Tetrahedron Vol. 48, No. 13, pp. 2739-2760, 1992
Printed in Great Britain

0040-4020/92 $3.00+.00

Synthesis and Reactivity of α-Halomethyl Ketimines

Norbert DE KIMPE,* Wim DE COCK and Christian STEVENS§
Laboratory of Organic Chemistry, Faculty of Agricultural Sciences,
State University of Gent, Coupure Links 653, B-9000 Gent, BELGIUM

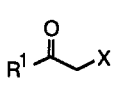
(*Received in UK 27 January* 1992)

Abstract

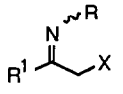
The synthesis of N-(1-halo-2-alkylidene)amines, i.e. α-halomethyl ketimines, is described for the first time, utilizing the $TiCl_4$-induced condensation of α-halomethyl ketones with primary amines. The reactivity of these new α-halomethylketimines was studied with respect to nucleophiles such as iodide, cyanide, alcohols, alkoxides, amines and thiolates. α-Halomethyl ketimines are powerful ambident electrophiles which underwent a variety of reactions leading to functionalized imines and heterocycles.

INTRODUCTION

α-Chloromethyl and α-bromomethyl ketones 1 are very useful substrates for the introduction of 2-oxoalkyl units in organic molecules. Especially chloroacetone, bromoacetone and phenacyl halides are popular for achieving this goal.[1] However, depending upon the reaction conditions, base-induced side reactions can become important leading to lower yields of desired end products and making time consuming separations necessary.[1] One way of avoiding these side reactions might be to mask these α-halomethyl ketones as a less reactive derivative, which still allows the desired nucleophilic substitution to take place without competition with other types of reactions. If the final products are convertable into the substituted methyl ketone, the reaction scheme via masking offers an attractive alternative approach. α-Halo imines have been used successfully by us as masked deri-



1 (X = Cl, Br)

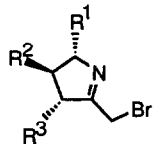


2 (X = Cl, Br)

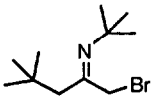
vatives of α-halo ketones.[2] In this communication, the synthesis of α-halomethyl ketimines 2 is described and their chemistry is evaluated as a

masking auxilliary for the corresponding α-halo ketones 1.

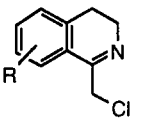
Only a few reports have appeared in the literature on the use of α-halomethyl ketimines. Woodward's synthesis of vitamine B_{12} utilized a cyclic α-bromomethyl ketimine, i.e. 2-(bromomethyl)-1-pyrroline 3, generated from the corresponding α-hydroxymethyl derivative via the mesylate.[3] Other examples entail the bulky bromomethyl ketimine 4[4] and 1-(chlorome-



3



4



5

thyl)-3,4-dihydroisoquinolines,[5] obtained by the classical Bischler-Napieralski procedure. Some α-fluoromethyl ketimines[6-9] belong also to the title class of compounds but are less interesting in the given context because the fluoro atom is less easily displaced.

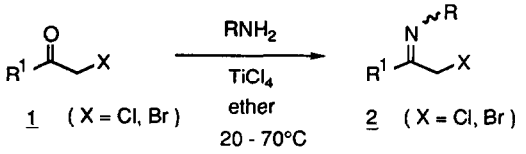
On the contrary, a rather large number of imino compounds, other than imines sensu stricto, e.g. hydrazone and oxime-type compounds, derived from α-halomethyl ketones have been reported in the literature. These derivatives include, among others, hydrazones,[10-13] semicarbazones,[14] azines,[15,16] oximes,[17-22] oxime benzoates[23] and oxime ethers.[24-26] All of these types of compounds have been utilized successfully in synthetic organic chemistry.[1]

The purpose of this communication is to uncover the potential of the basic class of α-halomethyl ketimines, i.e. imines derived from 1-halo-2-alkanones and phenacyl chloride.

RESULTS AND DISCUSSION

α-Haloimines are accessible by two major synthetic strategies, namely α-halogenation of imines and titanium(IV) chloride mediated condensation of α-haloketones and primary amines.[1] The first method does not permit the synthesis of the title α-halomethyl ketimines 2 because the halogenation of methyl ketimines with one molar equivalent of N-halosuccinimides in carbon tetrachloride leads to a mixture of α-mono- and α,α-dihalogenation (together with starting material) at the 1-position.[27,28] These α-halogenated methyl imines are labile compounds and cannot be sufficiently purified by vacuum distillation (decomposition) or column chromatography. Therefore, attention was paid to the more general entry into α-haloimines involving condensation of 1-halo-2-alkanones 1 with primary amines in the presence of stoechiometric quantities of titanium(IV) chloride.[29] Titanium(IV) chloride has a pronounced directing effect on the reaction in

that it results in imine formation without occurrence of the normal substitution reaction.



1 (X = Cl, Br) 2 (X = Cl, Br)

Chloroacetone condensed smoothly with isopropyl- and t-butylamine in ether but the resulting α-chloromethyl ketimines 2a and 2b are extremely labile. Freshly prepared α-chloromethyl ketimines 2a and 2b are colorless liquids, which are obtained in purities of at least 95%, and decompose rapidly and suddenly at 40°C (e.g. during evaporative removal of the solvent) or at ambient temperature in neat form. However they can be kept neat for several hours or days at -20°C or in solution (ether, pentane) for several weeks. Preference is given to the direct use of these reactive α-haloimines 2 in further reactions (vide infra). Also the labile N-(1-chloro-2-pentylidene)amines 2c,d (R=i-Pr, t-Bu) have been prepared and handled in the same way. The condensation of more bulky α-haloketones, e.g. 1-chloropinacolone and 1-bromopinacolone, with primary amines proceeded as expected except for the condensation of 1-chloropinacolone with t-butylamine which required more drastic reaction conditions. The usual reaction conditions (ether, RT) did not afford α-chloro ketimine 2f but a condensation in benzene for 7 days under reflux with a 10-fold excess of t-butylamine in the presence of $TiCl_4$ provided a reaction mixture consisting of α-chloro ketimine 2f and the starting α-chloro ketone from which the desired α-chloro ketimine 2f was isolated in 51% yield after distillation. Most of these α-chloro- and α-bromopinacolone imines 2e-h are stable compounds as a result of more sterical hindrance in the molecule. Phenacyl chloride was condensed with isopropylamine in ether in the presence of stoechiometric quantities of titanium(IV) chloride to yield the corresponding labile α-chloro ketimine 2i.

The synthesis of the various α-halomethyl ketimines 2 is described in Table I. The α-halo imines 2 were characterized by spectrometric methods (^1H NMR, ^{13}C NMR, IR, MS). α-Halomethyl ketimines are easily converted back to the corresponding α-halomethyl ketones upon acidic hydrolysis.

α-Halomethyl ketimines 2 derived from α-halopinacolones (R^1=t-Bu) occur in solution (^1H NMR; $CDCl_3$, CCl_4) as one geometrical isomer, the Z-form, based on accepted concepts of sterical hindrance for imines. Also imines derived from chloroacetone occur as one geometrical isomer which

Table I. Synthesis of α-Halomethyl Ketimines 2

	R^1	R	X	Method[a]	Molar Equiv. of RNH_2	Reaction Conditions	Yield	B.p. °C/mmHg
2a	Me	i-Pr	Cl	A (no H_2O)[b]	4	RT/1 h	70%	-[c]
2b	Me	t-Bu	Cl	A (no H_2O)[b]	4	RT/1 h	80%	-[c]
2c	n-Pr	i-Pr	Cl	A (H_2O)[d]	4	RT/1.5 h	75%	-[c]
2d	n-Pr	t-Bu	Cl	B (H_2O)[d]	4	RT/1.5 h	71%	-[c]
2e	t-Bu	i-Pr	Cl	B (H_2O)[d]	4	60°C/1.5 h	86%	73-75/20
2f	t-Bu	t-Bu	Cl	A (H_2O)[d,e]	10	70°C/7 days	51%	85-90/23
2g	t-Bu	i-Pr	Br	B (H_2O)[d]	4	RT/1 h	73%	75-78/15
2h	t-Bu	cycloHex	Br	B (no H_2O)[b]	3	RT/1.5 h	72%	-[c]
2i	C_6H_5	i-Pr	Cl	B (H_2O)[d]	4	RT/30 min	84%	-[c]
2j	t-Bu	i-Pr	I	-[f]	-[f]	50°C/1 h	95%	-[c]

a) Method A refers to the addition of titanium(IV) chloride to an ethereal solution of the α-halomethyl ketone and the primary amine. Method B refers to the addition of the primary amine to a mixture of the α-halomethyl ketone and titanium(IV) chloride in ether.

b) No aqueous workup was performed, i.e. direct filtration of the reaction mixture and evaporation of the solvent.

c) Thermolabile compounds which decomposed upon vacuum distillation.

d) Workup was performed with diluted aqueous sodium hydroxide.

e) The condensation was performed in benzene instead of ether.

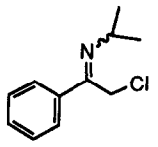
f) N-(1-iodo-3,3-dimethyl-2-alkylidene)isopropylamine 2j was prepared by substitution of N-(1-bromo-3,3-dimethyl-2-alkylidene)isopropylamine 2g with sodium iodide in acetone.

has most probably the Z-configuration by comparison with the data of α-chloromethyl ketimines 2e,f. On the other hand, N-isopropyl ketimines 2i and 2c, derived from phenacyl chloride and 1-chloro-2-pentanone, display signals in the ^1H NMR spectrum which are attributable to E and Z isomers. N-(2-chloro-1-phenyl-1-ethylidene)isopropylamine 2i showed a 1:1 ratio of E/Z isomers, while N-(1-chloro-2-pentylidene)isopropylamine 2c occurred as a 7:3 mixture of E/Z isomers. The attribution of the E/Z isomers was performed by the ASIS-method (Aromatic Solvent Induced Shift), as exemplified for the CH_2Cl-signals (^1H NMR) of N-(1-chloro-2-pentylidene)isopropylamine 2c (Table II).

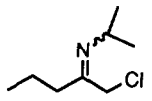
A SFORD experiment (^{13}C NMR, $CDCl_3$) allowed the determination of the CH_2Cl-signals of the E and Z isomers of α-chloromethyl ketimine 2c (δ 3.81 for $C\underline{H}_2Cl$ of the Z-isomer and δ 3.90 for $C\underline{H}_2Cl$ of the E-isomer).

Table II. Aromatic Solvent Induced Shift of the CH_2Cl-signals of α-Chloromethyl Ketimine 2c.

	δ (CCl_4)	δ (C_6H_6)	$\delta = \delta_{CCl_4} - \delta_{C_6H_6}$
Z	3.87	3.52	0.35
E	3.98	3.89	0.09



2i E/Z 1:1



2c E/Z 7:3

During gas chromatographic analysis (SE 30, s.s., 3m, H_2), even the more stable bulky α-halomethyl ketimines 2, e.g. α-chloro ketimine 2e, are partially reduced to the corresponding dehalogenated imines, i.e. methyl ketimines.

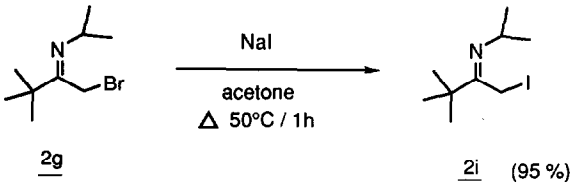
The reactivity of α-halomethyl ketimines 2 was determined toward nucleophiles such as iodide, cyanide, alkoxides, alcohols, amines and thiolates.

The displacement of the halogen was first verified with the sterically hindered α-haloimine 2g. The reaction of α-bromomethyl ketimine 2g with sodium iodide in acetone at 50° for 1h led to α-iodomethyl ketimine 2i in 95% yield. This experiment proved the suitability of α-halomethyl ketimines 2 for nucleophilic substitutions, even when the N-substituent is cis with respect to the reaction centre and when there is considerable steric hindrance (2 : R^1 = t-Bu; R = i-Pr).

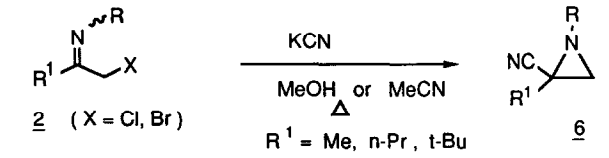
The reaction of aliphatic α-halomethyl ketimines 2 with potassium cyanide or acetone cyanohydrin in methanol or acetonitrile under reflux afforded α-cyanoaziridines 6 in 60-90% yield. The formation of α-cyanoaziridines 6 resulted from nucleophilic addition of cyanide across the imino function of 2 followed by intramolecular nucleophilic substitution. Cyanation of α-haloimines is an established method for the synthesis of α-cyanoaziridines,[30,31] which are of interest because of their immunostimulating properties.[31] The synthesis of α-cyanoaziridines 6[41] from α-halomethyl ketimines 2 is compiled in Table III, while the spectrometric data of α-cyanoaziridines 6 are given in the experimental part.

The aromatic α-chloromethyl ketimine 2i (R^1 = Ph; R = i-Pr) did not give aziridine formation upon treatment with potassium cyanide in methanol under reflux, but underwent nucleophilic substitution to afford α-cyano-

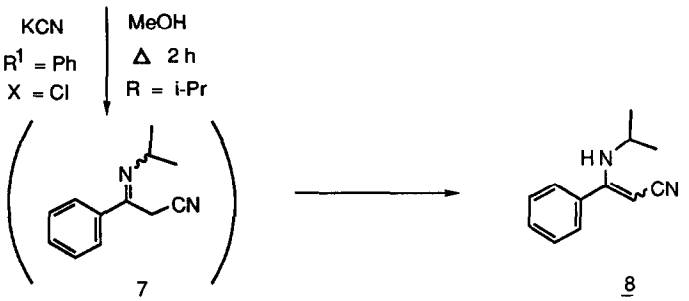
imine 7 which was isolated as the more stable β-cyanoenamine 8 (one geometrical isomer).[42] As compared to α-halomethyl ketones, the title α-halo-



2g 2i (95 %)



2 (X = Cl, Br) 6



7 8

methyl ketimines show a deviating reactive behavior towards cyanide. In general, α-haloketones react with cyanide to yield α-cyanoepoxides.[1] However, phenacyl halides or α-halogenated pinacolones condense with cyanide to give α-cyanoketones,[32,33] while α-chloroacetone yields self-condensation with cyanide.[34] The results of the cyanation of imines derived from α-chloroacetone and α-halopinacolones are different from those of the corresponding α-haloketones, while the results in the aromatic series are comparable.

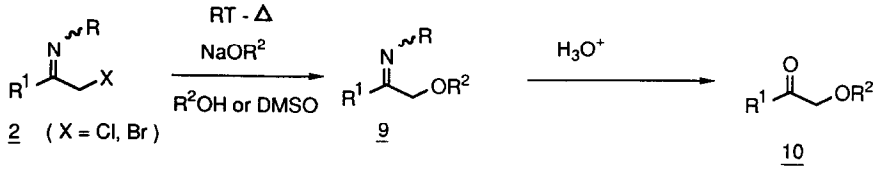
The reaction of α-halomethyl ketimines 2 with sodium methoxide or sodium phenoxide in methanol under reflux afforded the corresponding α-methoxy- or α-phenoxyketimines 9. The α-isopropoxyketimine 9 (R^2 = i-Pr) was obtained by reaction of α-bromoketimine 2g with sodium isopropoxide in isopropanol. A variant of this method, entailing possibilities for the introduction of a great variety of α-alkoxy substituents, concerned the reaction of α-bromomethyl ketimine 2g with sodium methoxide (generated from equimolecular amounts of sodium hydride and methanol) in dimethyl

Table III. Synthesis of α-Cyanoaziridines 6

Compound[a]	R^1	R	X[b]	Reactions Conditions	Yield (%)	B.p. (°C/mmHg)
6b	Me	t-Bu	Cl	KCN/MeOH/RT/18 h	10	65- 67/15[d]
6e	t-Bu	i-Pr	Cl	KCN/MeOH/ /3 h	60	90- 94/23
6g	t-Bu	i-Pr	Br	KCN/MeOH/ /3 h	70	90- 94/23
6g	t-Bu	i-Pr	Br	KCN/CH_3CN/ /3 h	82[e]	90- 94/23
6g	t-Bu	i-Pr	Br	$Me_2C(CN)OH$/MeOH/ /1.5 h	90[e]	90- 94/23
6h	t-Bu	Cyclohex	Br	KCN/MeOH/ /1 h	72	110-130/11[f]
6d	Pr	t-Bu	Cl	KCN/MeOH/ /1.5 h	86[e]	-

a) The letter designation refers to the starting α-haloimine used (note that 6e and 6g are the same structures).
b) α-Halogen in the starting material.
c) 2 Molar equivalents of cyanide source were used.
d) Lit.[41] bp. : 60°C/15 mmHg.
e) Yield before distillation.
f) Molecular distillation (bath temperature).

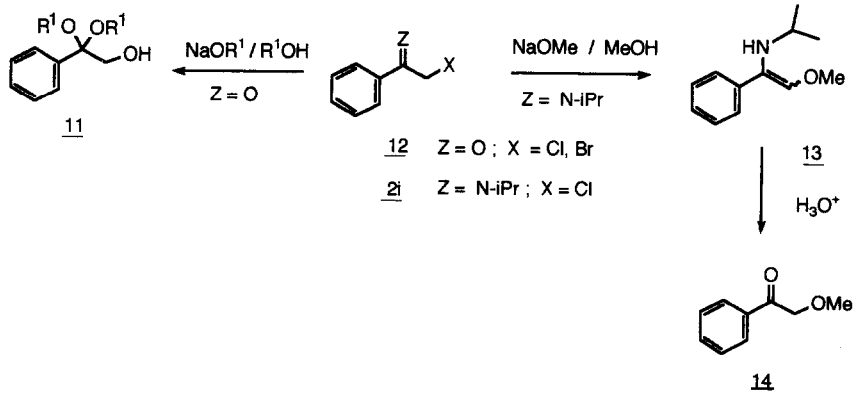
sulfoxide at 75°C, providing α-alkoxylation exclusively. α-Alkoxy ketimines 9 are extremely sensitive to hydrolysis. As the reaction products of the alkoxylations are always worked up by water, the final reaction mixture always contains variable and substantial amounts of α-alkoxy ketones 10. Total conversion of α-alkoxy ketimines 9 into α-alkoxy ketones 10 was easily achieved by treatment with aqueous acid. Bulky substituted α-alkoxy ketimines 9, e.g. 9 (R^1 = t-Bu), seemed to be more resistant to hydrolysis, while the α-methoxy phenacyl imine 9 (R^1 = Ph; R = i-Pr; R^2 = Me) occurred as the enamine form 13 (one geometrical isomer).



2 (X = Cl, Br) 9 10

Compared to the straightforward and simple α-alkoxylations of α-halomethyl ketimines 2, the reactions of α-halomethyl ketones with alkoxides are more complex (Favorskii, rearrangement, α-hydroxyacetal formation, ...)[1] in that several reaction products are possible, depending upon the substitution pattern in the substrate. The use of α-haloimines allows to

change reaction pathways in different directions than the parent α-halo ketones, as exemplified for the phenacyl halide derivatives 12 (formation of α-hydroacetal 11 via an intermediate α-alkoxyoxirane vs. α-alkoxylation).



On the other hand, α-halomethyl ketimines 2 rearrange with methanol without added extra base to afford α-(N-alkyl)aminoacetals 16 in 75-79% yield. The reaction mechanism proceeds via an intermediate α-methoxyaziridine 15,[35] which methanolyzes into 16.

The results of the alkoxylations of α-halomethyl ketimines 2 are presented in Table IV.

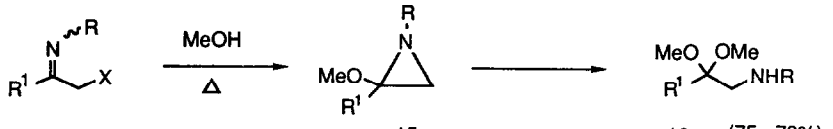
α-Chloromethyl ketimines, e.g. 2a and 2e, were easily substituted by thiolates in methanol to give the corresponding α-sulfenylated imines (17; 18), which were easily hydrolyzed to the α-sulfenylated ketones (19; 20) in quantitative yield. The synthesis of α-sulfenylated ketones via this route has no advantage over the direct route from α-haloketones.[1]

Also functionalized thiolates can be used in substitution reactions with α-halomethyl ketimines 2. In this way, α-bromomethyl ketimine 2g (R = i-Pr; R^1 = t-Bu; X = Br) reacted with the sodium salts of 2-mercapto-2-thiazoline (MeOH, RT 4h) or 2-mercapto-1-methylimidazole (MeOH, RT 4h) or with methyl thioglycolate (MeCN; Et_3N; RT 1.5h) to afford the corresponding functionalized ketimines 21, 22 and 23, respectively.

The latter compound was thermolabile and decomposed during preparative gas chromatographic analysis into a desulphurized compound which was tentatively identified as the N-isopropyl imine of methyl 5,5-dimethyl-4-oxo-2-hexenoate.

Finally, the reactivity of α-halomethyl ketimines 2 was evaluated towards amines in view of the potential to use the resulting α-amino ketimines as substrates for the synthesis of vicinal diamines, which are useful for a

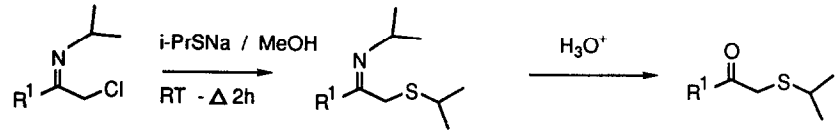
variety of applications. Secondary amines, such as pyrrolidine, reacted only sluggishly (reflux 17h) with α-bromomethyl ketimine 2g in benzene to



2d X= Cl (Δ 15 h)
2g X= Br (Δ 17 h)

15

16 (75 - 79%)

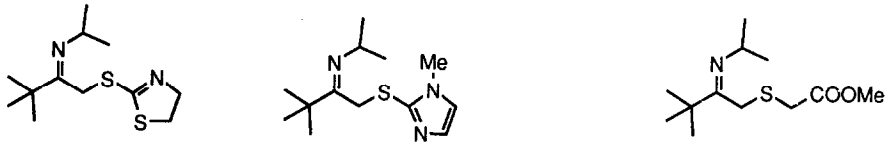


2a R^1 = Me
2e R^1 = t-Bu

17 R^1 = Me (70 %)
18 R^1 = t-Bu (75 %)

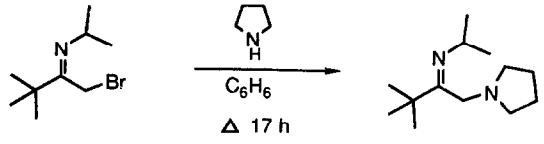
19 R^1 = Me
20 R^1 = t-Bu

afford N-[3,3-dimethyl-1-(1-pyrrolidino)-2-butylidene]isopropylamine 24 in 85% yield. Primary amines reacted similarly with α-halomethyl ketimi-



21 22 23

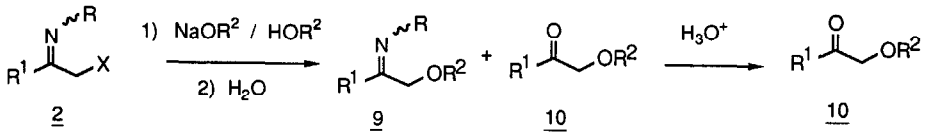
nes 2 to give the substitution products 25, initially, but the latter rearranged to α-(alkylamino)aldimines 26. These α-(alkylamino)aldimines



2g 24 (85 %)

26 were not very stable as they oxidized spontaneously in the air to α-diimines 27.[37,38] This type of rearrangement (via tautomerism) of α-amino ketones[38,39] or α-amino imines[38,39] has been observed previously

Table IV : Reaction of α-Halomethyl Ketimines 2 with Alkoxides



2 9 10 10

R^1	R	X	R^2	Solvent	Reaction Conditions	Equiv./conc. $NaOR_2$[a]	9 (%)[b]	10 (%)[b]	Yield[c] (%)
Pr	t-Bu	Cl	Me	MeOH	kt° 3 h	3E/2N	-	100	65[d]
t-Bu	i-Pr	Cl	Me	MeOH	Δ 3.5 h	3E/2N	-	100	67[d]
t-Bu	i-Pr	Br	Me	MeOH	Δ 30 min	3E/2N	100	-	75[e]
t-Bu	i-Pr	Br	Me	DMSO	75°C 3 h	2E	85	15	56
t-Bu	i-Pr	Br	Me	DMSO[f]	75°C 2 h	2E	100	-	-
t-Bu	i-Pr	Br	i-Pr	i-PrOH	Δ 5 h	2E/0.8N	-	-	57[e]
t-Bu	i-Pr	Br	C_6H_5	MeOH	Δ 3 h	1.5E	60	40	60
t-Bu	i-Pr	Br	C_6H_5	MeOH	Δ 6 h	1.5E	-	100	85
C_6H_5	i-Pr	Cl	Me	MeOH	Δ 2 h	3E/2N	100[g]	-	65

a) When no concentration is given, a 10% solution (w/v) of the substrate in the given solvent was used.

b) Ratio in the reaction mixture.

c) Yield determined after hydrolysis of the reaction mixture.

d) Yield without hydrolysis procedure.

e) Bp. : R^2 = i-Pr : 72-74°C/11 mmHg and R^2 = Me : 55-58°C/11 mmHg.

f) Reaction of 2E NaH/2E MeOH in DMSO.

g) Predominantly the enamine form.

in the literature. In general the reaction of α-halomethyl ketimines 2 with primary amines afforded a mixture of α-(alkylamino)aldimines 26 and α-diimines 27. Executing the reaction under nitrogen prevented α-amino aldimines 26 from oxidation into α-diimines 27. The results of the synthesis of α-amino aldimines 26 and α-diimines 27 are compiled in Table V. As compared to the results given here, α-bromopinacolone reacted with excess t-butylamine in acetonitrile under reflux (10h) to afford the substitution product, i.e. 1-(N-t-butylamino)-3,3-dimethyl-2-butanone, in 74% yield (purification by preparative gaschromatography). This α-t-butylaminoketone did not rearrange to the corresponding α-hydroxy aldimine.

In conclusion, α-halomethyl ketimines 2 were shown to be versatile substrates for undergoing nucleophilic substitutions. The advantage of the usage of α-halomethyl ketimines over other corresponding imino compounds, e.g. oximes, hydrazones, etc., stems from the ease with which the corresponding carbonyl compounds are regenerated (aqueous acid).

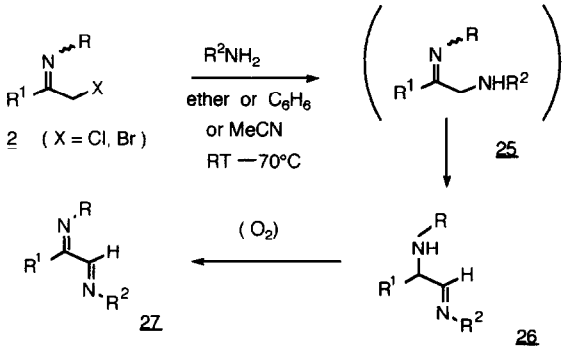


Table V. Condensation of Primary Amines with α-Halomethyl Ketimines 2

R^1	R	R^2	X	Reaction Conditions	Reaction Products (%)			Yield (%)
					2	26	27	
t-Bu	i-Pr	i-Pr	Br	C_6H_6/70°/4 h	-	67	33	70
t-Bu	i-Pr	i-Pr	Br	CH_3CN/55°/3h/N_2	-	95	-	83
t-Bu	i-Pr	i-Pr	Br	Et_2O/40°/18.5h	28	17	54	-
t-Bu	i-Pr	t-Bu	Br	CH_3CN/55°/3h/N_2	-	90	10	84
t-Bu	i-Pr	t-Bu	Br	Et_2O/40°/23h	65	-	35	-
C_6H_5	i-Pr	i-Pr	Cl	Et_2O/RT /40h	-	-	100	75

EXPERIMENTAL SECTION

Infrared spectra were recorded with a Perkin Elmer model 1310 spectrophotometer. ^{1}H NMR spectra were measured with a Varian T-60 NMR spectrometer while ^{13}C NMR spectra were recorded with a Varian FT-80 NMR spectrometer (20 MHz). Mass spectra were obtained with a Varian MAT 112 mass spectrometer (70 eV) using a direct inlet system or by using a GC-MS coupling (capillary column).

Synthesis of 1-Halo-2-alkanones

1-Chloro-2-propanone and phenacyl chloride were commercially available. 1-Chloro-2-pentanone was synthesized according to our previously published method.[40] 1-Chloro-3,3-dimethyl-2-butanone and 1-bromo-3,3-dimethyl-2-butanone were prepared by chlorination (sulfuryl chloride) or bromination (bromine) of pinacolone, according to standard procedures.[1]

Synthesis of α-Halomethyl Ketimines 2

Method A : A solution of the α-haloketone (0.05 mol) and the primary amine (0.2 mol) in diethyl ether (70-90 ml) was treated dropwise at 0°C under vigorous stirring with a solution of titanium(IV) chloride (0.03 mol) in 10 ml pentane. After the addition was complete, the reaction mixture was stirred further at room temperature for 1-1.5 h. Some syntheses of more bulky substrates required an elevated temperature (Table I). The workup was performed by pouring at once the reaction mixture into 100 ml of ice cold 0.5 N sodium hydroxide followed by immediate mixing of both layers. The aqueous phase was extracted three times with ether and the combined extracts were dried ($MgSO_4$) and evaporated in vacuo at ambient temperature. Once concentrated the imines derived from α-chloroacetone should be treated immediately with the appropriate solvent for further experiments. The latter α-halo imines often decompose violently when left in the pure state at room temperature for a few minutes. These α-halo imines 2 are preferally used immediately (purity > 94%) for further reactions or kept at -20°C for a few days.
More data on the synthesis of α-halomethyl ketimines are given in Table I.

Method B : A stirred mixture of α-halomethyl ketone (0.05 mol) and titanium(IV) chloride (0.03 mol) in 70-90 ml of ether was treated dropwise at 0°C with a solution of the primary amine (0.2 mol for isopropylamine and t-butylamine; 0.15 mol for cyclohexylamine) in 20 ml of ether. After stirring at the temperature and for the time indicated in Table I, the reaction mixture was worked up as described for Method A. Some α-halomethyl ketimines 2 were very labile and decomposed rapidly (even at room temperature), preventing the obtention of mass spectrometric data and

elemental analysis.

Spectrometric data of α-Halomethyl Ketimines 2 :

N-(1-Chloro-2-propylidene)isopropylamine 2a :

IR (NaCl) : 1665 cm^{-1} (C=N). ^1H NMR (δ, CCl_4) 1.05 (6H,d,J=6.5Hz,Me_2); 1.90 (3H,s,CH_3CN); 3.56 (1H,septet,J=6.5Hz,N-CH); 3.92 (2H,s,CH_2Cl). ^{13}C NMR (C_6D_6) : 10.77 (q,Me); 20.33 (q,Me_2); 48.19 and 48.39 (d and t, $\underline{C}HMe_2$ and CH_2Cl); 157.43 (s,C=N). Mass spectrum m/z (%) : 133/5 (M^+; 2); 120(3); 118(10); 85(2); 84(32); 82(2); 76(2); 75(2); 52(7); 49(2); 43(21); 42(100); 41(15); 40(9); 39(9).

N-(1-Chloro-2-propylidene)t-butylamine 2b :

IR (NaCl) : 1660 cm^{-1} (C=N). ^1H NMR (δ, CCl_4); 1.27 (9H,s,t-Bu); 2.04 (3H,s,CH_3CN); 3.93 (2H,s,CH_2Cl). ^{13}C NMR ($CDCl_3$) : 17.66 (q,Me); 30.07 (q,Me_3); 53.14 (t,$\underline{C}H_2Cl$); 55.19 (s,$\underline{C}Me_3$); 160.23 (s,C=N). Mass spectrum m/z (%) : 147/9 (M^+; 11); 132/4(18); 98(25); 94(5); 93(11); 92(16); 91(28); 57(100); 56(18); 55(5); 42(28); 41(32); 40(11).

N-(1-Chloro-2-pentylidene)isopropylamine 2c :

IR (NaCl) : 1655 cm^{-1} (C=N). ^1H NMR (δ, CCl_4) : 1.08 and 1.10 (6H,2xd, J=6Hz,Me_2,E/Z : 7/3 resp.); 1.2-1.8 (2H,m,$C\underline{H}_2$-Me); 2.4 (2H, t,$C\underline{H}_2CN$); 3.4-4 (1H,2xseptet,overlap,J 6Hz,N-CH,E/Z : 7/3 resp.); 3.87 and 3.98 (2H,2xs, CH_2-Cl,Z/E : 3/7 resp.). ^{13}C NMR ($CDCl_3$) : 14.32 and 13.69 (q,CH_3,E/Z : 7/3); 20.46 and 20.02 (2xt,$\underline{C}H_2$-Me,E/Z : 7/3); 30.16 and 28.98 (2xt,CH_2-CN, E/Z : 7/3); 23.84 and 23.61 (2xq,Me_2,Z/E : 3/7); 35.63 and 49.12 (2xt, CH_2Cl,Z/E : 3/7); 50.6 and 50.5 (2xd,N-$\underline{C}$H,E/Z : 7/3); 164.85 and 162.78 (2xs,C=N,E/Z : 7/3).

N-(1-Chloro-2-pentylidene)t-butylamine 2d :

IR (NaCl) : 1660 cm^{-1} (C=N). ^1H NMR (δ, $CDCl_3$) : 0.9-1.1 (3H,m,CH_3); 1.29 (9H,s,tBu); 1.4-2.6 (4H,CH_2-CH_2,m); 4.01 (2H,s,CH_2Cl).

N-(1-Chloro-3,3-dimethyl-2-butylidene)isopropylamine 2e :

IR (NaCl) : 1648 cm^{-1} (C=N). ^1H NMR (δ, $CDCl_3$) : 1.13 (6H,d,J=6Hz,Me_2); 1.15 (9H,s,t-Bu); 3.85 (1H,septet,J=6Hz,N-CH); 3.95 (2H,s,CH_2Cl). ^{13}C NMR ($CDCl_3$) : 23.70 (q,Me_2); 28.04 (q,Me_3); 31.42 (t,CH_2Cl); 40.00 (Me_3,s); 50.92 (d,N-$\underline{C}$H); 167.12 (s,C=N). Mass spectrum m/z (%) : 175/7 (M^+; 5); 160/2(6); 140(10); 126(16); 118/20(65); 84(93); 78(13); 76(35); 57(67); 43 (100); 42(16); 41(44); 40(21). Elem. analysis : 7.97% N calcd., 8.08% N found.

N-(1-Chloro-3,3-dimethyl-2-butylidene)t-butylamine 2f :
IR (NaCl) : 1650 cm^{-1} (C=N). ^1H NMR (δ, CCl_4) : 1.14 (9H,s,t-Bu); 1.29 (9H,s,t-Bu-N); 3.95 (2H,s,CH_2Cl). ^{13}C NMR ($CDCl_3$) : 29.16 (q,C-C$\underline{Me}_3$); 31.25 (q,N-C$\underline{Me}_3$); 33.69 (t,CH_2Cl); 41.05 (s,C-CMe_3); 55.71 (s,N-$\underline{C}Me_3$); 165.84 (s,C=N).

N-(1-Bromo-3,3-dimethyl-2-butylidene)isopropylamine 2g :
IR (NaCl) : 1640 cm^{-1} (C=N). ^1H NMR (δ, CCl_4) : 1.12 (6H,d,J=6Hz,Me_2); 1.16 (9H,s,$\underline{t}$-Bu). 3.74 (2H,s,CH_2Br); 3.83 (1H,septet,J=6Hz,N-CH). ^{13}C NMR ($CDCl_3$) : 16.82 (t,CH_2Br); 23.38 (q,Me_2); 28.32 (q,Me_3); 40.21 (s,$\underline{C}Me_3$); 50.76 (d,N-$\underline{C}H$); 166.92 (s,CN). Mass spectrum m/z (%) : 219/21 (M^+; 0.5); 218/20(0.5); 204/6(2); 162/4(33); 140(22); 126(11); 120/2(38); 84(71); 83(16); 57(66); 43(100); 42(55); 51(71); 40(38). Elem. analysis : 6.36% N calcd.; 6.24% N found.

N-(1-Bromo-3,3-dimethyl-2-butylidene)cyclohexylamine 2h :
IR (NaCl) : 1655 cm^{-1} (C=N). ^1H NMR (δ, CCl_4) : 1.19 (9H,s,t-Bu); 1.2-2 (10H,m,$(CH_2)_5$); 3.5 (1H,m,N-CH); 3.77 (2H,s,CH_2Br). ^{13}C NMR ($CDCl_3$) : 16.79 (t,CH_2Br); 24.35 (t,$(CH_2)_2$); 25.86 (t,CH_2); 33.32 (t,$(CH_2)_2$); 28.38 (q,Me_3); 40.32 (s,$\underline{C}Me_3$); 59.19 (d,N-CH); 167.15 (s,CN).

N-(2-Chloro-1-phenyl-1-ethylidene)isopropylamine 2i :
IR (NaCl) : 1625 cm^{-1} (C=N). ^1H NMR (δ, CCl_4) : 1.04 and 1.22 (6H,2xd, J=6Hz,Me_2,E/Z : 1/1); 3.42 and 3.95 (1H,2xseptet,J=6Hz,N-CH,E/Z : 1/1); 4.17 and 4.25 (2H,2xs,CH_2-Cl,E/Z : 1/1); 6.9-7.5 (3H,m,meta and para CH=); 7.6-7.8 (2H,m,ortho CH=). ^{13}C NMR ($CDCl_3$) : 23.54 and 23.82 (2xq,Me_2, E/Z : 1/1); 52.63 and 51.80 (2xd,NCH,E/Z : 1/1); 33.13 and 49.76 (2xt, CH_2Cl,E/Z : 1/1); 128.46-128.34-126.84-126.93-128.66-129.79 (d,=CH,ortho-meta-para); 138.39 and 135.56 (2xs,$C_{quat.}$ arom.); 158.96 and 163.58 (2xs, C=N,E/Z : 1/1).

Reaction of α-Bromomethyl Ketimine 2g with Sodium Iodide
A solution of 0.01 mol of α-bromomethyl ketimine 2g in 20 ml of dry acetone was treated with 0.02 mol of sodium iodide. The mixture was heated at 50° under stirring for 1 hour after which the solvent was evaporated under vacuo. The residue was extracted two times with dry ether and the combined extracts were evaporated to leave α-iodomethyl ketimine (95% yield; purity ≥ 95%). IR (NaCl) : 1630 cm^{-1} (C=N). ^1H NMR (δ, CCl_4) : 1.05 (6H,d,J=6Hz, Me_2); 1.15 (9H,s,t-Bu); 3.53 (2H,s,CH_2-I); 3.71 (1H,septet,i-Pr). ^{13}C NMR ($CDCl_3$) : 5.04 (t,CH_2-I); 22.68 (q,Me_2); 28.73 (q,Me_3); 40.53 (s,$\underline{C}Me_3$); 50.53 (d,N-CH); 167.25 (s,C=N).

Cyanation of α-Halomethyl Ketimines 2

The cyanation of α-halomethyl ketimines 2 is exemplified by the conversion of N-(1-bromo-3,3-dimethyl-2-butylidene)isopropylamine 2g into 2-t-butyl-2-cyano-1-isopropylaziridine 6g (R = i-Pr; R^1 = t-Bu). A solution of 0.04 mol of α-bromomethyl ketimine 2g in 80 ml of dry methanol was treated with 0.08 mol of potassium cyanide. The heterogeneous mixture was stirred under reflux for 3 hours, after which the solvent was half evaporated under vacuo. The residual mixture was poured into 200 ml of water and extraction was performed with dichloromethane (3 times). The combined extracts were dried (K_2CO_3) and evaporated to afford a clear oil, which consisted of almost pure α-cyanoaziridine 6g. Distillation in vacuo gave pure α-cyanoaziridine 6g, b.p. 90-94°C/23 mmHg (70% yield).

1-t-Butyl-2-methylaziridine-2-carbonitrile 6b :

IR (NaCl) : 2237 cm^{-1} (C≡N). ^1H NMR (δ, $CDCl_3$) : 1.22 (9H,s,t-Bu); 1.51 (3H,s,Me); 1.81 and 2.23 (each 1H,broad,∿s,$C\underline{H}_2$). ^{13}C NMR ($CDCl_3$) : 23.87 (q,Me); 27.28 (q,Me_3); 35.05 (t,CH_2); 46.15 (s,$\underline{C}$-CN); 121.51 (s,$\underline{C}$≡N); 54.57 (s,$\underline{C}Me_3$). Mass spectrum m/z (%) : no M^+; 123 (M^+-Me,5); 98(8); 96(9); 92 (4); 91(5); 89(20); 83(9); 82(25); 71(5); 80(12); 69(9); 58(18); 57(100); 56(18); 55(19); 43(21); 42(30); 41(50).

2-t-Butyl-1-isopropylaziridine-2-carbonitrile 6g :

IR (NaCl) : 2232 cm^{-1} (C≡N). ^1H NMR ($CDCl_3$) : 1.01 (9H,s,t-Bu); 1.17 (6H, d,J=6Hz,Me_2); 1.6 and 2.06 (each 1H,broad, s,$C\underline{H}_2$); 2.15 (1H,sept.,J=6Hz, N$C\underline{H}$). ^{13}C NMR ($CDCl_3$) : 21.88 and 22.36 (2xq,Me_2); 25.81 (q,Me_3); 32.25 (s,$\underline{C}Me_3$); 35.97 (t,dxd,$C\underline{H}_2$); 42.83 (s,$\underline{C}$-CN); 57.55 (d,N-$\underline{C}$H); 118.80 (s, $\underline{C}$≡N). Mass spectrum m/z (%) : 166 (M^+, 4); 151(36); 125(17); 123(44); 109 (54); 97(38); 82(88); 70(14); 67(18); 57(88); 56(35); 43(55); 42(41); 41 (96); 40(100); 39(35). Elem. analysis : calcd. 16.85% N; found 16.69% N.

2-t-Butyl-1-cyclohexylaziridine-2-carbonitrile 6h :

IR (NaCl) : 2235 cm^{-1} (C≡N). ^1H NMR ($CDCl_3$) : 1.00 (9H,s,t-Bu); 1.6 and 2.04 (each 1H,broad, s,$C\underline{H}_2$); 1.1-2.1 (11H,m,$(CH_2)_5CH$). ^{13}C NMR ($CDCl_3$) : 25.83 (q,Me_3); 32.27 (s,$\underline{C}Me_3$); 32.78, 32.10, 25.96, 24.39 and 24.07 (5xt, $(CH_2)_5$); 35.44 (t,$\underline{C}H_2$); 42.29 (s,$\underline{C}$-CN); 64.62 (d,N-$\underline{C}$H); 118.98 (s,$\underline{C}$≡N). Mass spectrum m/z (%) : 206 (M^+, 3); 191(9); 163(14); 150(9); 149(4); 130(9); 129(13); 109(21); 98(11); 97(100); 84(16); 83(53); 82(31); 81(9); 69(7); 68(13); 67(16); 57(28); 56(16); 55(88); 54(11); 53(11). Elem. analysis : calcd. 13.58% N; found 13.49% N.

1-t-Butyl-2-propylaziridine-2-carbonitrile 6d :
IR (NaCl) : 2232 cm^{-1} (C≡N). ^1H NMR ($CDCl_3$) : 0.95 (3H,t,J=7Hz,Me); 1.18 (9H,s,t-Bu); 1-1.75 (4H,m,$(CH_2)_2$); 1.78 and 2.2 (each 1H,each d,CH_2, J=0.7Hz). ^{13}C NMR ($CDCl_3$) : 13.66 (q,Me); 19.35 and 39.54 (each t,$(CH_2)_2$); 27.39 (q,Me_3); 27.45 (s,C-CN); 34.34 (t,CH_2); 54.29 (s,CMe_3); 120.88 (s, C≡N). Mass spectrum m/z (%) : 166 (M^+, 2); 151(8); 110(16); 109(5); 95 (10); 83(22); 71(7); 70(6); 68(4); 58(12); 57(100); 56(8); 55(10); 43(15); 42(12); 41(42); 40(11); 39(11).

3-(N-Isopropyl)amino-3-phenylpropanenitrile 8
Mp. 77°C; IR (KBr) : 3300 cm^{-1} (ν_{NH}); 2287 cm^{-1} ($\nu_{C\equiv N}$). ^1H NMR (δ, $CDCl_3$) : 1.25 (6H,d,J=6Hz,Me_2); 3.55 (1H,septet,J=6Hz,NCH); 4.04 (1H,s,CH-C≡N); 4.57 (1H,m,NH); 7.5 (5H,m,Ph). ^{13}C NMR (δ, $CDCl_3$) : 21.69 (q,Me_2); 44.97 (d,NCH); 60.34 (d,CH-C≡N); 122.05 (s,C≡N); 127.87, 128.54 and 130.08 (3xd,3xCH=); 136.12 (s,$C_{quat.}$); 161.48 (s,C=CH-CN). Mass spectrum m/z (%) : no M^+; 149(13); 148(43); 146(10); 133(10); 132(17); 131(9); 117(12); 107(56); 106(30); 105(45); 104(32); 91(25); 88(20); 86(14); 79(25); 77(19); 59(20); 58(11); 57(14); 56(36); 55(24); 51(10); 45(9); 44(18); 43(32); 42 (11); 41(32); 40(100).

Reaction of α-Halomethyl Ketimines with Alkoxides
The alkoxylations of α-halomethyl ketimines 2 are exemplified by the following experiment. A solution of 4.38 g (0.02 mol) α-bromomethyl ketimine 2g in 30 ml 2N sodium methoxide in methanol (0.06 mol) was stirred under reflux for 30 minutes. The reaction mixture was poured into 150 ml 1N sodium hydroxide and extraction was performed with dichloromethane (three times). The combined extracts were dried (K_2CO_3) and evaporated to leave a clear oil, which was analyzed by ^1H NMR and gas chromatography. Vacuum distillation afforded α-methoxymethyl ketimine 9 (R^1 = t-Bu; R = i-Pr; R^2 = Me) in 75% yield; bp. 55-68°C/11 mmHg.
Data on related reactions are compiled in Table IV.

N-(1-Methoxy-3,3-dimethyl-2-butylidene)isopropylamine 9 (R^1 = t-Bu; R = i-Pr; R^2 = Me)
IR (NaCl) 1650 cm^{-1} ($\nu_{C=N}$). ^1H NMR (δ, CCl_4) : 1.08 (9H,s,t-Bu); 1.05 (6H, d,J=6Hz,Me_2); 3.30 (3H,s,OMe); 3.75 (1H,septet,J=6Hz,NCH); 3.87 (2H,s, OCH_2).

N-(1-Phenoxy-3,3-dimethyl-2-butylidene)isopropylamine 9 (R^1 = t-Bu; R = i-Pr; R^2 = Ph)
IR (NaCl) : 1650 cm^{-1} ($\nu_{C=N}$). ^1H NMR (δ, CCl_4) : 1.14 (9H,s,t-Bu); 1.11 (6H,d,J=6Hz,Me_2); 3.75 (1H,septet,J=6Hz,NCH); 4.47 (2H,s,OCH_2); 6.6-7.4

(5H,m,C_6H_5).

Both ketimines 9 (R^1 = t-Bu; R = i-Pr; R^2 = Me, Ph) were further characte-

[redacted]

3,3-Dimethyl-1-methoxy-2-butanone 10 (R^1 = t-Bu; R^2 = OMe)

IR (NaCl) 1720 cm^{-1} ($\nu_{C=O}$); ^1H NMR (δ, CCl_4); 1.14 (9H,s,t-Bu); 3.32 (3H,s, OMe); 4.11 (2H,s,OCH_2).

3,3-Dimethyl-1-phenoxy-2-butanone 10 (R^1 = t-Bu; R^2 = Ph)

IR (NaCl) 1724 cm^{-1} ($\nu_{C=O}$); ^1H NMR (δ, CCl_4) : 1.21 (9H,s,t-Bu); 4.69 (2H, s,CH_2); 6.6-7.4 (5H,m,C_6H_5).

The reaction of N-(2-chloro-1-phenyl-1-ethylidene)isopropylamine 2i with sodium methoxide in methanol (3 equiv. 2N) under reflux for 2 hours afforded the crude substitution product 13 [65% yield; ^1H NMR (CCl_4) 1.0 (6H,d, J=6Hz,Me_2); 3.1 (1H,septet,J=7Hz,NCH); 3.49 (3H,s,OMe); 5.67 (1H,s,O-C<u>H</u>=); 6.9-8 (5H,m,C_6H_5)], which was hydrolyzed with aqueous oxalic acid (see procedure above) to give 2-methoxy-1-phenyl-1-ethanone 14 (R^1 = Ph; R^2 = Me) in 60% overall yield. IR (NaCl) : 1705 cm^{-1} ($\nu_{C=O}$); ^1H NMR (δ, CCl_4) : 3.33 (3H,s,OMe); 4.52 (2H,s,OCH_2); 7-7.5 (3H,m,m/p protons); 7.7-8 (2H,m,o protons).

Compounds 10 (R^1 = n-Pr; R^2 = Me) and 10 (R^1 = t-Bu; R^2 = i-Pr) were identical with authentic samples.

Reaction of α-Halomethyl Ketimines 2 with Methanol

A 20% solution (w/v) of α-halomethyl ketimines 2d and 2g in dry methanol was refluxed during 1.5 h and 17 h, respectively (protection by $CaCl_2$ tube). The solvent was removed in vacuo and the residue was treated with aqueous 1N sodium hydroxide. Extraction with dichloromethane, drying (K_2CO_3) and evaporation of the solvent afforded almost pure α-amino acetals 16 in 75-79% yield. Due to the lability of these compounds they were only partially characterized.

N-Isopropyl-2,2-dimethoxy-3,3-dimethyl-1-butylamine 16 (R^1 = t-Bu; R = i-Pr) :

IR (NaCl) : 3350 cm^{-1} (ν_{NH}), 2840 cm^{-1} (ν_{OMe}). ^1H NMR (δ, CCl_4) : 0.96 (9H,s,t-Bu); 1.02 (6H,d,J=6Hz,Me_2); 2.1 (1H,broad,NH); 2.6 (1H,septet, J=6Hz,NCH); 2.76 (2H,s,CH_2); 3.34 (6H,s,2xOMe). Mass spectrum m/z (%) : no M^+; 172 (M^+-MeO·; 8); 156(12); 146(12); 131($tBuC(OMe)_2^+$; 96); 126(16); 116 (20); 115(20); 114(20); 101(20); 100(40); 99(60); 74(72); 72(56); 70(44); 69(44); 67(44); 57(24); 56(16); 55(12); 43(88); 41(52); 40(100). Elem. analysis : calcd. 6.89% N; found 6.72% N.

N-t-Butyl-2,2-dimethoxy-1-pentylamine 16 (R^1 = n-Pr; R = t-Bu)
IR (NaCl) : 3360 cm^{-1} (ν_{NH}); 2850 cm^{-1} (ν_{OMe}). ^1H NMR (δ, CCl_4) : 1.09 (9H,s,t-Bu); 2.5 (2H,s,CH_2N); 0.8-1.8 (7H,m,$(CH_2)_2Me$); 3.12 (6H,s,2xOMe); NH invisible.

Reaction of α-Chloromethyl Ketimines 2 with Thiolates
The synthesis of ketimine 21 is representative for all other analogous reactions with thiolate-type reagents. To a solution of sodium methoxide in methanol (1 ml, 2N) was added 0.0021 mol of 2-mercapto-2-thiazoline. After stirring for 5 minutes, 0.002 mol α-bromomethyl ketimine 2g was added and stirring was continued at room temperature for 1 hour. The reaction mixture was poured into 1N sodium hydroxide and extraction was performed with dichloromethane. After drying (K_2CO_3) and evaporation of the solvent, the residual oil consisted of pure N-[1-(2-thiazolin-2-yl)-thio-3,3-dimethyl-2-butylidene]isopropylamine 21 (95% yield; purity > 96%). An additional purification can be performed passing the crude product through a short silica gel column using ether/pentane as eluens.
IR (NaCl) : 1640 and 1565 cm^{-1} ($\nu_{C=N}$). ^1H NMR (δ, $CDCl_3$) : 1.14 (9H,s, t-Bu); 1.1 (6H,d,J=6Hz,Me_2); 3.73 (1H,septet,J=6Hz,NCH); 3.92 (s,2H,CH_2S); 3.42 and 4.25 (each 2H,AA'MM',CH_2CH_2). ^{13}C NMR (δ, $CDCl_3$) : 23.87 (q,Me_2); 25.86 and 35.76 (each t,CH_2-CH_2); 27.92 (q,Me_3); 40.19 (s,$\underline{C}Me_3$); 51.15 (d, NCH); 63.94 (t,$\underline{C}H_2C$=N); 164.44 and 166.54 (each s,S-$\underline{C}$=N and $CH_2\underline{C}$=N).
The labile compounds 22 and 23 were obtained analogously in purities of > 94%.

N-[1-(1-Methylimidazol-2-yl)thio-3,3-dimethyl-2-butylidene]isopropylamine 22
IR (NaCl) : 2635 cm^{-1} ($\nu_{C=N}$). ^1H NMR (δ, CCl_4) : 1.12 (9H,s,t-Bu); 1.08 (6H,d,J=6Hz,Me_2); 3.53 (3H,s,Me); 3.70 (1H,septet;J=6Hz,NCH); 3.85 (2H,s, SCH_2); 6.7-6.9 (2H,m,CH=CH).

N-[1-(Methoxycarbonylmethyl)thio-3,3-dimethyl-2-butylidene]isopropylamine 23
IR (NaCl) : 1649 cm^{-1} ($\nu_{C=N}$). ^1H NMR (δ, CCl_4) : 1.08 (6H,d,J=6Hz,Me_2); 1.11 (9H,s,t-Bu); 3.19 and 3.39 (2x2H,2xs,2xCH_2); 3.72 (3H,s,OMe).
In similar way, α-chloromethyl ketimines 2a,e were transformed into α-sulfenylated ketimines 17 and 18 by reaction with sodium isopropyl thiolate in methanol.

N-(1-Isopropylthio-2-propylidene)isopropylamine 17 :
IR (NaCl) : 1647 cm^{-1} ($\nu_{C=N}$); ^1H NMR (δ, $CDCl_3$) : 1.13 (6H,d,J=6Hz, N-CH$\underline{Me}_2$); 1.27 (6H,d,J=7Hz,SCH$\underline{Me}_2$); 1.98 (3H,s,Me); 2.87 (1H,septet,J=7Hz, S-C$\underline{H}$); 3.27 (2H,s,CH_2S); 3.65 (1H,septet,J=6Hz,NCH).

N-(3,3-Dimethyl-1-isopropylthio-2-butylidene)isopropylamine 18 :
IR (NaCl) : 1635 cm^{-1} ($\nu_{C=N}$); 1.10 (6H,d,J=6Hz,NCH$\underline{Me}_2$); 1.14 (9H,s,t-Bu); 1.29 (6H,d,J=7Hz,SCH$\underline{Me}_2$); 3.92 (1H,septet,J=7Hz,S-C$\underline{H}$); 3.24 (2H,s,CH_2S); 3.83 (1H,septet,J=6Hz,NCH).
Both α-isopropylthio ketimines 17 and 18 were hydrolyzed with aqueous oxalic acid under reflux (1-2 h) in the presence of dichloromethane to afford the corresponding α-sulfenylated ketones 19 and 20. These ketones were identical to authentic substances prepared by reaction of α-chloroacetone or α-bromopinacolone with sodium isopropylthiolate in methanol.

Reaction of α-Bromomethyl Ketimine 2g with Pyrrolidine
A solution of 0.44 g (0.002 mol) of α-bromomethyl ketimine 2g in 10 ml benzene, containing 0.7 g (0.01 mol) of pyrrolidine, was refluxed during 17 hours. The reaction mixture was poured into 1N NaOH and was extracted with dichloromethane. After drying (K_2CO_3), evaporation of the solvent afforded N-[3,3-dimethyl-1-(1-pyrrolidino)-2-butylidene]isopropylamine 24 (85% yield). An analytical sample was obtained by preparative gas chromatography (s.s. column, 3 m, H_2 carrier gas), which revealed a purity of more than 95%.
IR (NaCl) : 1650 cm^{-1} ($\nu_{C=N}$); ^1H NMR (δ, CCl_4) : 1.01 (6H,d,J=6Hz,Me_2); 1.1 (9H,s,t-Bu); 1.5-1.9 (4H,m,$(CH_2)_2$); 2.3-2.7 (4H,m,CH_2N-CH_2); 3.16 (2H,s,2H, s,CH_2-C=N); 4.06 (1H,septet,J=6Hz,NCH). Elem. analysis : calcd. 13.32% N; found 13.51% N.

Reaction of α-Halomethyl Ketimines 2 with Primary Amines
A solution of 0.02 mol of α-halomethyl ketimine 2 in 30 ml ether, acetonitrile or benzene (Table V) was treated with 0.2 mol of the appropriate primary amine. The mixture was stirred at the temperature and during the time indicated in Table V. The reaction mixture was treated with aqueous 1N sodium hydroxide, extracted with dichloromethane, dried ($MgSO_4$), filtered and evaporated in vacuo to afford an oily reaction product, which was investigated by ^1H NMR and preparative gas chromatography (purity > 94%), which easily separated α-diimines 27 and α-aminoaldimines 26. On standing at room temperature the proportion of α-diimine 27 increased at the expense of α-aminoaldimine 26, due to air oxidation. The latter process could be avoided by working under an inert atmosphere (N_2). Imines 26 and 27 are very labile compounds which decompose on standing at room temperature.

N-[2-(N-isopropyl)amino-3,3-dimethyl-1-butylidene]isopropylamine 26 (R = i-Pr; R^1 = t-Bu; R^2 = i-Pr)
IR (NaCl) : 3310 cm^{-1} (ν_{NH}); 1675 cm^{-1} ($\nu_{C=N}$). ^1H NMR (δ, $CDCl_3$) : 0.94 (9H,s,t-Bu); 1.15 and 1.20 (2x6H,2xd,J=6Hz,2xMe_2); 1.8 (1H,broad,NH); 2.70 (1H,septet,J=6Hz,CH-NH); 3.38 (1H,septet,J=6Hz,C=N-CH); 2.85 (1H,d,J=6.5 Hz, t-Bu-CH); 7.6 (1H,d,J=6.5Hz,CH=N). ^{13}C NMR (δ, $CDCl_3$) : 22.73 and 24.20 (2xq;2xMe_2); 26.78 (q,Me_3); 34.06 (s,CMe_3); 47.20 (d,CH-NH); 61.34 (d,C=N-CH). 67.88 (d,t-Bu-CN); 163.25 (d,C=N).

N-[2-(N-isopropyl)amino-3,3-dimethyl-1-butylidene]t-butylamine 26 (R = i-Pr; R^1 = R^2 = t-Bu)
IR (NaCl) : 3300 cm^{-1} (ν_{NH}); 1662 cm^{-1} ($\nu_{C=N}$). ^1H NMR (δ, CCl_4) : 0.88 and 1.14 (2x9H,2xs,2xt-Bu); 0.95 and 1.08 (2x3H,2xd,J=6Hz,Me_2); 1.77 (1H, broad, NH); 2.55 (1H,septet,J=6Hz,NCH); 2.73 (1H,d,J=4.5Hz,t-BuCH); 7.6 (1H,d, J=4.5Hz,CH=N).

N,N-Diisopropyl-3,3-Dimethyl-1,2-butanediimine 27 (R = R^2 = i-Pr; R^1 = t-Bu)
IR (NaCl) : 1660-1690 cm^{-1} ($\nu_{C=N}$). ^1H NMR (δ, $CDCl_3$) : 1.12 (9H,s,t-Bu); 0.97 and 1.22 (2x6H,2xd,J=6Hz,2xMe_2); 3.1-3.9 (2H,septet,overlap,2NCH); 8.00 (1H,s,CH=N).

N^1-t-Butyl-N^2-isopropyl-3,3-dimethyl-1,2-butanediimine 27 (R = i-Pr; R^1 = R^2 = t-Bu)
The ^1H NMR spectrum was deduced from the spectrum of the 65/35 mixture of 2g and 35 (R = i-Pr; R^1 = R^2 = t-Bu). ^1H NMR (δ, CCl_4) : 1.1 (6H,d,covered,Me_2); 1.11 and 1.22 (2x9H,2xs,2 t-Bu); 8.0 (1H,s,CH=N).

N,N-Diisopropyl-2-phenyl-1,2-ethanediimine 27 (R = R^2 = i-Pr; R^1 = Ph)
Mp. : 73°C. IR (NaCl) : 1618 cm^{-1} ($\nu_{C=N}$). ^1H NMR (δ, $CDCl_3$) : 1.10 (2x6H, 2xd,J=7Hz,2xMe_2); 3.49 and 3.53 (2x1H,2xseptet,J=7Hz,2xNCH); 6.8-7.8 (5H,m, Ph). ^{13}C NMR (δ, $CDCl_3$) : 23.55 and 23.72 (2xq,2xMe_2); 52.57 and 61.11 (2xd,2xNCH); 127.71 and 127.91 (2xd,o and m CH=); 128.21 (d,p CH=); 134.76 (s,C_{quat}); 161.83 (d,CH=N); 166.48 (s,C=N). Mass spectrum m/z (%) : no M^+; 201 (M^+-Me, 21); 159(12); 146(4); 132(3); 118(4); 104(100); 77(15); 70(3); 51(5); 43(40); 41(23). Elem. analysis : calcd. 12.95% N; found 13.11% N.

REFERENCES

* "Onderzoeksdirecteur" (Research Director) of the Belgian "National Fund for Scientific Research".
§ "Aspirant" of the Belgian "National Fund for Scientific Research".

1. De Kimpe N. and Verhé R.; "The Chemistry of α-Haloketones, α-Haloaldehydes and α-Haloimines", Patai S., Rappoport Z., Eds., J. Wiley and Sons, Inc. Chichester, 1988.
2. For some leading references, see : De Kimpe, N., Yao, Z., Schamp, N.; Tetrahedron Lett. 1986 27, 1707-1710; De Kimpe, N., Sulmon, P., Schamp, N.; Angew. Chem. Int. Ed. Engl. 1985, 24, 881-882; De Kimpe, N., Verhé, R., De Buyck, L., Schamp, N.; Tetrahedron Lett. 1985, 26, 2709-2712; De Kimpe, N., Verhé, R., De Buyck, L., Schamp, N., Charpentier-Morize, M.; Tetrahedron Lett. 1982, 23, 2853-2856.
3. Woodward, R.B.; Pure Appl. Chem. 1968, 17, 519-547.
4. Quast, H., Frank, R., Heublein, A., Schmitt, E.; J. Liebigs Ann. Chem. 1980, 1814-1835.
5. Child, R., Pyman, F.L.; J. Chem. Soc. 1931, 36-49; Harwood, H.J., Johnson, T.B.; J. Am. Chem. Soc. 1933, 55, 2555-2559; Dey, B.B., Gorindachari, T.R.; Arch. Pharm. (Weinheim) 1939, 277, 177-192.
6. Welch, J.T., Seper, K.W.; J. Org. Chem. 1986, 51, 119-120.
7. Salon, M.C., Hamman, S., Beguin, C.G.; Org. Magn. Reson. 1983, 21, 265-270.
8. Burger, K., Huebl, D., Gertitschke, P.; J. Fluorine Chem. 1985, 27, 327-332.
9. Margaretha, P.; Helv. Chim. Acta 1982, 65, 290-292.
10. Faragher, R., Gilchrist, T.L.; J. Chem. Soc. Perkin Trans. I 1979, 249-257.
11. Gilchrist, T.L., Richards, P.; Synthesis 1983, 153-154.
12. Rossey, G., Wick, A., Wenkert, E.; J. Org. Chem. 1982, 47, 4745-4749.
13. Masi, P., Suarato, A., Giardino, P., Bernardi, L., Arcomone, F.; Il Farmaco, Ed. Sci. 1979, 34, 907-913.
14. Migliara, O., Petruso, S., Spiro, V.; J. Heterocyclic Chem. 1979, 16, 833-834.
15. Tsuge, O., Tashiro, M., Kamata, K., Hokama, K.; Org. Prep. Proced. Int. 1971, 3, 289-293.
16. Tsuge, O., Kamara, K., Yogi, S.; Bull. Chem. Soc. Japan 1977, 50, 2153-2157.
17. Oppolzer, W., Petrzilka, M., Bättig, K.; Helv. Chim. Acta 1977, 60, 2964-2967.
18. Nair, M.G., Saunders, C., Chen, S.-Y., Kislink, R.L., Gaumont, Y.; J. Med. Chem. 1980, 23, 59-65.
19. Gaudiano, G., Modelli, R., Ponti, P.P., Ticozzi, C., Umani-Ronchi, A.; J. Org. Chem. 1968, 33, 4431-4438.
20. Masaki, M., Fukui, K., Ohta, M.; J. Org. Chem. 1967, 32, 3564-3568.
21. Sadet, J., Lipszyc, J., Chenu, E., Gansser, C., Deyson, G., Hayat, M., Viel, C.; Eur. J. Med. Chem. - Chim. Therap. 1978, 13, 277-288.

22. Francotte, E., Mérenyi, R., Vandenbulcke-Coyette, B., Viehe, H.G.; Helv. Chim. Acta **1981**, 64, 1208-1218.
23. Fischer, H.P., Grob, C.A.; Helv. Chim. Acta **1962**, 45, 2528-2538.
24. Severin, T., Lerche, H.; Synthesis **1982**, 305-307.
25. Shatzmiller, S., Lidor, R., Shalom, E., Bahar, E.; J. Chem. Soc. Chem. Commun. **1984**, 795-796.
26. Buschman, E., Zeeh, B., Becker, R., Schaefer, P.; Ger. Offen. 2,924,401 (Cl. C07C131/00), 18 Dec. 1980, Appl. 16 June 1979; Chem. Abstr. **1981**, 94, 191936.
27. De Kimpe, N., Schamp, N., Coppens, W.; Bull. Soc. Chim. Belg. **1975**, 84, 227-234.
28. De Kimpe, N., Schamp, N.; Bull. Soc. Chim. Belg. **1975**, 84, 235-242.
29. De Kimpe, N., Verhé, R., De Buyck, L., Moëns, L., Schamp, N.; Synthesis **1982**, 43-46.
30. De Kimpe, N., Sulmon, P., Verhé, R., De Buyck, L., Schamp, N.; J. Org. Chem. **1983**, 48, 4320-4326.
31. De Kimpe, N., Sulmon, P., Schamp, N.; Bull. Soc. Chim. Belg. **1986**, 95, 567-586 and references cited therein.
32. Behringer, H., Ruff, M., Wiedenmann, R.; Chem. Ber. **1964**, 97, 1737-1744.
33. Widman, O., Wahlberg, E.; Chem. Ber. **1911**, 44, 2067.
34. Galons, H., Combet-Farnoux, C., Girardeau, J.-F., Miocque, M.; Compt. Rend. Acad. Sci. **1978**, Paris, C, 286, 663-666.
35. De Kimpe, N., Verhé, R., De Buyck, L., Moëns, L., Sulmon, P., Schamp, N.; Synthesis **1982**, 765-767.
36. Wiley, R.H., England, D.C., Behr, L.C.; Organic Reactions **1960**, 6, 367-409.
37. This type of spontaneous air oxidation is also known in similar systems such as the conversion of α-aminoketones into α-iminoketones : Singh, S.B., Mehrotra, K.N.; Can. J. Chem. **1981**, 59, 2475-2478.
38. For an example of an oxidation of an enediamine into a 1,2-diimine, see : Julian, P.L., Meyer, E.W., Magnani, A., Cole, W.; J. Am. Chem. Soc. **1945**, 67, 1203-1211.
39. Stevens, C.L., Pillai, P.M., Munk, M.E., Taylor, K.G.; "Amino Ketone Rearrangements" in "Mechanisms of Molecular Migrations", Vol. 3, Thyagarajan, B.S., Ed.; Wiley-Interscience **1971**, p. 271-296.
40. De Kimpe, N., De Cock, W., Schamp, N.; Synthesis **1987**, 188-199.
41. Szeimies, G.; Chem. Ber. **1973**, 106, 3695-3724.
42. Deswarte, S., Bellec, C., Souchay, P.; Bull. Soc. Chim. Belg. **1975**, 84, 321-331.