(3%) ; 91(2%) 84(15%) ; 77(4%) ; 57(100%) ; 51(2%).
14l[c]	-	-	-	-[d]	-	8.05	1665	no M^+ ; m/e 250(67%) ; 235(48%) ; 196(16%) ; 195(100 %) ; 194(39%) ; 167(14%) ; 152(6%) ; 77(5%) ; 58(5%) ; 57(21%) ; 41(8%).

a. All N-1-(2-chloroalkylidene)amines **14** were new compounds and gave satisfactory elemental analyses.

b. The low yield of **14c** was due to decomposition during distillation in vacuo[17]. α-Chloro aldimine **14c** was accompanied by 4 % N-t.butyl 2-chloro-2-methylpropane imidoylchloride (b.p. 75-77°C/17 mmHg).

c. $R_1CH_2=C_6H_5$ and $R_2=C_6H_5$: N-1-(2-chloro-2,2-diphenylethylidene)t.butylamine **14l**.

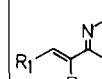
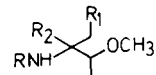
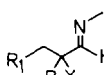
d. N-1-(2-chloro-2,2-diphenylethylidene)t.butylamine **14l** was obtained in nearly quantitative yield (>98 % pure as revealed by the NMR spectrum) and was used as such.

the nonhalogenated aldimines **13**. α-Chloro aldimines **14** displayed an absorption at 1660–1680 cm^{-1} (which often occurred as a doublet), while aldimines **13** gave a value of 1670–1680 cm^{-1}.

Mass spectra displayed the typical 100% peak of *m/e* 57 [$C(CH_3)_3^+$] for the N-*t*-butyl derivatives, next to the fragment ion resulting from fission of the C_1–C_2 bond ($\rightarrow tBu-\overset{+}{N}\equiv CH$ *m/e* 84; in general $R-\overset{+}{N}\equiv CH$). Molecular ions were less abundant or absent (when present molecular ions were only visible at increased amplitude).

We now report on our attempts to extend the rearrangement (via an aziridine intermediate) mentioned above to secondary[16] α-chloro aldimines **14**. With the desired α-chloro aldimines **14** in hand, attention was then turned to the chemical behaviour of these products towards other nucleophilic reagents. The reactivity of N-1-(2-chloroalkylidene)amines **14** with respect to nuc-

Table 2. Reactivity of N-1-(2-chloroalkylidene)amines **14**[a]

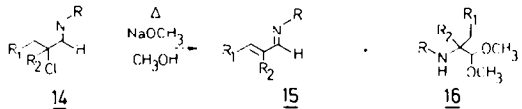
	Starting Compounds			Reagent concentration/ equivalents	Reaction time (reflux)	Recovery of starting material	 15 (elimination)	 16 (rearrangement)	 (substitution)
	R_1	R_2	R						
14a	H	CH_3	tBu	$NaOCH_3/CH_3OH$ 2N/2E	20 hr.	0 %	40 %	33 %	0 %
14a	H	CH_3	tBu	KOtBu/tBuOH 1N/3E	20 hr.	5 %	90 %	0 %	0 %
14a	H	CH_3	tBu	KOtBu/Et_2O 5E	24 hr.	0 %	95 %	0 %	0 %
14a	H	CH_3	tBu	$NaOC_6H_5/CH_3OH$ 1N/2E	24 hr.	0 %	0 %	63 %[b,c]	0 %
14a	H	CH_3	tBu	C_6H_5OH	4 hr.	0 %	0 %	0 %	26 % ($X=OC_6H_5$)[c]
14a	H	CH_3	tBu	$NaSC_6H_5/CH_3OH$ 2N/4E	27 hr.	0 %	0 %	0 %	88 % ($X=SC_6H_5$)
14a	H	CH_3	tBu	NaN_3/acetone 5E	120 hr.	5 %	0 %	0 %	90 % ($X=N_3$)[c]
14a	H	CH_3	tBu	$Cl_2CHCOOMe$/ NaOMe-ether	36 hr.	95 %	0 %	0 %	0 %
14a	H	CH_3	tBu	excess gaseous NH_3/ether	10 hr.	100 %	0 %	0 %	0 %
14b	H	CH_3	cycloHex	$NaOCH_3/CH_3OH$ 2N/2E	20 hr.	0 %	38 %	51 %	0 %
14b	H	CH_3	cycloHex	KOtBu/tBuOH 1N/3E	21 hr.	0 %	90 %	0 %	0 %
14b	H	CH_3	cycloHex	KOtBu/Et_2O 5E	24 hr.	0 %	90 %	0 %	0 %
14b	H	CH_3	cycloHex	$NaOCH_3/iPr_2O$ 5E	20 hr.	100 %	0 %	0 %	0 %
14b	H	CH_3	cycloHex	$NaSC_6H_5/CH_3OH$ 2N/4E	18 hr.	0 %	0 %	0 %	77 % ($X=SC_6H_5$)
14b	H	CH_3	cycloHex	CH_3MgI/ether 4E	18 hr.	45 %	0 %	0 %	42 % ($X=CH_3$)
14e	H	CH_3	$CH_2C_6H_5$	$NaOCH_3/CH_3OH$ 2N/2E	20 hr.	0 %	37 %[d]	40 %	0 %
14f	CH_3	CH_3	tBu	$NaOCH_3/CH_3OH$ 2N/3E	24 hr.	0 %	94 %[c,e]	0 %	0 %
14g	CH_3	Et	tBu	$NaOCH_3/CH_3OH$ 2N/3E	24 hr.	0 %	87 %	0 %	0 %
14h	CH_3	Et	cycloHex	$NaOCH_3/CH_3OH$ 2N/2E	24 hr.	0 %	89 %	0 %	0 %
14h	CH_3	Et	cycloHex	KOtBu/tBuOH 1N/3E	20 hr.	0 %	90 %	0 %	0 %
14h	CH_3	Et	cycloHex	KOtBu/ether 5E	28 hr.	90 %	5 %[c]	0 %	0 %
14h	CH_3	Et	cycloHex	NaI/acetone 3E	overnight	90 %[c]	0 %	0 %	0 %
14i	$(CH_2)_4$		tBu	$NaOCH_3/CH_3OH$ 2N/2E	18 hr.	0 %	98 %	0 %	0 %
14i	$(CH_2)_4$		tBu	$NaOCH_3/iPr_2O$ 5E	120 hr.	100 %	0 %	0 %	0 %
14j	$(CH_2)_4$		cycloHex	$NaOCH_3/CH_3OH$ 2N/2E	16 hr.	0 %	67 %	4 %	0 %
14k	H	C_6H_5	tBu	$NaOCH_3/CH_3OH$ 2N/2E	16 hr.	0 %	0 %	0 %	88 % ($X=OCH_3$)
14k	H	C_6H_5	tBu	CH_3OH	overnight	0 %	0 %	0 %	80 % ($X=OCH_3$)[f]
14l[g]	-	-	-	$NaOCH_3/CH_3OH$ 2N/2E	18 hr.	0 %	0 %	0 %	90 % ($X=OCH_3$)
14l	-	-	-	CH_3OH	overnight	0 %	0 %	0 %	90 % ($X=OCH_3$)[f]
14	($R_1=CH_3$; $R_2=H$; R=tBu)			$NaOCH_3/CH_3OH$ 2N/2E	22 hr.	0 %	10 %	30 %	54 % ($X=OCH_3$)[c]

[a] Yields given in the table were isolated yields except otherwise stated ; [b] Mixture of 17% 2-tbutylamino-1,1-dimethoxy--2-methylpropane **16a** and 56% 2-tbutylamino-1-methoxy-1-phenoxy-2-methylpropane **22** (mixed acetal) ; [c] glc analysis : internal calibration ; [d] isolated as N-(benzylidene)2-methyl-1-propenylamine **17** ; [e] mixture of 64 % N-1-(2-methyl-2-butenylidene)tbutylamine **15f** and 30 % N-1-(2-ethyl-2-propenylidene)tbutylamine **15'f** ; [f] isolated as the α-methoxy-acetal ; [g] N-1-(2-chloro-2,2-diphenylethylidene)tbutylamine.

leophiles, bases or the combined action of both was investigated.

RESULTS AND DISCUSSION

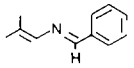
Treatment of N - 1 - (2 - chloro - 2 - methylpropylidene)amines **14a** and **14b** with sodium methoxide in methanol (2N; 2 equivalents; reflux) led to elimination and rearrangement. Elimination produced α,β-unsaturated aldimines **15**, while rearrangement gave



14 **15** **16**

rise to α-(dimethoxymethyl)amines **16**. These isobutyraldehyde derivatives (see Table 2) were formed in essentially equal amounts.

An analogous reaction was found for N - 1 - (2 - chloro - 2 - methylpropylidene)benzylamine **14e**; although no α,β-unsaturated aldimine was obtained since double bond migration and dehydrochlorination produced benzylidene derivative **17**. Migration of the C=N bond from the



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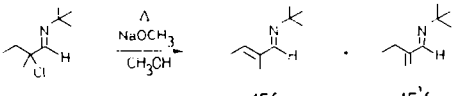
alkylidene to the benzylidene moiety is a base induced process, which has been used to convert α,β-unsaturated carbonyl compounds into the corresponding saturated compounds via alkylidene-benzylamines.[18]

More highly-substituted representatives ($R_1 \neq H$) gave almost exclusively elimination products **15**, while no rearrangement product **16** was observed. Thus, treatment of secondary α-chloro aldimines with sodium methoxide in methanol provided a useful method for the synthesis of α,β-unsaturated aldimines **15**, which have recently been found to be of synthetic value (see for instance reactions of lithiated α,β-unsaturated aldimines[19,20]). A survey of the preparation and spectroscopic properties of N-1-(2-alkenylidene)amines **15** is given in Table 3. When "unsymmetrical" α-chloro aldimines were used, i.e. when $R_1CH_2 \neq R_2$, a mixture of two α,β-unsaturated aldimines was obtained. For instance N - 1 - (2 - chloro - 2 - methylbutylidene)*t*-butylamine **14f** ($R_1 = CH_3$; $R_2 = CH_3$; R = *t*-Bu) gave a mixture of 64% N - 1 - (2 - methyl - 2 - butenylidene)*t*-butylamine **15f** and 30% N - 1 - (2 - ethyl - 2 - propenylidene)*t* - butylamine **15'f**.

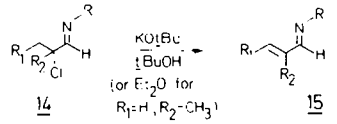


14f **15f** **15'f**

The NMR spectrum of α,β-unsaturated aldimines **15f, g, h** showed that only one cis/trans isomer (C=C bond) was formed, namely, the *E*-isomer. This argumentation was based on the δ-value of the β-methyl group ($\delta \sim 1.8$ ppm) which corresponded to a trans methyl group with respect to the imino function (anisotropy effect); [11,21] for instance the trans β-methyl group of the N-*t*-butyl aldimine derived from crotonaldehyde resonated at 1.87 ppm (NMR; CCl_4).

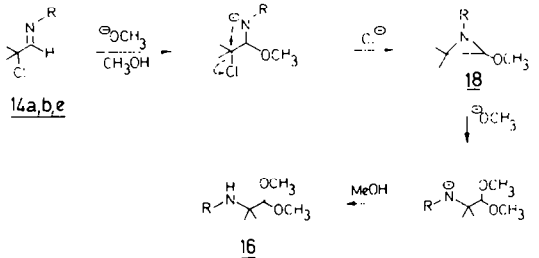
The formation of the rearrangement products **16** in the case of the isobutyraldehyde derivatives ($R_1 = H$; $R_2 = CH_3$) was overcome when the reaction was carried out with potassium *t*-butoxide in *t*-butanol. Yields varied from 90 to 95%. However, N - 1 - (2 - chloro - 2 - phenylpropylidene)*t*-butylamine **14k**, on treatment with potassium *t* - butoxide in *t* - butanol under reflux (for 19 hr), afforded an unappreciable reaction mixture from which only N-*t*-butyl formamide and acetophenone were isolated by preparative gas chromatography. The isolation of these products indicated a breakdown process, which was not further investigated.

Only the dimethyl derivatives (e.g. **14a** and **14b**) gave high yield conversions to α,β-unsaturated aldimines **15** by treatment with potassium *t*-butoxide in diethyl ether under reflux. Higher substituted derivatives did not give elimination even at higher temperature. In this respect, N - [(1' - chloro - 1 - cyclohexyl)methylidene]t - butylamine **14i** and N - 1 - (2 - chloro - 2 - ethylbutylidene)cyclohexylamine **14h** were totally recovered after reflux during 20 hr with a fivefold excess of sodium methoxide in diisopropylether. Additionally, triethylamine in ether or benzene did not provide dehydrochlorination of **14b**. The occurrence of α,β-unsaturated aldimines **15** is in accordance with the preference of the α-halo imino system to



14 **15**

give elimination.[12] When possible elimination yielded the most stable olefin. Products **15** and **15'** were produced in a 2:1 ratio. A more interesting facet of the chemistry of these α-chlorinated aldimines **14** was their rearrangement to compounds **16**. This rearrangement supported the conversion of α,α-dichloro aldimines **2** into the dimethoxymethyl derivatives **7**, which was proposed to occur via an aziridine intermediate, following elimination and migration of the double bond from the conjugated to the deconjugated position (**3**⇄**4**). With the results of the secondary α-chloro aldimines **14**, we wanted to prove that indeed the α-halo imino system (see for instance **4**) was able to undergo rearrangement via aziridines. As shown in the scheme, the rearrangement of compounds **14a, b, e** proceeded via nucleophilic addition, followed by intramolecular nucleophilic substitution and ring opening of the intermediate aziridine **18** by means of an attack of methoxide at the reactive side of the three membered ring (methoxysubstituted carbon atom). A similar ring opening was recently observed on treatment of N-isopropylallenimine with phenol.[22] This reaction was explained by a Markownikow addition of phenol to the exocyclic double bond to yield a phenoxyaziridine, which subsequently reacted with phenol to the expected acetal.



14a,b,e **18** **16**

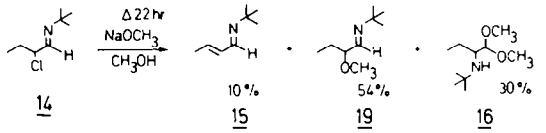
Table 3. Preparation[a] and spectroscopic properties of N-1-(2-alkenylidene)amines **15**

	R_1	R_2	R_3	Yield	B.p.	N.M.R. (CCl_4) (δ, ppm)	I.R. (NaCl) $\nu_{C=N}$ $\nu_{C=C}$ (cm^{-1})	Mass spectrum m/e (%)
15a	H	CH_3	tBu	40 % 90 %[b]	40- 50°C/ 22 mmHg	δ1.16 (9H, s, tBu) ; 1.84 (3H, m, CH_3-C=) ; 5.45 (1H, m, =CH cis with respect to C=N) ; 5.24 (1H,m, =CH trans with respect to C=N) ; 7.80 (1H, s, CH=N)	1647 1628	m/e 125(M^+ ; 60%) ; 110(80%) ; 95(6%) ; 83(3%) ; 70(36%) ; 69(24%) ; 68(8%) ; 57(100%) ; 56(12%).
15b	H	CH_3	C_6H_{11}	38 % 90 %[b]	90-100°C/ 12 mmHg	δ1-2(10H, m, $(CH_2)_5$) ; 1.88 (3H, m, CH_3-C=) ; 3.00 (1H, m, N-CH) ; 5.30 (1H, m, =CH trans with respect to C=N) ; 5.54 (1H, m, =CH with respect to C=N) ; 7.93 (1H, s, CH=N)	1646 1623	m/e 151(M^+ ; 56%) ; 150(28%) ; 136(52%) ; 122(36%) ; 110(68%) 108(100%) ; 96(16%) ; 95(16%) 94(36%) ; 83(24%) ; 82(36%) ; 70(32%) ; 69(12%) ; 68(20%) ; 67(16%) ; 55(54%) ; 41(33%).
15f	CH_3	CH_3	tBu	64 %[c]	-	δ1.18 (9H, s, tBu) ; 1.76 (3H, s, =C-CH_3) ; 1.18 (3H, d, J 6.8Hz, CH_3-C=C-C=N) ; 5.80 (1H, q, J 6.8Hz, CH=C) ; 7.70 (1H, s, CH=N)	1655 1630	m/e 139(58%) ; 124(37%) ; 84(26%) ; 83(42%) ; 82(16%) ; 57(100%).
15f	H	Et	tBu	30 %[c]	-	δ1.05(3H, t, J 7.3Hz, CH_3) ; 1.19(9H, s, tBu) ; 2.31 (2H, q, J 7.3Hz, CH_2) ; 5.26 and 5.47(2H, 2 x m, =C^{H}_{H}) ; 7.82 (1H, s, CH=N)	1650 1625	m/e 139(M^+ ; 79%) ; 124(93%) ; 84(29%) ; 83(43%) ; 82(29%) ; 57(100%).
15g	CH_3	Et	tBu	87 %[c]	-	δ0.95(3H, t, J 7Hz, CH_3) ; 1.19(9H, s, tBu) ; 1.85(3H, d, J 7.2Hz, CH_3-C=) ; 2.42 (2H, q, J 7Hz, CH_2-C=) ; 5.75(1H, q, J 7.2Hz, =CH) ; 7.53(1H, s, CH=N)	1650 1635	m/e 153(M^+ ; 69%) ; 138(50%) ; 110(5%) ; 98(18%) ; 97(75%) ; 96(41%) ; 82(100%) ; 69(19%) ; 56(87%) ; 54(25%).
15h	CH_3	Et	cycloHex	89 % 90 %[b]	111-116°C/ 12 mmHg	δ0.96(3H, t, J 7HZ, CH_3) ; 1.1-2(10H, m, $(CH_2)_5$) ; 1.83(3H, d, J 7Hz, CH_3-C=) ; 2.36(2H, q, J 7Hz, CH_2-C=) ; 2.9(1H, m, CH-N) ; 5.75 (1H, q, J 7Hz, CH=C) ; 7.69 (1H, s, CH=N)	1651 1634	m/e 179(M^+ ; 100%) ; 178(12%) 164(83%) ; 150(30%) ; 136(50%) 122(44%) ; 110(32%) ; 108(20%) 98(22%) ; 97(18%) ; 96(96%) ; 94(14%) ; 82(89%) ; 70(14%) ; 69(12%) ; 68(10%) ; 67(26%) ; 55(76%) ; 54(16%) ; 53(20%) ; 41(89%).
15i	$(CH_2)_4$		tBu	98 %	94 - 97°C/ 12 mmHg	δ1.15(9H, s, tBu) ; 1.4-1.8 (4H, m, $(CH_2)_2$) ; 1.9-2.4 (4H, m, $(CH_2)_2$C=) ; 6.00 (1H, m, CH=C) ; 7.70(1H, s, CH=N)	1650 1630	m/e 165(M^+ ; 60%) ; 150(65%) ; 109(100%) ; 108(50%) ; 94(40%) 93(15%) ; 92(20%) ; 91(15%) ; 82(10%) ; 81(15%) ; 80(8%) ; 79(8%) ; 77(10%) ; 67(15%) ; 58(15%) ; 57(80%).
15j	$(CH_2)_4$		cycloHex	67 %	90 - 95°C/ 0.5 mmHg	δ1-2(14H, m, ring protons) ; 2-2.5(4H, m, $(CH_2)_2$C=) ; 2.9 (1H, m, N-CH) ; 6.00 (1H, m, CH=C) ; 7.72 (1H, s, CH=N)	1648 1630	m/e 191(M^+ ; 100%) ; 190(38%) 177(9%) ; 162(38%) ; 148(45%) 136(16%) ; 134(23%) ; 122(14%) 110(26%) ; 108(26%) ; 95(9%) ; 94(14%) ; 83(13%) ; 81(13%) ; 79(10%) ; 67(13%) ; 56(16%) ; 55(25%) ; 43(31%).

[a] reagent : $NaOCH_3/CH_3OH$ 2N (2 equivalents) under reflux ; all α,β-unsaturated aldimines 15 gave satisfactory elemental analyses ; [b] reagent : KOtBu/tBuOH 1N (3 equivalents) under reflux ; [c] yield determined by gas chromatography (internal calibration).

The occurrence of only elimination for **14f–j** was as expected, while the competition between elimination and rearrangement for the isobutyraldehyde derivatives **14a**, **14b** and **14e** originated in the formation of a less favourable terminal double bond. The unfavourable elimination was therefore accompanied by the aziridine-rearrangement.

Additional insight into the competition between elimination and rearrangement of α-chloro imino compounds was provided by the reaction of primary α-chloro aldimine **14** ($R_1 = CH_3$; $R_2 = H$; R = *t*-Bu) with methoxide in methanol: a mixture of 10% N - 1 - (2 - butenylidene)*t* - butylamine **15** ($R_1 = CH_3$; $R_2 = H$), 54% N - 1 - (2 - methoxybutylidene)*t* - butylamine **19** ($R_1 = CH_3$; $R_2 = H$) and 30% 2-*t*-butylamino-1,1-dimethoxybutane **16** ($R_1 = CH_3$; $R_2 = H$) was obtained. The presence of mainly the substitution product **19** was rather surprising as previously reported results showed a preference for elimina-

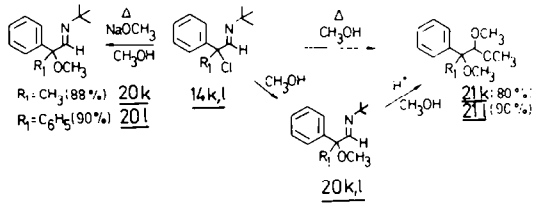


14 15 19 16

tion. The low yield of α,β-unsaturated aldimine **15** can be accounted for the decrease in substitution with respect to the secondary α-chloro aldimines and α,α-dichloro aldimines which favoured elimination. As a matter of fact, the occurrence of the rearranged compound **16** ($R_1 = CH_3$; $R_2 = H$) was then not surprising and proved again the validity of the proposed aziridine rearrangement. The α-substitution was thought to follow a second order mechanism since the formation of a positive charge in the α-position of an imino function is less favourable.

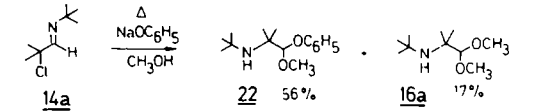
The reaction of α-chloro-α-phenylsubstituted aldimines **14k** and **14l** with sodium methoxide in methanol took a different way as only α-substitution was observed. N - 1 - (2 - chloro - 2 - phenylpropylidene)*t* - butylamine **14k** yielded exclusively N - 1 - (2 - methoxy - 2 - phenylpropylidene)*t* - butylamine **20k** (88%), while N - 1 - (2 - chloro - 2,2 - diphenylethylidene)*t* - butylamine **14l** provided the substitution product N - 1 - (2 - methoxy - 2,2 - diphenylethylidene)*t* - butylamine **20l** (90%).

The substitution in the α-position of the imino function was thought to proceed via a S_N1 mechanism as the resulting carbonium ion is stabilized by delocalization with the aromatic π-orbitals. Subsequently, attack of the nucleophile would yield final products **20**. This proposition was supported by refluxing α-chloro aldimines **14k** and **14l** in methanol. Work-up revealed the presence of exclusively α-methoxy-acetals **21**, resulting from α-substitution. Hydrogen chloride, produced by this nucleophilic substitution, caused further conversion of α-methoxy aldimines **20** into α-methoxy-acetals **21**.



20k,l

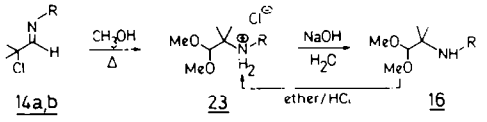
The reaction of α-chloro aldimines was also studied with less basic alkoxides such as sodium phenoxide. Refluxing **14a** with a twofold excess of sodium phenoxide in methanol (overnight) did not yield α,β-unsaturated aldimine **15a** but gave exclusively rearrangement products **16a** and **22**. The mixed acetal **22** is presumably formed by addition of phenoxide to the C=N bond followed by ring closure (S_Ni), the resulting phenoxyaziridine being attacked by methanol (no trace of diphenylacetal was found).



14a

In order to avoid the interaction of methanol, we carried out the reaction of **14a** and sodium phenoxide in dimethoxyethane, but in this case no reaction occurred (a reflux period of 40 hr). Higher substituted α-chloro aldimines yielded complex reaction mixtures when heated with sodium phenoxide in methanol and were therefore not further investigated. A similar complex reaction mixture was obtained when N - 1 - (2 - chloro - 2 - methylpropylidene)*t* - butylamine **14a** was refluxed with phenol. Two main products could be determined by glc namely N - 1 - (2 - methyl - 2 - phenoxypropylidene)*t* - butylamine (25%) and N - *t* - butyl 2 - chloro - 2 - methylpropanamide (16%).

As shown above, reaction of α-chloro α-phenyl aldimines **14k** and **14l** with methanol gave rise to α-substitution, which was followed by formation of acetals **21k** and **21l**. Although, when ordinary α-chloro aldimines, such as **14a**, were treated with methanol under reflux during a long period (5 days), a 70% yield of a crystalline material **23a** was obtained. The NMR spectrum ($CDCl_3$) of this solid material was practically completely similar to that of **16a**, except that a deshielding of all peaks was observed along with a broad peak at higher δ-value (8.20 ppm). The product was found to be the hydrochloride of the rearrangement product **16a**. Treatment of **23a** with sodium hydroxide in water gave indeed **16a**. The structural elucidation was further proved by comparison with an authentic sample, prepared from **16a** and gaseous hydrogen chloride in ether. A similar result was obtained with imine **14b** (yield of **23b**: 93%).

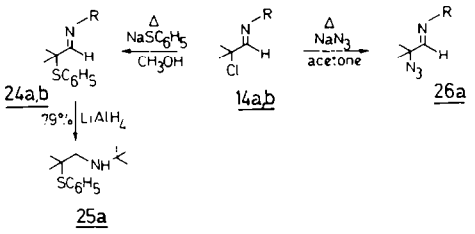


14a,b 23 16

As described above, the formation of compounds **23** can be explained by the aziridine rearrangement, the liberated hydrogen chloride being captured by the amine. Thus appropriate choice of the reaction medium can convert isobutyraldehyde derivatives **14** ($R_1 = H$, $R_2 = CH_3$) to the dehydrochlorinated product, the rearranged product or a mixture of both.

As shown by the results given above, α-chlorinated aldimines established a preference for elimination reactions by treatment with reagents which had nucleophilic and basic properties. Rearrangement of dimethyl derivatives **14a**, **14b** and **14e** via an aziridine intermediate could be promoted by methoxide in methanol. We were able to furnish exclusively nucleophilic substitution in the α-position of the imino grouping by treatment with sodium thiophenolate in methanol and sodium azide in acetone. Compounds **14a** and **14b** reacted fastly with sodium thiophenolate in refluxing methanol to produce high yields of substitution products **24a,b**. Compound **24a** was easily reduced to the corresponding amine **25a** ($LiAlH_4$/ether).

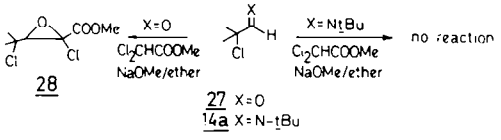
The reaction of sodium azide with N - 1 - (2 - chloro - 2 - methylpropylidene)*t* - butylamine **14a** proceeded very slowly and needed a refluxtime of 5 days producing 90% N - 1 - (2 - azido - 2 - methyl - propylidene)*t* - butylamine



24a,b 14a,b 26a

25a

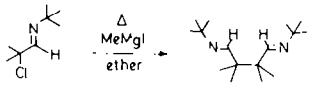
26a (together with a recovery of 5% starting material). The azido compound **26a** was obtained in pure form by preparative gas chromatography. The purity was checked by GLC on several different columns. The structure of compound **26a** was in accordance with the infrared and mass spectrum. Nevertheless, the NMR spectrum showed a 4/1 ratio of two compounds, from which the main compound was consistent with the azide structure **26a**. The product existed in CCl_4-solution probably in equilibrium with an isomeric compound (ringstructure?). On the contrary, when amines were used as nucleophilic agents, no reaction occurred after a prolonged period. Even ammonia in ether did not give any reaction. Also other reagents such as potassium xanthogenate in methanol, methyl acetoacetate in dimethoxyethane with NaH, diazomethane in ether, sodium iodide in acetone, and methyl dichloroacetate in NaOMe and ether did not react in the expected manner. Especially the latter reagent was expected to give the Darzens type condensation product since the corresponding oxygen analogue α-chloro isobutyraldehyde **27** reacted smoothly to afford chlorinated epoxides **28**.[23]



28

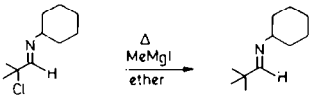
27 X=O
14a X=N-tBu

When N - 1 - (2 - chloro - 2 - methylpropylidene)*t* - butylamine **14a** was allowed to react with excess methyl magnesium iodide in refluxing ether, a high yield conversion to "dimer" **29** was obtained (70%). A similar result was reported by Duhamel *et al.*, who prepared di-imine **29** by reaction of N - 1 - (2 - bromo - 2 -



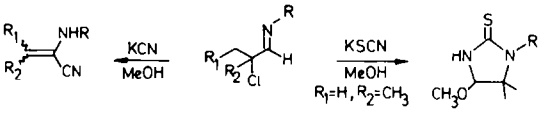
14a 29

methylpropylidene)*t* - butylamine with lithium (32% yield).[24] Furthermore, the same authors extended this "dimerization" by condensation of α-bromo aldimines with sodium in liquid ammonia[25] and used this result to prove that the conversion of primary α-halogenated aldimines with Grignard reagents to pyrroles was initiated by a "dimerization" under influence of the organomagnesium compound.[24-26] Surprisingly N - 1 - (2 - chloro - 2 - methylpropylidene)cyclohexylamine **14b**, on treatment with CH_3MgI in refluxing ether gave no "dimerization" but yielded 42% N - 1 - (2,2 - dimethylpropylidene)cyclohexylamine (besides recovery of 45% starting material).



14b 30

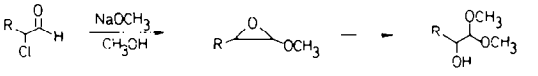
As previously described, the versatility of the α-chloro imino system **14** was demonstrated by the synthesis of α-cyano - enamines **31** and 1 - alkyl - 4 - methoxy - 5,5 - dimethyl - 2 - imidazolidinethion **32**. The former were prepared by reaction of **14** with potassium cyanide in methanol,[27] while the latter were synthesised by a one-step synthesis, using **14a, b, c, d, e** and potassium thiocyanate in methanol.[1]



31 14 32

N - 1 - (2 - chloroalkylidene)amines can therefore be dedicated as useful synthesizing blocs in synthetic organic chemistry.

One of the purposes of this mechanistical study was to compare the reactivity of the α-halo imino system **14** with the corresponding oxygen analogues, i.e. α-halo aldehydes. From the theoretical point of view a variety of reactions is possible with a system, consisting of the combination of an imino (or carbonyl) function and a halogenated carbon atom. The reactivity of α-halogenated aldehydes was thouroughly studied by Kirrmann and Stevens, who mainly described the alkoxide-induced rearrangement of α-halo aldehydes **33**



33 34 35

to α-hydroxy acetals **35**.[28-31] The reaction proceeded via epoxides **34**, which were isolated when no excess of alcohol was used.

Besides the overwhelmingly occurring nucleophilic addition followed by epoxide-formation, other types of reactions such as elimination,[32] "Favorskii-type" rearrangement,[33] Tichtchenko dismutation,[33] Darzens-type condensations[23,24] and α-substitution[35,36] were rarely reported. Only α-halo-isobutyraldehyde was described to give α-substitution with malonate or acetylacetate, which led on further reaction respectively to γ-butyrolactones[37] and 2,3-dihydrofuran derivatives.[38] As shown above α-chloro aldimines **14** do not easily undergo nucleophilic addition at the carbon–nitrogen double bond. This is in contrast to the O-analogues and is resulting from the less pronounced polarization of the C=N bond with respect to the C=O bond.

The difference of the reactivity of α-halogenated aldehydes and aldimines is mainly based on the difference in electronegativity of the heteroatom of the C=X bond (X=O, N). Owing to the decreased polarization of the C=N bond, the reactions of **14** with alkoxides in alcohol took a different way and gave mainly elimination to produce α,β-unsaturated aldimines **15**. The elimination appeared in competition with the rearrangement (following A_N, S_Ni and aziridine opening) when a less favourable terminal double bond had to be produced (dimethyl derivatives **14a, b, c**). In our opinion, the formation of only 10% elimination, starting from the primary α-chloro aldimine **14** ($R_1 = CH_3$; $R_2 = H$; R = *t*-Bu) is a problem of destabilization (disubstituted alkene with respect to a trisubstituted one for secondary derivatives), while the high yields of α-substitution may probably account for a less pronounced steric hindrance in primary compounds **14** ($R_2 = H$) as in secondary derivatives **14** ($R_2 \neq H$). Only

strong nucleophiles (thiophenolate, azide) performed α-substitution, which was also found in cases, whereby a stabilisation of the carboniumion in the α-position of the C=N bond was possible by phenyl substitution.

EXPERIMENTAL

IR spectra were recorded on a Perkin Elmer model 257 spectrophotometer. NMR spectra were obtained on a Varian T-60 spectrometer, while mass spectra were measured with A.E.I. MS20 or A.E.I. MS30 mass spectrometers (70 eV). The A.E.I. MS20 apparatus was coupled with a Pye Unicam 104 gas chromatograph (SE30 5%; 1.5 m). M.ps were determined on a Kofler hot stage and were uncorrected. All aldehydes used were commercially available compounds or were prepared according to standard methods: 2-methylbutanal[39] and 2-phenylpropanal.[40] N - 1 - (2 - chlorobutylidene)*t* - butylamine **14** ($R_1 = CH_3$; $R_2 = H$; R = *t*-Bu) was prepared by condensation of 2-chlorobutanal[28] with *t*-butylamine in diluted ethereal medium.[4]

Preparation of N - 1 - (2 - chloroalkylidene)amines **14**

A mixture of 0.1 mole aldehyde **12** and 0.1 mole primary amine was mixed at room temperature and stirred for 5 min (eventually with cooling). It was not necessary to isolate N-1-(alkylidene)amines **13**. Although, aldimines **13** could be isolated by addition of ether and $MgSO_4$, the resulting suspension being stirred for 1 hr; filtration and evaporation *in vacuo* yielded an oil, which was distilled to give **13**. The isolation of aldimines **13** could be overcome by addition of 150 ml carbon tetrachloride to the initial reaction mixture obtained by adding the primary amine to the aldehyde. After addition of $MgSO_4$, the suspension was stirred for 2 hr and subsequently filtered and washed with carbon tetrachloride. The filtrate was then treated portionwise with 0.11 mole N-chlorosuccinimide while the temperature was maintained at room temperature by means of a water bath. After stirring thouroughly for 3 hr the mixture was filtered and washed with a small amount of dry CCl_4. The solvent was then removed *in vacuo* and the remaining oil was distilled with the water pump. Yields of N - 1 - (2 - chloroalkylidene)amines **14** were given in Table 1. In the case of compound **14a**, the distilled product was contaminated with a small amount (1–3%) of N,N-dichloro-*t*-butylamine *t*-$BuNCl_2$ which was identified by NMR and mass spectrometry (GS–MS coupling).

Reaction of N-1-(2-chloroalkylidene)amines **14** *with sodium methoxide in methanol*

A mixture of 0.1 mol N-1-(2-chloroalkylidene)amine **14** and 160 ml 2N sodium methoxide in methanol (2.0 equivalents) was refluxed for a period indicated in Table 2. Methanol was partly evaporated and the residue was poured into water, followed by extraction with diethyl ether. The combined extracts were dried ($MgSO_4$) and evaporated *in vacuo* leaving an oil which was first analyzed by gas liquid chromatography and distilled. The reaction mixture derived from N - 1 - (2 - chloro - 2 - methylpropylidene)*t* - butylamine **14a** contained highly volatile compounds, which were lost partially by distillation of methanol *in vacuo*. Therefore the whole reaction mixture was poured into water and extracted four times with pentane. The combined extracts were dried ($MgSO_4$), filtered and distilled using a 20 cm Vigreux column. There was obtained 40% N - 1 - (2 - methylpropenylidene)*t* - butylamine **15a**, b.p. 40–50°C/12 mmHg, (see Table 3 for data) and 33% 2 - *t* - butylamino - 1,1 - dimethoxy - 2 - methylpropane **16a**, b.p. 70–80°C/15 mmHg. NMR (CCl_4): 1.15 (9H, s, *t*-Bu); 1.05 (6H, s, $(CH_3)_2$); 3.45 (6H, s, $(OCH_3)_2$); 3.81 (1H, s, C<u>H</u>$(OMe)_2$); NH invisible. IR (NaCl): 3360 cm^{-1} (ν_{NH} very weak); 2840 cm^{-1} (ν_{OCH_3}). MS: no M^+; *m/e* 174 (0.1%); 157 (1%); 141 (2%); 114 (21%); 102 (6%); 100 (3%); 86 (3%); 85 (2%); 75 (2%); 70 (7%); 58 (100%); 57 (12%). Calc. for $C_{10}H_{23}NO_2$: C, 63.45; H, 12.25; N, 7.40; Found: C, 63.59; H, 12.39; N, 7.24%.

Other compounds obtained from the reaction of **14** with sodium methoxide im methanol and which were not tabulated (spectral data) are given below. 2 - Cyclohexylamino - 1,1 - dimethoxy - 2 - methylpropane **16b**: NMR (CCl_4): 0.93 (6H, s, $(CH_3)_2$); 1–2 (10H, m, $(CH_2)_5$); 2.5 (1H, m, N–C<u>H</u>); 3.50 (6H, s, $(OCH_3)_2$); 3.86 (1H, s, C<u>H</u>$(OMe)_2$); NH invisible. IR (NaCl): no ν_{NH}; 1468, 1454, 1190, 1110, 1080 cm^{-1} (strong). MS: no M^+; *m/e* 184 (4%); 168 (1%); 167 (2%); 140 (87%); 102 (3%); 83 (4%); 75 (3%); 70 (5%); 58 (100%); 55 (10%); 41 (10%). Calc. for $C_{12}H_{25}NO_2$: C, 66.93; H, 11.70; N, 6.50. Found: C, 66.80; H, 11.59; N, 6.66%.

2-*Benzylamino*-1,1-*dimethoxy*-2-*methylpropane* **16c**. NMR (CCl_4): 1.03 (6H, s, $(CH_3)_2$); 3.43 (6H, s, $(OCH_3)_2$); 3.93 (1H, s, C<u>H</u>$(OMe)_2$); 3.67 (2H, s, NCH_2); 7–7.2 (5H, m, C_6H_5); NH invisible. IR (NaCl): 3330 cm^{-1} (ν_{NH}); 2835 cm^{-1} (ν_{OCH_3}); 1608, 1577, 1500 cm^{-1} ($\nu_{aromatic}$). MS: no M^+; *m/e* 192 (4%); 148 (65%); 91 (100%); 77 (2%); 75 (4%); 65 (7%); 59 (3%); 55 (3%); *b.p.* 74–80°C/0.01 mmHg. Calc. for $C_{13}H_{21}NO_2$: C, 69.92; H, 9.48; N, 6.27. Found: C, 70.09; H, 9.62; N, 6.02%.

N - (benzylidene)2 - methyl - 1 - propenylamine **17**: NMR (CCl_4): 1.80 and 2.03 (2×3H, 2×s broadened, $(CH_3)_2C=$); 6.54 (1H, m, C<u>H</u>=C); 7.0–7.8 (5H, m, C_6H_5); 7.98 (1H, s, C<u>H</u>=N). IR (NaCl): 1661 cm^{-1} ($\nu_{C=N}$); 1608, 1577, 1499, 1453, 1386 cm^{-1}. MS: *m/e* 159 (M^+; 100%); 158 (54%); 144 (16%); 143 (11%); 131 (4%); 117 (23%); 104 (33%); 91 (18%); 90 (25%); 89 (16%); 82 (53%); 77 (9%); 65 (4%); 63 (6%); 57 (5%); 55 (18%); 51 (8%); b.p. 64–70°C/0.01 mmHg.

N - 1 - (2 - butenylidene)*t* - butylamine **15** ($R_1 = CH_3$; $R_2 = H$; R = *t*-Bu) was identified by its spectral data and by comparison with an authentic sample prepared from crotonaldehyde and *t*-butylamine.

N - 1 - (2 - methoxybutylidene)*t* - butylamine **19**: NMR (CCl_4): 1.16 (9H, s, *t*-Bu), 0.90 (3H, t, J 6 Hz, CH_3); 1.46 (2H, m, CH_2); 3.29 (3H, s, OCH_3); 3.45 (1H, m, CH–OMe); 7.38 (1H, d, J 6 Hz, C<u>H</u>=N). IR (NaCl): 1675 cm^{-1} ($\nu_{C=N}$); 2830 cm^{-1} (ν_{OCH_3}). MS: *m/e* 157 (M^+; 2%); 142 (5%); 126 (14%); 114 (4%); 112 (6%); 86 (6%); 85 (2%); 84 (4%); 73 (73%); 72 (2%); 71 (4%); 70 (4%); 58 (13%); 57 (100%); 56 (6%); 55 (4%); 53 (4%). Calc. for $C_9H_{19}NO$: C, 68.74; H, 12.18; N, 8.91. Found: C, 68.94; H, 12.20; N, 8.83%.

2 - *t* - butylamino - 1,1 - *dimethoxybutane* **16** ($R_1 = CH_3$; $R_2 = H$; R = *t*-Bu) NMR (CCl_4): 0.85 (3H, t, J 6.5 Hz); 1.4 (2H, m, $(CH_2)_2$): 2.62 (1H, dxt, $J_{ab} = 4$ Hz, J_{ac} undistinctly, C<u>H</u>$_a$–N); 4.06 (1H, d, $J_{ab} = 4$ Hz, OCH_b–O); 3.35 and 3.39 (6H, 2xs, $(OCH_3)_2$); 1.05 (9H, s, *t*-Bu); NH invisible. IR (NaCl): 2835 cm^{-1} (ν_{OCH_3}); 3340 cm^{-1} (ν_{NH}). MS: *m/e* 189 (M^+; 0.3%); 158 (2%); 142 (2%); 128 (1%); 114 (32%); 102 (7%); 85 (2%); 75 (3%); 73 (1%); 72 (1%); 70 (4%); 58 (100%); 57 (10%); 41 (7%). Calc. for $C_{10}H_{23}NO_2$: C, 63.45; H, 12.25; N, 7.40. Found: C, 63.15; H, 12.23; N, 7.48%.

Reaction of N-1-(2-chloroalkylidene)amines **14** *with potassium t-butoxide in ether*

A mixture of 0.01 moles α-chloro aldimine **14** and 0.05 moles KOt-Bu in 50 ml dry ether was refluxed for a time indicated in Table 2. After filtration, the ether was evaporated and the remaining oil was analyzed by GLC and distilled.

Reaction of N-1-(2-chloroalkylidene)amines **14** *with potassium t-butoxide in t-butanol*

A similar procedure as described for the reaction with sodium methoxide in methanol was used (see Table 2).

Reaction of α-chloro aldimines with methanol

This procedure is only valid for the isobutyraldehyde derivatives **14** ($R_1 = H$; $R_2 = CH_3$). In a typical experiment, a solution of 2.0 g (0.0124 moles) N - 1 - (2 - chloro - 2 - methylpropylidene)*t* - butylamine **14a** in 50 ml dry methanol was refluxed during a period of 100 hr (protection by a calcium chloride rube). Evaporation of the solvent under vacuum afforded a viscous oil which solidified partially on standing. Crystallisation was further promoted by the addition of dry diethyl ether. After standing overnight, the white crystalline material was collected by filtration and treated with chloroform. The unsoluble material was found to be *t*-butylamine hydrochloride. Evaporation of the chloroform *in vacuo* provided again an oil which solidified on standing: 1.9 g 2 - *t* - butylamino - 1,1 - dimethoxy - 2 - methylpropane hydrochloride **23a** (yield 70%), m.p. 164°C. NMR ($CDCl_3$): 1.57 (6H, s, $(CH_3)_2$); 1.64 (9H, s, *t*-Bu); 3.65 (6H, s, $(OCH_3)_2$); 4.88 (1H, s, O–C<u>H</u>–O); 8.20 (2H, s, broad, $\overset{+}{N}H_2$). IR (KBr): 3600–2500 cm^{-1} (broad); medium absorption at

2700, 2600, 2510, 2415 cm^{-1}; strong peaks at 1568, 1558, 1405, 1386, 1155, 1110, 1080, 975 cm^{-1}. Treatment of **23a** in chloroform with 2N NaOH gave, after usual work up pure **16a** (see above). Compound **23b**, i.e. 2 - cyclohexylamino - 1,1 - dimethoxy - 2 - methylpropane hydrochloride, was obtained in similar manner (yield 93%); m.p. 196°C (decomp.). NMR ($CDCl_3$): 1–2.2 (10H, m, $(CH_2)_5$); 1.53 (6H, s, $(CH_3)_2$); 3.5 (1H, m, N–CH); 3.66 (6H, s, $(OCH_3)_2$); 4.74 (1H, s, $CH(OMe)_2$); 7.6 (2H, s broad $\overset{+}{N}H_2$). IR (KBr): 3600, 2500 cm^{-1} (broad); 1566, 1459, 1405, 1199, 1188, 1168, 1114, 1080 cm^{-1}.

Reaction of α-chloro-α-phenyl aldimines **14k** *and* **14l** *with methanol*

In a typical experiment, 223 mg (0.001 mol) N - 1 - (2 - chloro - 2 - phenylpropylidene)*t* - butylamine **14k** was mixed with 5 ml dry methanol and refluxed. The solution immediately became acid. After refluxing overnight, the solvent was removed under vacuum by repeatedly addition of carbon tetrachloride and evaporation. A colorless oil was obtained, which was found to be pure 1,1,2 - trimethoxy - 2 - phenylpropane **21k** (NMR, GLC). Yield 80%. NMR (CCl_4): 1.48 (3H, s, CH_3); 3.03 and 3.06 (6H, 2xs, $(OCH_3)_2$); 3.46 (3H, s, OCH_3); 3.96 (1H, s, $CH(OMe)_2$); 7–7.5 (5H, m, C_6H_5). IR (NaCl): 2835 cm^{-1} (ν_{OCH_3}). MS: no M^+; 179 (2%); 135 (13%); 121 (1%); 119 (1.5%); 105 (3%); 103 (1%); 91 (1%); 77 (4%); 75 (100%; $CH_3O–\overset{+}{C}H–OCH_3$); 51 (2%); 47 (5%); 43 (8%). Calc. for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.21; H, 8.49%.

1,1,2-Trimethoxy-2,2-diphenylethane **21l** was obtained in similar manner, yield 90%. NMR (CCl_4): 3.10 (3H, s, $CH_3O–C(C_6H_5)_2$; 3.29 (6H, s, $(OCH_3)_2$); 4.56 (1H, s, $CH(OMe)_2$); 6.0–6.8 (10H, m, 2 C_6H_5). IR (NaCl): 2835 cm^{-1} (ν_{OCH_3}). MS: no M^+; *m/e* 241 (1%); 212 (0.3%); 197 (10%); 167 (1%); 165 (1%); 153 (0.5%); 122 (0.5%); 105 (5%); 92 (0.5%); 77 (5%); 75 (100%); 51 (1%); 47 (3%). Calc. for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 74.77; H, 7.12%.

*Reaction of N - 1 - (2 - chloro - 2 - methylpropylidene)*t *- butylamine* **14a** *with sodium azide in acetone*

To a solution of 0.03 moles **14a** in 50 ml acetone was added 0.15 moles sodium azide. The suspension was refluxed for 5 days. Filtration and evaporation gave a residue which consisted of 90% N - 1 - (2 - azido - 2 - methylpropylidene)*t* - butylamine **26a** and 5% starting material **14a** (NMR, GLC). Compound **26a** was isolated by preparative GLC. NMR (CCl_4): 1.16 (9H, s, *t*-Bu); 1.32 (6H, s, $(CH_3)_2$); 7.47 (1H, s, CH=N). Compound **26a** seemed to be in equilibrium with an unknown compound which showed the following NMR 1.21 (9H, s, *t*-Bu); 1.29 (6H, s, $(CH_3)_2$); 7.70 (1H, s, CH=N). Product **26a** was found to give only one single peak on different GLC columns. IR (NaCl): 2205 cm^{-1} (azide); 1647 cm^{-1} ($\nu_{C=N}$). MS: no M^+; 140 (2%; $-N_2$); 139 (2%); 125 (2.5%; $-HN_3$); 110 (2%); 98 (2%); 84 (16%; *t*-BuN≡CH); 83 (12%) 70 (12%); 57 (100%); 56 (28%); 42 (8%); 41 (22%).

Reaction of α-chloro aldimines **14** *with sodium thiophenolate in methanol*

In a typical experiment, 7.5 g (0.04 mol) N - 1 - (2 - chloro - 2 - methylpropylidene)cyclohexylamine **14b** was treated with 4 equivalents 2N sodium thiophenolate in methanol (obtained by addition of 17.6 g (0.16 mol) thiophenol to 80 ml 2N sodium methoxide in methanol). The solution was refluxed under a nitrogen atmosphere during 18 hr. Half of the methanol was evaporated (Rotavapor) and the mixture was then poured into water, extracted three times with ether, dried. Evaporation of the solvent yielded an oil which was distilled to afford 8.0 g N - 1 - (2 - methyl - 2 - phenylthiopropylidene)cyclohexylamine **24b** (yield 77%); b.p. 180–190°C/12 mmHg. NMR (CCl_4): 1–2 (10H, m, $(CH_2)_5$); 1.35 (6H, s, $(CH_3)_2$); 3.0 (1H, m, N–CH); 7.1–7.6 (5H, m, C_6H_5); 7.56 (1H, s, CH=N). IR (NaCl): 1662 cm^{-1} ($\nu_{C=N}$). MS: 261 (M^+; 12%); 227 (16%); 217 (9%); 152 (55%); 151 (45%); 119 (9%); 110 (36%); 83 (100%); 70 (90%); 55 (95%); 41 (97%). Calc. for $C_{16}H_{23}NS$: C, 73.51; H, 8.87; N, 5.36. Found: C, 73.14; H, 8.70; N, 5.54%. Compound **24a** was obtained in similar manner: yield 88%; 147–156°C/12 mmHg. NMR (CCl_4): 1.03 (9H, s, *t*-Bu); 1.33 (6H, s, $(CH_3)_2$); 7.1–7.5 (5H, m, C_6H_5); 7.50 (1H, s, CH=N). IR (NaCl): 1658–1680 cm^{-1} ($\nu_{C=N}$). MS: 235 (M^+; 7%); 220 (1%); 152 (45%); 151 (65%); 120 (6%); 119 (7%); 118 (8%); 117 (10%); 111 (9%); 110 (29%); 96 (4%); 84 (5%); 73 (5%); 70 (32%); 57 (100%); 41 (32%). Calc. for $C_{14}H_{21}NS$: C, 71.44; H, 8.99; N, 5.95. Found: C, 71.16; H, 8.70; N, 6.09%. Compound **24a** was further characterized by reduction with $LiAlH_4$ in ether to N-*t*-butyl N - (2 - methyl - 2 - phenylthio)propylamine **25a** (yield 79%). NMR (CCl_4): 1.06 (9H, s, *t*-Bu); 1.21 (6H, s, $(CH_3)_2$); 2.43 (2H, s, CH_2N); 7.2–7.7 (5H, m, C_6H_5); NH invisible. IR (NaCl): 1480, 1494, 1395, 1371, 1240, 1140, 1032 cm^{-1}. MS: *m/e* 237 (M^+; 0.4%); 222 (0.1%); 165 (2%); 151 (1%); 123 (1%); 112 (2%); 111 (1%); 110 (2%); 109 (1.5%); 86 (54%); 77 (1%); 72 (10%); 70 (3%); 57 (11%); 55 (7%); 51 (0.5%); 41 (7%); 30 (100%). Calc. for $C_{14}H_{23}NS$: N, 5.90. Found: N, 6.11%.

Reaction of α-chloro aldimines **14** *with methyl magnesium iodide*

The procedure is illustrated by the following experiment. To a mixture of 4.025 g (0.025 mol) N - 1 - (2 - chloro - 2 - methylpropylidene)*t* - butylamine in 10 ml dry ether was added a solution of methyl magnesium iodide in 50 ml ether (obtained from 2.4 g (0.1 mol) magnesium curlings and 14.2 g iodomethane). The solution was refluxed overnight, cooled, poured into saturated ammonium chloride solution and extracted with ether. After drying, evaporation of the solvent afforded an oil, which was distilled to give 2.2 g di-imine **29** (yield 70%); b.p. 130–135°C/12 mmHg (oil bath temperature: microdistillation apparatus). NMR (CCl_4): 0.99 (12H, s, $2\times(CH_3)_2$); 1.13 (18H, s, $2\times$*t*-Bu); 7.61 (2H, s, $2\times$CH=N). IR (NaCl): 1662 cm^{-1} ($\nu_{C=N}$). MS: 252 (M^+; 0.02%); 237 (0.06%); 195 (0.2%); 181 (0.2%); 154 (19%); 139 (6%); 127 (100%); 112 (28%); 98 (4%); 84 (2.5%); 71 (25%); 69 (19%); 57 (40%); 56 (6%); 55 (4%); 41 (13%).

A similar procedure starting from **14b** provided 42% N - 1 - (2,2 - dimethylpropylidene)cyclohexylamine **30** with 45% starting material. Compound **30**: NMR (CCl_4): 1.00 (9H, s, *t*-Bu); 1–2 (10H, m, $(CH_2)_5$); 2.8 (1H, m, CH–N); 7.40 (1H, s, CH=N). IR (NaCl): 1670 cm^{-1} ($\nu_{C=N}$). MS: 167 (M^+; 1%); 166 (1%); 152 (11%); 124 (7%); 110 (67%); 83 (100%); 57 (13%); 56 (8%); 55 (37%); 41 (18%).

Other compounds which have been obtained but which were not previously mentioned are given below:

2 - t - *butylamino* - 1 - *methoxy* - 2 - *methyl* - 1 - *phenoxypropane* **22**: NMR (CCl_4): 1.23 (9H, s, *t*-Bu); 1.25 (6H, s, $(CH_3)_2$); 2.7 (1H, s broad, NH); 3.35 (3H, s, OCH_3); 4.93 (1H, s, O–CH–O); 6.6–7.5 (5H, m, C_6H_5). IR (NaCl): 1605, 1592, 1490, 1475, 1222 cm^{-1}. MS: *m/e* 251 (M^+; 0.2%); 236 (0.4%); 220 (1%); 197 (4%); 164 (3%); 158 (13%); 142 (5%); 115 (8%); 114 (84%); 102 (31%); 100 (7%); 94 (8%); 86 (5%); 85 (7%); 77 (5%); 70 (24%); 58 (100%); 57 (13%). Calc. for $C_{15}H_{25}NO_2$: C, 71.67; H, 10.03; N, 5.57. Found: C, 72.00; H, 10.09; N, 5.52%.

*N - 1 - (2 - Methyl - 2 - phenoxypropylidene)*t *- butylamine*: NMR (CCl_4): 1.20 (9H, s, *t*-Bu); 1.46 (6H, s, $(CH_3)_2$); 6.80–7.30 (5H, m, C_6H_5); 7.76 (1H, s, CH=N). IR: $\nu_{C=N}$: 1670, 1600, 1590, 1495 (arom.). MS: 219 (M^+; 5%); 147 (4%); 135 (40%); 126 (59%); 112 (6%); 111 (10%); 107 (4%); 95 (8%); 94 (20%); 77 (9%); 70 (100%); 57 (60%). Calc. for $C_{14}H_{21}NO$: N, 6.39. Found: N, 6.51%.

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