Pergamon

Tetrahedron 54 (1998) 9207–9222

TETRAHEDRON

A general and practical method of synthesis of 2-disubstituted-1-chloro- and 1-bromoenamines

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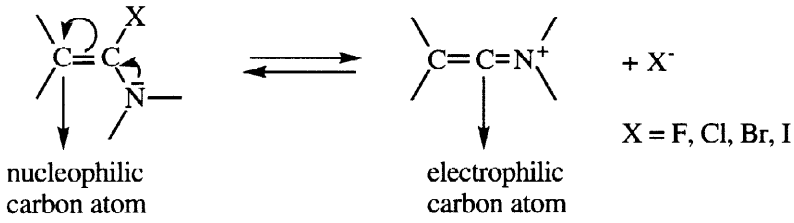
Received 29 April 1998; accepted 3 June 1998

Abstract : Disubstituted-α-chloroenamines are useful synthetic intermediates which had earlier been prepared by the reaction of tertiary amides with phosgene. The toxicity of the latter led us to systematically investigate new synthetic routes towards α-chloro- and α-bromoenamines. The reactions of various halogenating agents ($SOCl_2$, diphosgene, triphosgene, $OPCl_3$, $OPBr_3$) with tertiary amides followed by the addition of triethylamine have been studied. Thionyl chloride was found unsuitable for the preparation of α-chloroenamines. Of the other halogenating agents, $OPCl_3$ and $OPBr_3$ were found the most practical. The generality of the method is illustrated by the synthesis of fifteen α-chloroenamines and six α-bromoenamines.

Keywords : α-chloroenamines, α-bromoenamines, keteniminium salts, amides, chlorination, bromination

Introduction

α-Haloenamines which can be regarded as enamines derived from acid halides hold a special place among the various types of enamines and ketene acetals. They indeed behave as ambiphilic molecules which react as nucleophilic reagents at the β-carbon atom of the enamine function but also exhibit electrophilic reactivity at the α-carbon atom (Scheme 1).[1]



Scheme 1

It has been shown that fine tuning of the ambiphilicity of α-haloenamines could be easily performed by varying the nature of the halogen atom and of the amine substituents.[1c-f,2]

The first representatives of the class of α-chloroenamines had been described by von Braun and Heymons in 1929 but their products had not been fully purified and characterised.[3] It was only in the middle sixties that the synthesis and the properties of α-haloenamines were systematically investigated in Viehe's laboratory[4] and by our group.[1,2,5,6] Since then, they have been used by many researchers in various synthetic applications.[7,8]

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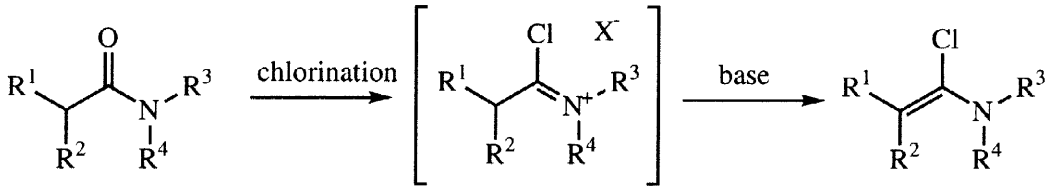
0040-4020/98/$19.00
PII: S0040-4020(98)00558-4

β-Substituted-α-haloenamines have received special attention since they are thermally stable and can be purified and stored. They are very convenient sources of keteniminium salts which are unrivalled reagents for [2+2] cycloadditions.[6,8] Also they are mild halogenating reagents of hydroxyl groups under neutral conditions.[5j,7f,7h]

In 1969 we published a general method of synthesis of β-disubstituted-α-chloroenamines.[5a] It involved the reaction of tertiary amides with phosgene followed by the dehydrochlorination of the intermediate amide chlorides with triethylamine. The hazard associated with the use of large amounts of phosgene as well as the ban on phosgene in many laboratories led us to re-examine the preparation of β-disubstituted-α-chloroenamines which are also the starting material of the synthesis of the other α-haloenamines. The synthetic route is conceptually the same as the previous one : it involves the reaction of a tertiary amide with a chlorinating agent followed by the elimination of hydrochloric acid from the resulting α-chloroiminium salt (Scheme 2).



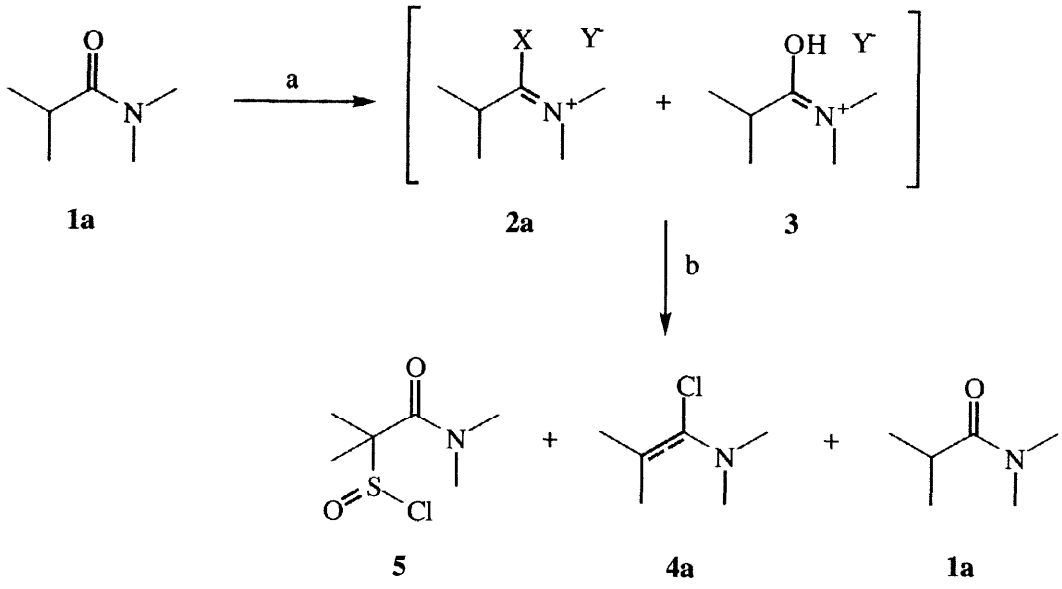
Scheme 2

The reaction of tertiary amides with standard chlorinating agents is abundantly documented.[9] However its application to the sequence of scheme 2 is not trivial since the α-chloroenamine generated in the second step can react with almost any electrophilic species of the reaction mixture of the chlorination reaction. We had therefore to undertake a careful study of the sequence of scheme 2 using a variety of chlorinating agents. This paper reports the most significant results of these studies which led to a general and practical synthesis of β-disubstituted-α-chloro and α-bromoenamines.

Results and discussion

1. Reactions with thionyl chloride

In contrast with an earlier report of Martin *et al*[10], we only observed a very low (≤ 20%) conversion of N,N,2-trimethylpropanamide **1a** into the corresponding iminium salt **2a** upon treatment with thionyl chloride at room temperature. Refluxing the mixture in benzene led to a complex mixture which did not contain **2a**. However reaction of **1a** with thionyl chloride in the presence of 20% DMF at room temperature yielded a 4:1 ratio of **2a** and protonated amide **3** (Scheme 3).

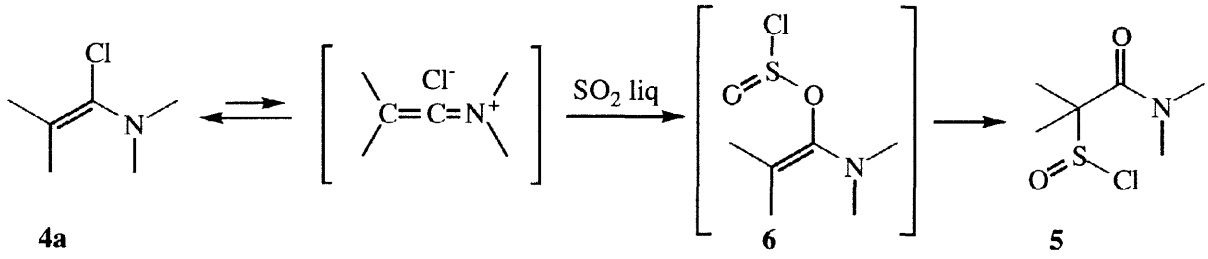


Reagents and conditions : (a) $SOCl_2$ (5 equiv.); DMF (0.2 equiv.), 4 hrs X,Y = Cl or OSOCl, crude ;
(b) removal of excess $SOCl_2$, Et_3N

Scheme 3

Treatment of the crude mixture with triethylamine led to tetramethyl-α-chloroenamine (TMCE) **4a** contaminated by amide **1a** (± 10 %), compound **5** (± 10 %) and some unidentified products. Distillation led to extensive decomposition and only 20% of pure **4a** could be obtained.

The formation of **5** can be explained by the intramolecular rearrangement of the N,O-keteneacetal **6** resulting from the deprotonation of **2a** (X=OSOCl). This interpretation is supported by an independent synthesis of **5** by dissolving **4a** in liquid SO_2 (Scheme 4).

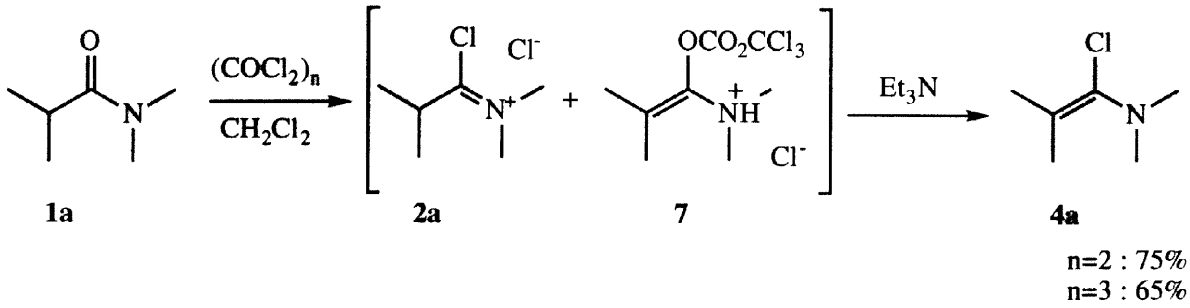


Scheme 4

These results clearly demonstrated that thionyl chloride is not a suitable chlorinating agent for the conversion of tertiary amides into α-chloroenamines.

2. Reactions with di- and triphosgene

Di- and triphosgene are easier to manipulate and to store than phosgene. Both reagents were found suitable for the preparation of TMCE **4a** from N,N,2-trimethylpropanamide **1a** (Scheme 5).



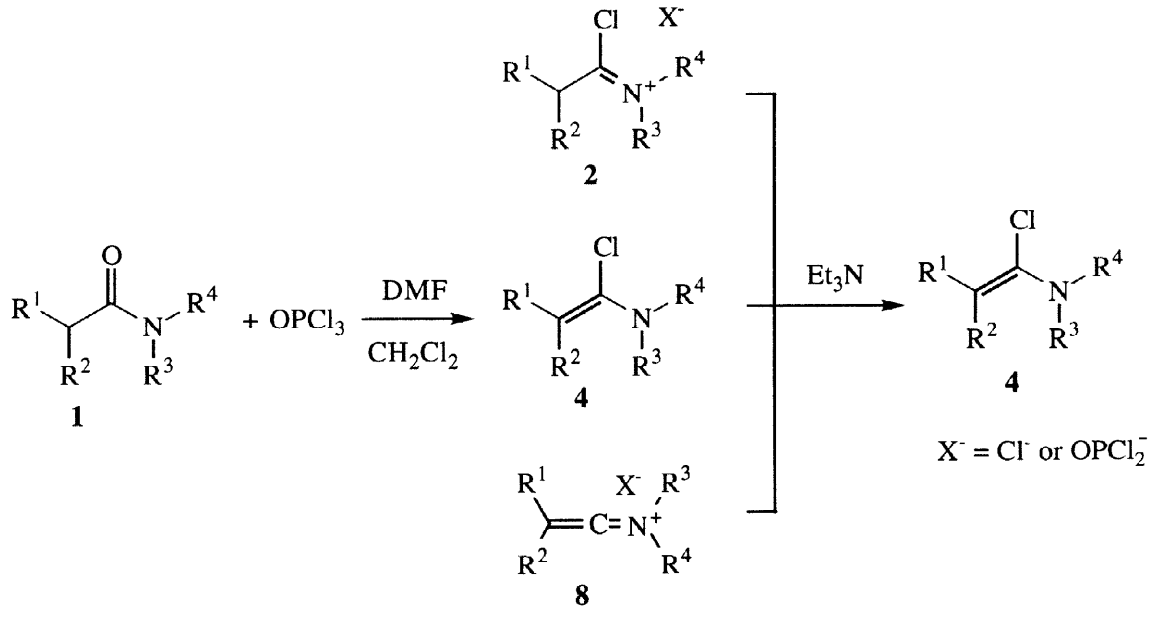
Scheme 5

The best results were obtained with 2 equivalents of diphosgene at room temperature (yields : 75%) or 3 equivalents of triphosgene in refluxing dichloromethane (yields : 65%). In both cases the formation of **2a** was accompanied by that of a minor product which was assigned structure **7**. Hydrolysis of the crude mixture of **2a** and **7** led to the quantitative recovery of **1a**.

3. Reactions with phosphorous oxychloride

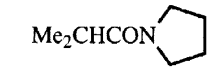
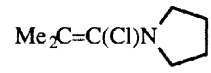
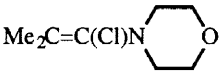
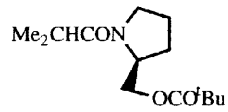
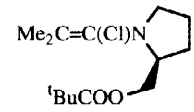
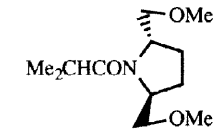
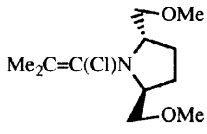
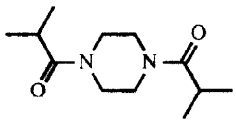
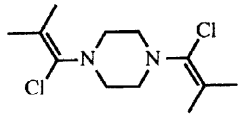
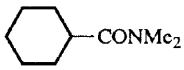
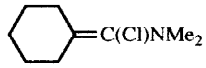
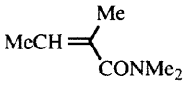
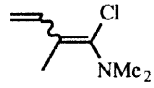
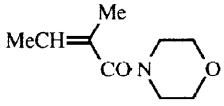
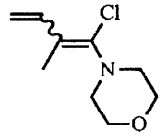
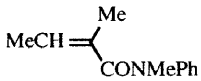
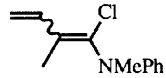
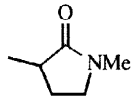
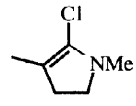
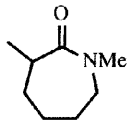
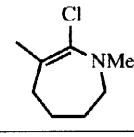
The reaction of tertiary amides with phosphorous oxychloride has been amply documented. NMR studies by Martin *et al* have convincingly demonstrated that the reaction generated α-chloroiminium salts.[10] The reaction can be catalysed by a small amount of DMF; in this case the chlorinating agent has been shown to be the α-chloroiminium salt derived from a fast reaction between DMF and $OPCl_3$.[11]

We have studied the reaction of a series of tertiary amides with $OPCl_3$ in the presence of a catalytic amount of DMF. The crude reaction mixtures were analysed by ^{1}H-NMR then treated with triethylamine to yield the corresponding α-chloroenamines **4** (Scheme 6, Table 1).



Scheme 6

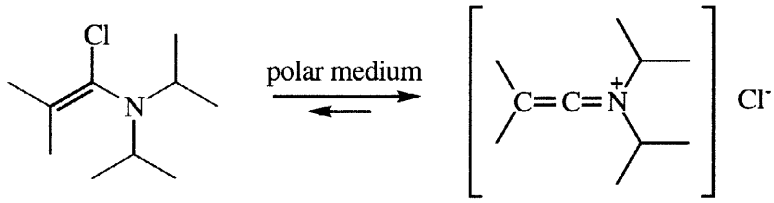
Table 1 : Synthesis of α-chloroenamines 4

	Amide **1**	1st step OPCl3 (equiv.)	DMF (equiv.)	T (°C)*	products (ratio)	2d step Et3N (equiv.)	α-chloroenamine **4**	Yield of **4** (%)
a	$Me_2CHCONMe_2$	1.6	0.02	20	**2a**	1.6	$Me_2C{=}C(Cl)NMe_2$	80-90
b		2.0	0.02	20	**2b**	1.6		83
c		2.0	0.05	20	**2c:4c** (5.6:1)	2.0		85
d	$Me_2CHCONMePh$	2.5	0.05	80	**2d:4d** (1:1.7)	1.1	$Me_2C{=}C(Cl)NMePh$	83
e	$Me_2CHCONiPr_2$	1.6	0.10	60	**2e + 8e**	1.1	$Me_2C{=}C(Cl)NiPr_2$	80
f		2.0	0.02	20	**2f**	2.0		62
g		2.5	0.20	50	**2g**	1.5		66
h		4.0	0.04	60	**2h + 4h**	3.0		78
i		1.1	0.02	20	**2i**	3.0		76
j	$Ph_2CHCONMe_2$	5.0	0.23	60	**2j**	2.5	$Ph_2C{=}C(Cl)NMe_2$	40
k		1.1	0.02	20	**2k**	3.0		80
l		1.1	0.02	20	**2l:4l** (1:2.6)	1.1		75
m		2.0	0.04	20	**2m:4m** (1:2.6)	2.0		88
n		1.1	0.02	20	**2n**	9.5		46
o		1.1	0.02	20	**2o**	2.0		81

* Temperature of the bath. All reactions were performed in CH_2Cl_2.

In the presence of small amounts of DMF, the chlorination was much faster. In most cases a 90% conversion was obtained in less that 12 hours. Less reactive amide (entries d, g, h, j) requested higher temperatures and (or) longer reaction times.

Amides **1c**, **1d**, **1h**, **1l**, **1m** gave less stabilised iminium salts which underwent partial deprotonation under the reaction conditions. Interestingly, the reaction mixture derived from **1e** contained the corresponding α-chloroiminium salt contaminated by keteniminium salt **8e** ($\bar{\upsilon}_{C=C=N+}$ 2020 cm^{-1}). The formation of **8e** can be explained by the ionisation of the corresponding α-chloroenamine **4e** boosted by the polarity of the medium and the steric relief in going from a trigonal to a dihedral carbon atom (Scheme 7).



4e **8e**

Scheme 7

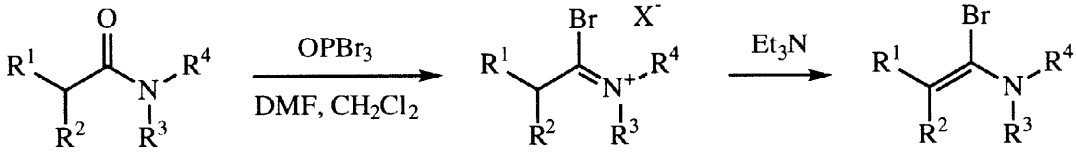
The mixture was then treated with an excess of triethylamine and the resulting triethylamine hydrochloride was precipitated off by addition of petroleum ether. In some cases (e.g. entries h and j) it was necessary to remove the excess of $OPCl_3$ before adding the base.

Except for **4h** and **4j** which are crystalline solids, all α-chloroenamines are thermally stable liquids which were purified by distillation. Their structures were confirmed by their spectral properties. A detailed discussion of their mass spectra has been recently published.[12]

This method is suitable for the preparation of large amounts of α-chloroenamines (e.g. : **4e** : 400 g, **4a** : 100 g).

4. Reactions with phosphorous oxybromide

The successful results obtained with $OPCl_3$ led us to examine the possibility of preparing the corresponding α-bromoenamines by using $OPBr_3$ as brominating reagent (Scheme 8, Table 2).



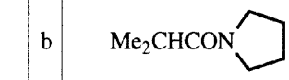
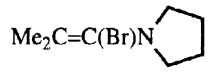
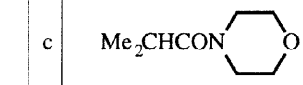
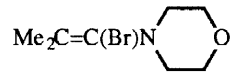
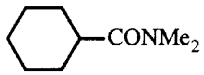
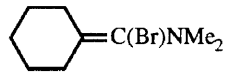
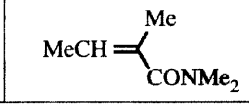
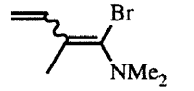
1 **10** **9**

$X^- = Br^-$ or $OPBr_2^-$

Scheme 8

The bromination reactions took place more rapidly than the corresponding chlorinations and, in general, less amounts of the halogenating agent were used. Addition of triethylamine yielded the corresponding α-bromoenamines **9**.

Table 2 : Synthesis of α-bromoenamines 9

	Amide **1**	1st step OPBr3 (equiv.)	DMF (equiv.)	T (°C)*	products (crude)	2d step Et3N (equiv.)	α-bromoenamine **9**	Yield of **9** (%)
a	$Me_2CHCONMe_2$	1.2	0.02	20	**10a**	1.4	$Me_2C{=}C(Br)NMe_2$	95
b		1.2	0.02	0	**10b**	2.5		61
c		1.2	0.02	20	**10c**	2.0		74
d	$Me_2CHCONⁱPr_2$	1.6	0.10	40	**10d****	2.2	$Me_2C{=}C(Br)NⁱPr_2$	72
e		1.1	0.02	20	**10e**	4.0		62
f		1.1	0.02	0	**10f**	1.8		24

* Temperature of the bath. All reactions were performed in CH_2Cl_2. ** Accompanied by small amounts of the corresponding ketenimínium bromide.

Conclusions

We have thus been successful in developing a general and practical method for the synthesis of the useful β-disubstituted-α-chloroenamines. In most cases, the method using phosphorous oxychloride gave the highest yields. This method will probably supersede that using phosgene as chlorinating agent because of the toxicity of the latter. We have also succeeded in preparing the corresponding α-bromoenamines which, up to now, were only available by halide exchange.[1c-d]

Experimental section

IR spectra were recorded on Perkin-Elmer 297 or 681 spectrophotometers. ^1H NMR spectra were obtained on Varian XL-200 or VXR-200 spectrometers (δ in ppm relative to internal TMS, $CDCl_3$, J in Hertz). ^{13}C NMR spectra were recorded at 50 MHz on Varian XL-200 or VXR-200 (δ in ppm relative to internal TMS, $CDCl_3$, J in Hertz). Multiplicities were reported as s (singlet), d (doublet), t (triplet), q (quadruplet), sept (septuplet), m (multiplet or massif). Mass spectra were measured on Varian MAT-44 or Finnigan MAT-TSQ70 spectrometers (electronic impact 70 eV or chemical ionisation with N_2O-CH_4 as ionising gas). Optical activities ([α]) were measured on PERKIN-ELMER 241 MC polarimeter (concentrations in g/100 ml). Distillations were performed using a 10 cm Vigreux column or a Büchi Kugelrohr GKR-50 apparatus. All dry solvents were distilled under argon or under reduced pressure. Dimethoxyethane was distilled from sodium/benzophenone ketyl. Dichloromethane, cyclohexane, petroleum ether, N,N-dimethylformamide and amines were distilled from calcium hydride. Acid chlorides were distilled immediately before use. All

reactions requiring anhydrous or inert conditions were carried out under a dry argon atmosphere in under reduced pressure flame-dried glassware.

Non commercial acid chlorides have been obtained according to known procedures. Most amides had been previously prepared but some of them spectral properties had not been reported. We have therefore included them in the experimental part. α-Chloro and α-bromoenamines are very sensitive to moisture. No satisfactory microanalyses could be obtained. However their purity can be assessed by titration with aqueous NaOH.

Synthesis of amides

General procedure

The amine and dry dichloromethane were introduced in a three-necked, round-bottomed flask equipped with a magnetic stirring bar, a pressure-equalising dropping funnel and a reflux condenser. After cooling the solution in an ice-water bath, the acid chloride was dropwise added via the dropping funnel. The resulting mixture was then stirred overnight at room temperature. The precipitate formed was filtered and washed with dichloromethane. The filtrate was successively washed with 3% sodium bicarbonate solution and water, dried over magnesium sulfate and concentrated under reduced pressure. The residue was purified either by distillation or by recrystallisation.

N,N,2-trimethylpropionamide (1a)

226 ml (90 g, 2 mols, 2 eq.) of a 40% w/w solution of dimethylamine in water (the flask were not dried!), 50 ml of dichloromethane, 105 ml (106.5 g, 1 mol) of 2-methylpropanoyl chloride; distillation; yield: 98 g (85%); $C_6H_{13}NO$ (115.17); RN 21678-37-5; colourless liquid; Bp. 62°C (10 torr); IR (CH_2Cl_2): 1645 (NC=O); ^1H NMR[10]: 3.04 (*s*, 3H, NCH_3); 2.94 (*s*, 3H, NCH_3); 2.81 (*sept*, *J* = 6.8, 1H, CH); 1.12 (*d*, *J* = 6.8, 6H, $CH(CH_3)_2$); ^{13}C NMR: 176.6 (*S*, C=O); 36.6 (*Qq*, *J* = 137, 3.4, NCH_3); 35.1 (*Qq*, *J* = 138, 3.4, NCH_3); 29.7 (*Dsept*, *J* = 127, 4.4, CH); 18.7 (*Qqd*, *J* = 127, 5.4, 4.4, $CH(CH_3)_2$).

1-isobutyrylpyrrolidine (1b)

167 ml (142.3 g, 2 mols, 2 eq.) of pyrrolidine, 200 ml of dichloromethane, 105 ml (106.5 g, 1 mol) of isobutyryl chloride; distillation; yield: 110 g (78%); $C_8H_{15}NO$ (141.21); RN 33931-47-4; colourless liquid; Bp. 116°C (12 torr); IR (CH_2Cl_2): 1630 (NC=O); ^1H NMR: 3.4-3.5 (*m*, 4H, NCH_2); 2.64 (*sept*, *J* = 6.8, 1H, CH); 1.75-2.05 (*m*, 4H, $NCH_2(CH_2)_2$); 1.13 (*d*, *J* = 6.8, 6H, CH_3); ^{13}C NMR: 174.5 (*S*, C=O); 45.3 (*T*, *J* = 142, NCH_2); 44.7 (*T*, *J* = 143, NCH_2); 31.4 (*Dsept*, *J* = 128, 4.0, $CH(CH_3)_2$); 25.3 (*Tquint*, *J* = 133, 3.5, NCH_2CH_2); 23.4 (*Tquint*, *J* = 133, 3.5, NCH_2CH_2); 18.1 (*Qdq*, *J* = 128, 5.5, 5.0, $CH(CH_3)_2$).

4-isobutyrylmorpholine (1c)

174 ml (174.2 g, 2 mols, 2 eq.) of morpholine, 100 ml of dichloromethane, 105 ml (107 g, 1 mol) of isobutyryl chloride; distillation; yield: 136.6 g (87%); $C_8H_{15}NO_2$ (157.21); RN 18071-39-1; colourless liquid; Bp. 120°C (15 torr); IR (CH_2Cl_2): 1635 (NC=O); ^1H NMR: 3.54-3.68 (*m*, 8H, NCH_2CH_2O); 2.79 (*sept*, *J* = 6.8, 1H, $CH(CH_3)_2$); 1.15 (*d*, *J* = 6.8, 6H, $CH(CH_3)_2$); ^{13}C NMR: 174.8 (*S*, C=O); 66.3 (*T*, *J* = 144, OCH_2); 45.3 (*T*, *J* = 139, NCH_2); 41.4 (*T*, *J* = 140, NCH_2); 29.2 (*D*, *J* = 125, $CH(CH_3)_2$); 18.7 (*Q*, *J* = 128, $CH(CH_3)_2$).

N,2-dimethyl-N-phenylpropionamide (1d)

433 ml (430 g, 4 mols, 2 eq.) of methylaniline, 200 ml of dichloromethane, 210 ml (213 g, 2 mols) of isobutyryl chloride; yield: 144 g (81%); $C_{11}H_{15}NO$ (177.24); RN 55577-65-6; white solid (recrystallised from benzene/cyclohexane 2:5); IR (CH_2Cl_2)[7a]: 1650 (NC=O); ^1H NMR[7a]: 7.18-7.47 (*m*, 5H, Ph); 3.26 (*s*, 3H, NCH_3); 2.52 (*sept*, *J* = 6.6, 1H, $CH(CH_3)_2$); 1.04 (*d*, *J* = 6.6, 6 H, $CH(CH_3)_2$); ^{13}C NMR: 177.6 (*S*, C=O); 144.6 (*S br.*, $C(C_5H_5)$); 130.1 (*Dd*, *J* = 161, 7.6, C_{ortho}); 128 (*Dt*, *J* = 162, 7.5, C_{para}); 127.6 (*Ddd*, *J* = 161, 7.2, 6.4, C_{meta}); 37.5 (*Q*, *J* = 139, NCH_3); 30.4 (*Dsept*, *J* = 130, 4.1, $CH(CH_3)_2$); 19.7 (*Qdq*, *J* = 128, 4.6, 5.2, $CH(CH_3)_2$).

2-methyl-N,N-diisopropylpropionamide (1e)

280 ml (202.4 g, 2 mols, 2 eq.) of diisopropylamine, 200 ml of dichloromethane, 105 ml (106.5 g, 1 mol) of isobutyryl chloride; yield: 162 g (95%); $C_{10}H_{21}NO$ (171.28); RN 682-98-0; white solid (recrystallised from ethyl acetate); IR (neat): 1630 (NC=O); ^1H NMR: 4.01 (*sept*, *J* = 6.7, 1H, NCH); 3.58 (*m*, 1H, NCH); 2.71 (*sept*, *J* = 6.7, 1H, $CHCH_3$); 1.35 (*d*, *J* = 6.8, 6H, $NCHCH_3$); 1.23 (*d*, *J* = 6.8, 6H, $NCHCH_3$); 1.11 (*d*, *J* = 6.7, 6H, $CCH(CH_3)_2$); ^{13}C NMR: 173.3 (*S*, C=O); 47.3 (*D*, *J* = 136, NCH); 45.3

(*Dsept*, J = 134, 4.0, NCH); 31.5 (*D*, J = 127, $CCH(CH_3)_2$); 21.1 (*Qdq*, ^1J = 127, $^2J = {}^3J$ = 4.6, $NCH(CH_3)_2$); 20.4 (*Qdq*, J = 127, 4.4, 4.4, $NCH(CH_3)_2$); 19.4 (*Qdq*, J = 128, 5.4, 4.2, $CCH(CH_3)_2$).

(S)-2-(tert-butoxycarbonylmethyl)-1-isobutyrylpyrrolidine (1f)

This amide was prepared in two steps:

(S)-2-(hydroxymethyl)-1-isobutyrylpyrrolidine

11.3 ml (11.6 g, 115 mmols) of L-2-pyrrolidinemethanol and 230 ml of dichloromethane were introduced in a three-necked, round-bottomed flask equiped with a magnetic stirring bar, a pressure-equalising dropping funnel and a reflux condenser. The resulting solution was cooled to -40°C and 19.2 ml (13.9 g, 140 mmols, 1.2 eq.) of dry triethylamine were added. A solution of 12.14 ml (12.3 g, 115 mmols) of 2-methylpropanoyl chloride in 230 ml of dichloromethane was dropwise added (during the addition, the internal temperature was maintained at -40°C). The reaction mixture was then allowed to warm up to 0°C. The formation of the amide was confirmed by IR and ^{1}H NMR. IR (CH_2Cl_2): 1620 (C=O); ^{1}H NMR: 4.17 (*m*, 1H, N-CH); 3.70-3.40 (*m*, 4H, N-CH_2 and CH_2OH); 2.70 (*sept*, J = 6.8, 1H, $CH(CH_3)_2$); 2.15-1.80 (*m*, 4H, N-CH_2-$(CH_2)_2$-); 1.75 (*d*, J = 6.8, 3H, $CHCH_3$); 1.25 (*d*, J = 6.8, 3H, $CHCH_3$).

(S)-2-(tert-butoxycarbonylmethyl)-1-isobutyrylpyrrolidine (1f)

To the crude reaction mixture obtained above and cooled to -30°C was added 19.2 ml (13.9 g, 140 mmols, 1.2 eq.) of dry triethylamine. 9.4 ml (13.8 g, 110 mmols) of pivaloyl chloride were then slowly added (over a period of 30 min.; the internal temperature was maintained at -30°C during the addition). The reaction mixture was allowed to warm up slowly to room temperature (over a period of 4 h) and refluxed for 12 hours. The solvent was removed under reduced pressure and triethylamine hydrochloride was precipitated by addition of ether. The precipitate was filtered off and washed with ether. The filtrate was extracted with a solution of 3% $NaHCO_3$. The organic phase was dried over magnesium sulfate and concentrated under reduced pressure. The crude product was purified by flash-chromatography (cyclohexane/ethyl acetate 3:2); yield: 15.5 g (53%); $C_{14}H_{25}NO_3$ (255.35); RN 149554-71-2; white solid; $[\alpha]_D^{20}$ = -56.7° (c=0.86, $CHCl_3$); IR (CH_2Cl_2): 1725 (OC=O); 1635 (NC=O); ^{1}H NMR (2 rotamers): 4.42-4.32 (*m*, 1H, NCH); 4.18 (*d*, J = 6.1, 2H, OCH_2); 3.53 (*t*, J = 6.0, 2H, NCH_2); 2.83 (*sept*, J = 6.8, $CH(CH_3)_2$ minor); 2.65 (*sept*, J = 6.8, 1H, $CH(CH_3)_2$ major); 2.1-1.8 (*m*, 4H, $NCH_2(CH_2)_2$); 1.22 (*s*, $C(CH_3)_3$ minor); 1.19 (*s*, 9H, $C(CH_3)_3$ major); 1.12 (*d*, J = 6.8, 6H, $CH(CH_3)_2$); ^{13}C NMR: 178 (*S*, OC=O); 175.9 (*S*, NC=O); 63.5 (*T*, J = 150, OCH_2); 55.1 (*D*, J = 145, NCH); 46.6 (*T*, J = 142, NCH_2); 38.3 (*S*, $C(CH_3)_3$); 32.1 (*Dsept*, J = 128, 4.0, $CH(CH_3)_2$); 26.7 (*Qsept*, J = 127, 5.0, $C(CH_3)_3$); 23.8 (*T*, J = 134, $NCH_2(CH_2)_2$); 19.0 (*Q*, J = 127, $CHCH_3$); 18.1 (*Q*, J = 127, $CHCH_3$).

(2R,5R)-2,5-bis(methoxymethyl)-1-isobutyrylpyrrolidine (1g)

This amide was prepared according to the general procedure with the following modifications: after cooling the solution of 2,5-bis(methoxymethyl)pyrrolidine hydrochloride in dichloromethane by an ice-water bath, triethylamine was added before the acid chloride. For the work-up, triethylamine hydrochloride was precipitated by addition of petroleum ether. 5.33 g (27 mmols) of 2,5-bis(methoxymethyl)pyrrolidine hydrochloride[13], 150 ml of dichloromethane, 11.4 ml (8.3 g, 82 mmols, 3 eq.) of triethylamine, 3.53 ml (3.5 g, 33 mmols, 1.2 eq.) of methylpropanoyl chloride; distillation; yield: 5.98 g (96%); RN 149554-72-3; Bp. 80°C (0.03 torr); $[\alpha]_D^{20}$ = +69.04 (c=1.09, $CHCl_3$); IR (CH_2Cl_2): 1634 (NC=O); ^{1}H NMR: 4.2 (*m*, 1H, NC*H*); 3.98 (*m*, 1H, NC*H*); 3.55 (*dd*, J = 9.2, 3.0, 1H, OC*H*H); 3.35 (*s*, 3H, OCH_3); 3.32 (*s*, 3H, OCH_3); 3.4-3.1 (*m*, 9H, CH_2OCH_3+$CHHOCH_3$); 2.75 (*sept*, J = 6.8, 1H, $CH(CH_3)_2$); 2.1-1.8 (*m*, 4H, $NCH(CH_2)_2$); 1.13 (*d*, J = 6.8, 3H, $CHCH_3$); 1.11 (*d*, J = 6.8, 3H, $CHCH_3$); ^{13}C NMR: 177.1 (*S*, C=O); 74.7 (*T*, J = 141, OCH_2); 71.37 (*T*, J = 142, OCH_2); 59.2 (*Qt*, J = 141, 2.8, OCH_3); 58.9 (*Qt*, J =141, 3.4, OCH_3); 57.3 (*D*, J =143, NCH); 56.4 (*D*, J =143, NCH); 32.7 (*Dsept*, J = 129, 4,0, $CH(CH_3)_2$); 27.1 (*T*, J = 136, $NCHCH_2$); 25.2 (*T*, J = 133, $NCHCH_2$); 20.7 (*Q*, J = 128, $CHCH_3$); 18.8 (*Q*, J = 127, $CHCH_3$); MS (IE, $C_{12}H_{23}NO_3$ (229.31)): m/z = 230 ($[M+H]^{+\bullet}$); 229 ($M^{+\bullet}$); 184 ($[M-CH_2OMe]^+$); 115 ($[184-Me_2CHCO+H]^+$); 71 ($[Me_2CHCO]^+$); Anal. calc. for $C_{12}H_{23}NO_3$: H 10.1, C 62.85, N 6.1; found: H 9.79, C 62.65, N 5.98.

N,N'-diisobutyrylpiperazine (1h)

300 ml (293.4 g, 3.7 mols, 9 eq.) of pyridine and 35 g (0.4 mol) of piperazine were introduced in a three-necked, round-bottomed flask equiped with a magnetic stirring bar, a pressure-equalising dropping funnel and a reflux condenser. To the resulting suspension was added (over at least a period of 1 hour) 84 ml (85 g, 0.8 mol, 2 eq.) of isobutyryl chloride. After the addition, 150 ml of benzene were added and the reaction mixture was refluxed for 15 minutes. After cooling down to about 50°C, the upper phase was separated by decantation. The lower phase (pyridine hydrochloride) was washed with 50 ml of benzene. The benzenic phases combined and

concentrated under reduced pressure were taken up in 60 ml of hot dichloromethane. After cooling to room temperature, the amide crystallised and was filtered. The filtrate was concentrated and the operation repeated; yield: 59 g (65%); $C_{12}H_{22}N_2O_2$ (226.31); RN 18940-58-4; white solid; Mp. 136-137°C; IR (CH_2Cl_2): 1640 (NC=O); ^{1}H NMR: 3.67-3.50 (*m*, 8H, NCH_2); 2.81 (*sept*, *J* = 6.8, 2H, CH); 1.15 (*d*, *J* = 6.8, 12H, CH_3); ^{13}C NMR: 174.9 (*S*, C=O); 44.6 (*T*, *J* = 140, NCH_2); 41.2 (*T*, *J* = 146, NCH_2); 30.0 (*D*, *J* = 127, CH); 19.2 (*Q*, *J* = 127, CH_3).

N,N-dimethylcyclohexanecarboxamide (1i)

226 ml (90 g, 2 mols, 2 eq.) of a 40% w/w solution of dimethylamine in water (the flask were not dried!), 50 ml of dichloromethane, 146.5 g (1 mol) of cyclohexanecarbonyl chloride; distillation; yield: 125 g (81%); $C_9H_{17}NO$ (155.24); RN 17566-51-7; colourless liquid; Bp. 39°C (0.05 torr); IR : 2854 (C-H); 2829 (C-H); 1640 (NC=O); ^{1}H NMR: 3.04 (*s*, 3H, NCH_3); 2.93 (*s*, 3H, NCH_3); 2.50 (*tt*, *J* = 11.1, 3.3, 1H, CH); 1.85-1.15 (*m*, 10H, $(CH_2)_5$); ^{13}C NMR: 175.0 (*S*, C=O); 39.7 (*D*, *J* = 123, CH); 36.1 (*Qq*, *J* = 136.8, 3.6, NCH_3); 34.5 (*Qq*, *J* = 137.6, 3.6, NCH_3); 28.2 (*T*, *J* = 128, $CHCH_2$); 25.1 (*T*, *J* = 126, CH_2).

N,N-dimethyltiglamide (1k)

68 ml (27 g, 0.6 mol, 2 eq.) of a 40% w/w solution of dimethylamine in water (the flask were not dried!), 25 ml of dichloromethane, 35.4 g (0.3 mol) of 2-methylbut-2-enoyl chloride[14]; distillation; yield: 33.5 g (88%); $C_7H_{13}NO$ (127.18); RN 32223-06-6; colourless liquid; Bp. 85°C (12 torr); IR (CH_2Cl_2): 1660 (C=C); 1620 (NC=O); ^{1}H NMR: 5.65 (*q*, *J* = 5.9, 1H, CH); 2.99 (*s*, 6H, $N(CH_3)_2$); 1.84 (*s*, 3H, CCH_3); 1.71 (*d*, *J* = 5.9, 3H, $CHCH_3$); ^{13}C NMR: 172.9 (*S*, C=O); 131.6 (*S*, CCH_3); 124.7 (*Dq*, *J* = 154, 5.8, $CHCH_3$); 38.8 (*Q*, NCH_3); 37.0 (*Q*, NCH_3); 13.1 (*Qd*, *J* = 128, 8.3, CCH_3); 12.3 (*Qd*, *J* = 127, 4.0, $CHCH_3$).

4-(2-methylbut-2-enoyl)morpholine (1l)

This amide was prepared according to the general procedure with the following modifications: 1) A mixture of morpholine and triethylamine was dropwise added to a -10°C cooled solution of the acid chloride in dichloromethane. 2) Triethylamine hydrochloride was precipitated by addition of low boiling petroleum ether. 95 g (0.8 mol) of 2-methyl-2-butenoyl chloride[14], 200 ml of dichloromethane, 76.7 ml (76.7 g, 0.88 mol, 1.1 eq.) of morpholine, 122.5 ml (89 g, 0.88 mol, 1.1 eq.) of triethylamine; distillation; yield: 98 g (78%); $C_9H_{15}NO_2$ (169.22); colourless liquid; Bp. 73°C (0.1 torr); IR (CH_2Cl_2): 1660 (C=C); 1620 (NC=O); ^{1}H NMR: 5.65 (*qq*, *J* = 6.8, 1.6, 1H, HC=C); 3.70-3.62 (*m*, 4H, NCH_2); 3.62-3.53 (*m*, 4H, OCH_2); 1.83 (*sdq*, *J* = 1.6, 1.2, 3H, CCH_3); 1.7 (*dq*, *J* = 6.8, 1.2, 3H, $CHCH_3$); ^{13}C NMR: 171.8 (*S*, C=O); 131.0 (*S*, CCH_3); 125.5 (*Dqq*, *J* = 154, 5.6, 6.9, $CHCH_3$); 66.3 (*T*, *J* = 144, OCH_2); 44.1 (*T*, NCH_2); 13.5 (*Qd*, *J* = 128, 8.2, CCH_3); 12.5 (*Qd*, *J* = 127, 3.7, $CHCH_3$).

N,2-dimethyl-N-phenylbut-2-enamide (1m)

The procedure described for amide (**1l**) was applied with the following amounts: 29 g (0.25 mol) of 2-methyl-2-butenoyl chloride[14], 70 ml of dichloromethane, 31.6 g (0.29 mol, 1.2 eq.) of aniline and 35.3 ml (25 g, 0.25 mol) of triethylamine; distillation; yield: 43 g (90%); $C_{12}H_{15}NO$ (189.25); RN 135578-96-0, 143726-38-9; colourless liquid; Bp. 85°C (0.2 torr); IR (CH_2Cl_2): 1630 (NC=O); ^{1}H NMR: 7.30 (*dd*, *J* = ~8, 2H, H_{meta}); 7.21 (*dd*, *J* = ~7, 1H, H_{para}); 7.06 (*d*, *J* = ~7, 2H, H_{ortho}); 5.74 (*q*, *J* = 6.8, 1H, CH); 3.33 (*s*, 3H, NCH_3); 1.57 (*s*, 3H, CCH_3); 1.47 (*d*, *J* = 6.8, 3H, $CHCH_3$); ^{13}C NMR: 172.6 (*S*, C=O); 144.4 (*S*, $NC(C_5H_5)$); 132.1 (*Sq*, *J* = 6, *C*CH); 129.7 (*Dqq*, *J* = 155, 8, 4, *C*H); 128.5 (*Dd*, *J* = 161, 8, C_{ortho}); 125.8 (*D*, C_{meta}); 37.1 (*Q*, *J* = 139, NCH_3); 13.5 (*Qd*, *J* = 128, 7.9, CCH_3); 12.7 (*Qd*, *J* = 127, 3.9, $CHCH_3$).

1,3-dimethyl-2-pyrrolidone (1n)

70.1 ml (50.6 g, 0.5 mol) of diisopropylamine and 250 ml of tetrahydrofuran were introduced in a three-necked, round-bottomed flask equiped with a magnetic stirring bar and a pressure-equalising dropping funnel. The resulting solution was cooled to 0°C and 200 ml (0.5 mol) of a 2.5 M solution of butyllithium in hexane were added dropwise. After 15 minutes at 0°C, the flask was cooled to -78°C and 48 ml (49.6 g, 0.5 mol) of N-methyl-2-pyrrolidone were slowly added via a syringe. The temperature was maintained at -78°C for 30 minutes. 34.3 ml (78.1 g, 0.55 mol, 1.1 eq.) of methyl iodide were then added at once. The reaction mixture was stirred at -30°C for 3 hours and then allowed to warm up to room temperature. The lower phase containing the desired product was separated by decantation. Water was added and the amide was extracted with chloroform. Organic layer was dried over magnesium sulfate, concentrated and distilled under reduced pressure; yield: 39.6 g (70%); $C_6H_{11}NO$ (113.15); RN 19597-07-0; colourless liquid; Bp. 90-95°C (20 torr); IR (CH_2Cl_2): 1663 (NC=O); ^{1}H NMR (2 isomers): 3.4 (*dd*, NCH_2 minor); 3.31 (*dd*, *J* = 8.4, *J* = 5.3, 2H, NCH_2); 3.0 (*s*, NCH_3 minor); 2.85 (*s*, 3H, NCH_3); 2.45 (*q*, *J* = 7.9, 1H, $CHCH_3$); 2.27 (*m*, 1H, NCH_2CHH); 2.05 (*dtd*, NCH_2CHH minor); 1.63 (*dtd*, *J* = 12.4, 8.6, 8.4, 1H, NCH_2CHH); 1.2 (*d*, *J* = 7.0, 3H, $CHCH_3$); ^{13}C NMR: 176.8 (*S*, C=O);

174.5 (*S*, C=O minor); 48.9 (*T*, *J* = 141, **NCH_2 minor**); 46.9 (*T*, *J* = 141, NCH_2); 35.9 (*D*, *J* = 130, $CHCH_3$); **34.0 (*D*, *J* = ~130,** CH minor); 29.2 (*Q*, *J* =138, **NCH_3**); **29.0** (*Q*, *J* = 138, NCH_3 minor); 26.5 (*Tdd*, *J* = 133, 4.9, 1.6, NCH_2CH_2); 17.1 (*Q*, $CHCH_3$ minor); 15.9 (*Qdt*, *J* = 127, ~4, ~1.7, $CHCH_3$).

1,3-dimethylcaprolactam (1o)

This amide was prepared according to the procedure described for (**1n**): 70.1 ml (50.6 g, 0.5 mol) of diisopropylamine, 250 ml of tetrahydrofuran, 200 ml (0.5 mol) of a 2.5 M solution of butyllithium in hexane, 64.2 ml (63.6 g, 0.5 mol) of N-methylcaprolactam and 34.3 ml (78.1 g, 0.55 mol, 1.1 eq.) of methyl iodide; yield 48 g (68%); $C_8H_{15}NO$ (141.21); RN 55917-05-0; colourless liquid; Bp. 109°C (11 torr); IR (CH_2Cl_2): 1639 (NC=O); ^{1}H NMR: 3.62 (*dd*, *J* = 14.8, 11.2, 1H, NC*H*H); 3.16 (*dd*, *J* = 14.8, 11.2, 1H, NCH*H*); 2.99 (*s*, 3H, NCH_3); 2.65 (*qt*, *J* = 6.8, 3.6, 1H, $CHCH_3$); 1.97-1.33 (*m*, 6H, $NCH_2(CH_2)_3$); 1.13 (*d*, *J* = 6.8, 3H, $CHCH_3$); ^{13}C NMR: 176.8 (*S*, C=O); 49.9 (*T*, *J* = 136, NCH_2); 37.4 (*D*, *J* = 124, CH); 35.2 (*Qt*, *J* = 138, 4.0, NCH_3); 31.9 (*T*, *J* = 126, CH_2); 28.8 (*T*, *J* = 125, CH_2); 26.6 (*T*, *J* = 124, $CHCH_2$); 17.9 (*Qt*, *J* = 127, 4.3, $CHCH_3$).

Synthesis of α-chloroenamines

General procedure

Freshly distilled phosphorus oxychloride, N,N-dimethylformamide and dry dichloromethane were introduced in a three-necked, round-bottomed flask equiped with a magnetic stirring bar, a pressure-equalising dropping funnel and a reflux condenser. A solution of the amide in dry dichloromethane was then dropwise added. The resulting mixture was stirred overnight at room temperature (the reaction was monitored by ^{1}H NMR). After cooling the flask in an ice-water bath, triethylamine was slowly added (the reaction was monitored by ^{1}H NMR). The cooling bath was removed and the mixture was allowed to warm up to room temperature. Low boiling petroleum ether was then added and the mixture was vigorously stirred for 3 hours. After cooling overnight to 4 °C, the precipitate of triethylamine hydrochloride was removed by filtration under argon. The precipitate was washed with petroleum ether. The solvents were removed under reduced pressure and the residue was purified by distillation.

N-(1-chloro-2-methylprop-1-enyl)-N,N-dimethylamine (4a)

162.4 ml (267.2 g, 1.74 mols, 2 eq.) of phosphorus oxychloride, 1.35 ml (1.28 g, 18 mmols, 0.02 eq.) of N,N-dimethylformamide, 300 ml of dichloromethane, 100 g (0.87 mol) of N,N,2-trimethylpropionamide **1a**, 8 hours at room temperature, then 132.8 ml (96.7 g, 0.96 mol, 1.1 eq.) of triethylamine; yield: 93 g (80%); RN 26189-59-3; Bp. 57°C (50 torr); colourless liquid; IR (CH_2Cl_2): 1673 (C=CCl); ^{1}H NMR: 2.39 (*s*, 6H, $N(CH_3)_2$); 1.77 (*s*, 6H, $C(CH_3)_2$); ^{13}C NMR: 140.4 (*S*, CCl); 123.8 (*S*, $C(CH_3)_2$); 42.3 (*Q*, *J* = 136, $N(CH_3)_2$); 19.8 (*Q*, *J* = 128, $C(CH_3)_2$); MS (EI, $C_6H_{12}ClN$ (133.62): m/z = 133 (90%, $M^{+\bullet}$); 128 (15%, $[M-Me]^+$); 98 (100%, $[M-Cl]^+$).

1-(1-chloro-2-methylprop-1-enyl)pyrrolidine (4b)

13 ml (140 mmols, 2 eq.) of phosphorus oxychloride, 100 µl (1.3 mmols, 0.02 eq.) of N,N-dimethylformamide, 15 ml of dichloromethane, 10 g (70 mmols) of 1-isobutyrylpyrrolidine **1b**, 3 hours at room temperature, then 15.6 ml (110 mmols, 1.6 eq.) of triethylamine; yield: 9.3 g (83%); RN 87443-04-7; colourless liquid; Bp. 60-70°C (15 torr); IR ($CHCl_3$): 1645 (C=CCl); ^{1}H NMR: 2.85 (*m*, 4H, NCH_2); 1.84-1.78 (*m*, 4H, NCH_2CH_2); 1.78 (*s*, 6H, $C(CH_3)_2$); ^{13}C NMR : 138.2 (*S*, CCl); 126.1 (*S*, $C(CH_3)_2$); 51.3 (*T*, *J* = 141, NCH_2); 25.8 (*T*, *J* = 131, NCH_2CH_2); 21.1 (*Q*, *J* = 125, $C(CH_3)_2$); MS (EI, $C_8H_{14}ClN$ (159.65)): m/z = 159 (45%, $M^{+\bullet}$); 144 (9%, $[M-Me]^+$); 131 (9%, $[M-C_2H_4]^+$); 130 (4%, $[M-C_2H_5]^+$); 124 (100%, $[M-Cl]^+$).

4-(1-chloro-2-methylprop-1-enyl)morpholine (4c)

13 ml (140 mmols, 2 eq.) of phosphorus oxychloride, 250 µl (3.5 mmols, 0.05 eq.) of N,N-dimethylformamide, 15 ml of dichloromethane, 11 g (70 mmols) of 4-isobutyrylmorpholine **1c**, 15 hours at room temperature, then 20 ml (140 mmols, 2 eq.) of triethylamine; yield: 10.4 g (85%); RN 58933-80-5; white solid; Bp. 37°C (0.15 torr); IR (CH_2Cl_2): 1670 (C=CCl); ^{1}H NMR: 3.74 (*dd*, *J* = ~4.1, 4H, OCH_2); 2.68 (*dd*, *J* = ~3.8, 4H, NCH_2); 1.89 (*s*, 3H, CCH_3); 1.77 (*s*, 3H, CCH_3); ^{13}C NMR: 137.6 (*S*, CCl); 125.2 (*S*, CCH_3); 66.3 (*T*, *J* = 143, OCH_2); 50 (*T*, *J* = 136, NCH_2); 20 (*Qq*, *J* = 127, 4.1, CCH_3); 19.7 (*Qq*, *J* = 127, 4.1, CCH_3); MS (EI, $C_8H_{14}ClNO$ (175.65)): m/z = 175 (56%, $M^{+\bullet}$); 174 (7%, $[M-H]^+$); 160 (8%, $[M-Me]^+$); 140 (100%, $[M-Cl]^+$).

N-(1-chloro-2-methylprop-1-enyl)-N-methyl-N-phenylamine (4d)

16.4 ml (175 mmols, 2.5 eq.) of phosphorus oxychloride, 250 µl (3.5 mmols, 0.05 eq.) of N,N-dimethylformamide, 25 ml of dichloromethane, 12.1 g (70 mmols) of N,2-dimethyl-N-phenylpropionamide **1d**; reflux for 14h, then 14 ml (100 mmols, 1.4 eq.) of triethylamine; yield: 11.4 g (83%); colourless liquid; Bp. 55°C (0.1 torr); IR (CH_2Cl_2): 1675 (C=CCl); ^{1}H NMR[7a]: 7.26 (*dd*, *J* = 8.3, *J* = 7.8, 2H, H_{meta}); 6.85 (*t*, *J* = 7.8, 1H, H_{para}); 6.79 (*d*, *J* = 8.3, 2H, H_{ortho}); 3.00 (*s*, 3H, NCH_3); 1.90 (*s*, 3H, CCH_3); 1.73 (*s*, 3H, CCH_3); ^{13}C NMR: 146.0 (*S*, CCl); 131.5 (*S*, NC); 130.0 (*Ssept*, ^2J = 6, CCH_3); 129.1 (*D*, *J* = 159, C_{meta}); 119.2 (*D*, *J* = 161, C_{para}); 113.7 (*D*, *J* = 155, C_{ortho}); 37.0 (*Q*, *J* = 137, NCH_3); 20.6 (*Qq*, *J* = 138, 4, CCH_3); 19.6 (*Qq*, *J* = 138, 4, CCH_3); MS (EI, $C_{11}H_{14}ClN$ (195.69)): m/z = 195 (94%, $M^{+\bullet}$); 180 (4%, $[M\text{-}Me]^+$); 160 (93%, $[M\text{-}Cl]^+$); 159 (7%, $[M\text{-}HCl]^{+\bullet}$).

N-(1-chloro-2-methylprop-1-enyl)-N,N-diisopropylamine (4e)

5.24 ml (56 mmols, 1.6 eq.) of phosphorus oxychloride, 250 µl (3.5 mmols, 0.1 eq.) of N,N-dimethylformamide, 10 ml of dichloromethane, 6 g (35 mmols) of 2-methyl-N,N-diisopropylpropionamide **1e**; reflux for 10h, then 5.4 ml (39 mmols, 1.1 eq.) of triethylamine; yield: 5.25 g (80%).

Example of a large scale preparation:

544.2 ml (895.2 g, 5.84 mols, 2 eq.) of freshly distilled phosphorus oxychloride, 4.5 ml (4.3 g, 0.059 mol, 0.02 eq.) of dimethylformamide and 1 L of dry dichloromethane were introduced in a 4 L three-necked, round-bottomed flask equiped with a mechanical stirrer, a pressure-equalising dropping funnel and a reflux condenser. A solution of 500 g (2.92 mols) of N,N-diisopropylisobutyramide **1e** in 400 mL of dry dichloromethane was then added dropwise. The resulting mixture was stirred overnight at room temperature. After cooling the flask in an ice-water bath, 446 mL (325 gr, 3.2 mols 1.1 eq) of triethylamine were slowly added. The cooling bath was removed and the mixture was allowed to warm up to room temperature. 500 ml of low boiling petroleum ether were then added and the mixture was vigorously stirred for 3 hours. After cooling to 4 °C overnight, the liquid phase was separated from the triethylamine hydrochloride precipitate via a cannula (the precipitate of triethylamine hydrochloride might also be removed by filtration under argon). The precipitate was washed with 3x300 mL of petroleum ether. The solvents were removed under reduced pressure and the residue was purified by distillation (89-90°C/15 mmHg) to give 400 g (72%) of the title compound as a reddish oil; RN 65785-45-7; IR (CH_2Cl_2): 1670 (C=CCl); ^{1}H NMR: 3.30 (*sept*, *J* = 6.5, 2H, NCH); 1.80 (*s*, 6H, $C(CH_3)_2$); 1.09 (*d*, *J* = 6.5, 12H, $CH(CH_3)_2$); ^{13}C NMR: 135.7 (*S*, CCl); 128.8 (*S*, $C(CH_3)_2$); 48.8 (*D*, *J* = 136, CH); 21.5 (*Qq*, *J* = 127, 4, $C(CH_3)_2$); 20.4 (*Qdq*, *J* = 126, 3, 5.1, $CH(CH_3)_2$); MS (EI, $C_{10}H_{20}ClN$ (189.72)): m/z = 189 (46%, $M^{+\bullet}$); 174 (4%, $[M\text{-}Me]^+$); 154 (100%, $[M\text{-}Cl]^+$); 146 (61%, $[M\text{-}^iPr]^+$).

(S)-1-(1-chloro-2-methylprop-1-enyl)-2-(tert-butoxycarbonylmethyl)pyrrolidine (4f)

3.6 ml (39 mmols, 2 eq.) of phosphorus oxychloride, 30 µl (0.39 mmol, 0.02 eq.) of N,N-dimethylformamide, 4.5 ml of dichloromethane, 5 g (19.5 mmols) of (S)-2-(tert-butoxycarbonylmethyl)-1-isobutyrylpyrrolidine **1f**, 15h at room temperature, then 5.5 ml (39 mmols, 2 eq.) of triethylamine; yield: 5.25 g (80%); RN 149554-68-7; pale yellow viscous liquid; Bp. 100°C (0.03 torr); IR (CH_2Cl_2): 1725 (C=O); 1675 (C=CCl); ^{1}H NMR: 4.25 (*m*, 1H, NCH); 3.95 (*d*, *J* = 4.6, 2H, OCH_2); 2.99-2.92 (*m*, 2H, NCH_2); 1.79 (*s*, 3H, CCH_3); 1.77 (*s*, 3H, CCH_3); 1.65-2.00 (*m*, 4H, $NCH_2\text{-}(CH_2)_2$); 1.20 (*s*, 9H, $C(CH_3)_3$); ^{13}C NMR: 178.4 (*S*, C=O); 135.6 (*S*, CCl); 127.5 (*Ssept*, ^2J = 6.5, CCH_3); 65.7 (*T*, *J* = 146, OCH_2); 58.9 (*D*, *J* = 139, NCH); 51.9 (*T*, *J* = 144, NCH_2); 38.7 (*S br.*, $C(CH_3)_3$); 28.1 (*T*, *J* = ~130, $NCH_2(CH_2)_2$); 27.1 (*Qsept*, *J* = 127, 4.7, $C(CH_3)_3$); 20.7 (*Q*, *J* = ~130, CCH_3); 20.3 (*Q*, *J* = ~130, CCH_3); MS (EI, $C_{14}H_{24}ClNO_2$ (273.8)): m/z = 273 (9%, $M^{+\bullet}$); 258 (trace, $[M\text{-}Me]^+$); 238 (16%, $[M\text{-}Cl]^+$); 189 (13%, [M-CO*t*-Bu]); 171 (5%, [M-*t*-BuCOOH]$^{+\bullet}$); 115 (100%, $[M\text{-}CH_2CO_2t\text{-}Bu]^+$).

(2R,5R)-1-(1-chloro-2-methylprop-1-enyl)-2,5-bis(methoxymethyl)pyrrolidine (4g)

3.05 ml (33 mmols, 2.5 eq.) of phosphorus oxychloride, 180 µl (2.6 mmols, 0.2 eq.) of N,N-dimethylformamide, 4.5 ml of dichloromethane, 3.07 g (13.4 mmols) of (2R,5R)-2,5-bis(methoxymethyl)-1-isobutyrylpyrrolidine **1g**, reflux for 18h, then 2.74 ml (19.7 mmols, 1.5 eq.) of triethylamine; yield: 2.2 g (66%); RN 149554-69-8; colourless liquid; Bp. 80°C (0.05 torr); IR (CH_2Cl_2): 1665 (C=CCl); ^{1}H NMR: 3.62-3.48 (*m*, 2H, NCH); 3.42-3.35 (*m*, 2H, OCH_2); 3.32 (*s*, 6H, OCH_3); 3.19 (*dd*, 2H, *J* = 9, 8, OCH_2); 2.10-1.65 (*m*, 4H, CH_2CH_2); 1.78 (*s*, 6H, $C(CH_3)_2$); ^{13}C NMR: 132.9 (*S*, CCl); 126.4 (*Ssept*, *J* = 6.4, $C(CH_3)_2$); 74.1 (*T*, *J* = 134, OCH_2); 59.2 (*Qt*, *J* = 141, 2.9, OCH_3); 57.5 (*D*, NCH); 27.2 (*T*, *J* = 132, CH_2CH_2); 20.6 (*Qq*, *J* = 128, 3.9, $C(CH_3)_2$); MS (EI, $C_{12}H_{22}ClNO_2$ (247.76)): m/z = 247 (9%, $M^{+\bullet}$); 232 (trace, $[M\text{-}Me]^+$); 212 (49%, $[M\text{-}Cl]^+$); 202 (100%, $[M\text{-}C_2H_5O]^+$).

N,N'-bis(1-chloro-2-methylprop-1-enyl)piperazine (4h)

26.8 ml (290 mmols, 16 eq.) of phosphorus oxychloride, 190 µl (2.5 mmols, 0.14 eq.) of N,N-dimethylformamide, 20 ml of dichloromethane, 8 g (36 mmols, 2 eq.) of N,N'-diisobutyrylpiperazine **1h**, reflux for 30h, removal of exces of $OPCl_3$ by distillation, then 7.5 ml (54 mmols, 3 eq.) of triethylamine; yield: 7.2 g (78%); RN 60180-60-1; white solid (recrystallised from dichloromethane/petroleum ether 1:6); IR (CH_2Cl_2): 1670 (C=CCl); ^{1}H NMR: 2.76 (*s br*, 8H, NCH_2); 1.84 (*s*, 6H, CCH_3); 1.76 (*s*, 6H, CCH_3); ^{13}C NMR: 138.0 (*S*, CCl); 125.0 (*Ssept*, *J* = 6.5, *C*CH_3); 49.8 (*T*, *J* = 138, NCH_2); 20.3 (*Qq*, *J* = 127, 4, *C*CH_3); 20.2 (*Qq*, *J* = 127, 4, *C*CH_3); MS (EI, $C_{12}H_{20}Cl_2N_2$ (263.21)): m/z = 262 (69%, $M^{+\bullet}$); 227 (70%, $[M\text{-}Cl]^+$).

N-[chloro(cyclohexylidene)methyl]-N,N-dimethylamine (4i)

7.2 ml (77 mmols, 1.1 eq.) of phosphorus oxychloride, 100 µl (1.3 mmols, 0.02 eq.) of N,N-dimethylformamide, 15 ml of dichloromethane, 10.9 g (70 mmols) of N,N-dimethylcyclohexanecarboxamide **1i**, 2 hours at room temperature, then 29.3 ml (210 mmols, 3 eq.) of triethylamine; yield: 9.2 g (76%); colourless liquid; Bp. 100°C (15 torr); IR (CH_2Cl_2): 1665 (C=CCl); ^{1}H NMR: 2.4 (*s*, 6H, NCH_3); 2.4-2.2 (*m*, 4H, CCH_2); 1.6-1.4 (*m*, 6H, $CH_2(CH_2)_3CH_2$); ^{13}C NMR: 138.1 (*S*, CCl); 130.9 (*S*, *C*CH_2); 42.9 (*Qq*, *J* = 135, 4.3, NCH_3); 30.6 (*T*, *J* = 128, *C*CH_2); 27.3 (*T*, *J* = 127, CCH_2CH_2); 26.6 (*Tquint*, *J* = 127, 4.2, $C(CH_2)_2CH_2$); MS (EI, $C_9H_{16}ClN$ (173.68)): m/z = 173 (60%, $M^{+\bullet}$); 158 (23%, $[M\text{-}Me]^+$); 138 (100%, $[M\text{-}Cl]^+$).

N-(1-chloro-2,2-diphenylvinyl)-N,N-dimethylamine (4j)

8.4 ml (91 mmols, 5 eq.) of phosphorus oxychloride, 310 µl (4 mmols, 0.23 eq.) of N,N-dimethylformamide, 10 ml of dichloromethane, 4.2 g (18 mmols) of N,N-dimethyl-2,2-diphenylpropionamide **1j** (commercial), reflux for 20h, removal of exces of $OPCl_3$ by distillation, then 2.5 ml (18 mmols) of triethylamine; yield: 1.9 g (40%); white solid (recrystallised from petroleum ether; Bp. 130°C (0.1 torr); IR (CH_2Cl_2): 1646 (C=CCl); ^{1}H NMR: 7.4-7.2 (*m*, 10H, C_6H_5); 2.55 (*s*, 6H, $N(CH_3)$); ^{13}C NMR: 143.9 (*S*, CCl); 141.0 (*S*, C=*C*C); 129.6 (*D*, *J* = 160, C_{meta}); 129.4 (*D*, *J* = 160, C_{ortho}); 128.0 (*S*, *C*Ph_2); 127.0 (*D*, *J* = 160, C_{para}); 42.4 (*Qq*, *J* = 136, 4, $N(CH_3)_2$); MS (EI, $C_{16}H_{16}ClN$ (257.76)): m/z = 257 (100%, $M^{+\bullet}$); 242 (trace, $[M\text{-}Me]^+$); 222 (65%, $[M\text{-}Cl]^+$).

N-(1-chloro-2-methylbuta-1,3-dienyl)-N,N-dimethylamine (4k)

7.2 ml (77 mmols, 1.1 eq.) of phosphorus oxychloride, 100 µl (1.3 mmols, 0.02 eq.) of N,N-dimethylformamide, 10 ml of dichloromethane, 8.9 g (70 mmols) of N,N-dimethyltiglamide **1k**, 3 hours at room temperature, then 29.3 ml (210 mmols, 3 eq.) of triethylamine; yield: 8.2 g (80%) (mixture of E and Z isomers); RN (E) 72184-21-9; (Z) 72184-22-6; colourless liquid; Bp. 55°C (15 torr); IR (CH_2Cl_2)[15]: 1820 (H_2C=CH); 1630 (C=CCl); 1000 (H_2C=CH); 980 (H_2C=CH); 920 (H_2C=CH); ^{1}H NMR[15] (Major): 7.03 (*dd*, *J* = 17.8, 10.9, 1H, CH); 5.2 (*ddd*, *J* = 17.8, 1.4, 0.6, 1H, CH*H*); 5.05 (*dd*, *J* = 10.9, 1.4, 1H, C*H*H); 2.44 (*s*, 6H, $N(CH_3)_2$); 1.86 (*s*, 3H, CCH_3); Minor: 6.92 (*dd*, *J* = 17.5, 10.9, 1H, CH); 5.26 (*ddd*, *J* = 17.5, 1.5, 0.6, 1H, CH*H*); 5.16 (*dd*, *J* = 10.7, 1.5, 1H, C*H*H); 2.45 (*s*, 6H, $N(CH_3)_2$); 1.91 (*s*, 3H, CCH_3); ^{13}C NMR (Major): 146.2 (*S*, CCl); 134.3 (*Dqd*, *J* = 159, 3.7, 3.7, CH); 126.2 (*S*, *C*CH_3); 113.4 (*DD*, *J* = 159, 155, CH_2); 42.7 (*Qq*, *J* = 136, 5.2, $N(CH_3)_2$); 13.9 (*Qd*, *J* = 128, 4.4, C*C*H_3); Minor: 143.9 (*S*, CCl); 135.5 (*Dqd*, *J* = 157, 3.6, 3.6, CH); 126.1 (*S*, *C*CH_3); 116.0 (*DD*, *J* = 160, 155, CH_2); 42.3 (*Qq*, *J* = 136, 4.7, $N(CH_3)_2$); 13.5 (*Qd*, *J* = 128, 4.5, CCH_3); MS[15] (EI, $C_7H_{12}ClN$ (145.63)): m/z = 145 (46%, $M^{+\bullet}$); 130 (100%, $[M\text{-}Me]^+$); 110 (58%, $[M\text{-}Cl]^+$).

4-(1-chloro-2-methylbuta-1,3-dienyl)morpholine (4l)

6.5 ml (70 mmols) of phosphorus oxychloride, 100 µl (1.3 mmols, 0.02 eq.) of N,N-dimethylformamide, 8 ml of dichloromethane, 5.92 g (70 mmols) of 4-(2-methylbut-2-enoyl)morpholine **1l**, 8 hours at room temperature, then 10 ml (72 mmols, 1.02 eq.) of triethylamine; yield: 4.8 g (73%) (mixture of E and Z isomers); Bp. 33°C (0.03 torr); IR (CH_2Cl_2): 1825 (H_2C=CH); 1625 (C=CCl); 990 (H_2C=CH); 920 (H_2C=CH); ^{1}H NMR (Major): 7.10 (*dd*, *J* = 17.8, 10.9, 1H, =CH); 5.25 (*dd*, *J* = 17.8, 1.2, 1H, *H*CH=); 5.11 (*dd*, *J* = 10.9, 1.2, 1H, HC*H*=); 3.79 (*dd*, *J* = 8.0, 4H, OCH_2); 2.82-2.70 (*m*, 4H, NCH_2); 1.90 (*s*, 3 H, CH_3); Minor: 6.94 (*dd*, *J* = 17.4, 10.9, 1H, CH); 5.33 (*dd*, *J* = 17.4, 1.3, 1H, *H*CH=); 5.24 (*dd*, *J* = 10.9, 1.3, 1H, HC*H*=); 3.79 (*dd*, *J* = 8.0, 4H, OCH_2); 2.82-2.70 (*m*, 4H, NCH_2); 1.97 (*s*, 3H, CH_3); ^{13}C NMR (Major): 143.2 (*S*, CCl); 134.0 (*Dqd*, *J* = 158, 3.7, 3.7, =CH); 127.2 (*S*, *C*CH_3); 114.0 (*DD*, *J* = 159, 155, H_2C=); 66.4 (*T*, *J* = 143, OCH_2); 50.5 (*T*, *J* = 136, NCH_2); 14.2 (*Qd*, *J* = 128, 4.5, CH_3); Minor: 140.9 (*S*, CCl); 135.1 (*Dqd*, *J* = 157, 3.6, 3.6, CH=); 125.5 (*S*, *C*CH_3); 116.5 (*DD*, *J* = 160, 155, H_2C=); 66.4 (*T*, *J* = 143, OCH_2); 50.2 (*T*, *J* = 135, NCH_2); 14.1 (*Qd*, *J* = 128, 4.5, CH_3); MS (EI, $C_9H_{14}ClNO$ (187.66)): m/z = 187 (100%, $M^{+\bullet}$); 172 (35%, $[M\text{-}Me]^+$); 152 (86%, $[M\text{-}Cl]^+$); 143 (3%, $[M\text{-}C_2H_4O]^{+\bullet}$); 142 (9%, $[M\text{-}C_2H_5O]^+$).

N-(1-chloro-2-methylbuta-1,3-dienyl)-N-methyl-N-phenylamine (4m)

13 ml (140 mmols, 2 eq.) of phosphorus oxychloride, 200 µl (2.6 mmols, 0.04 eq.) of N,N-dimethylformamide, 10 ml of dichloromethane, 13.23 g (70 mmols) of N,2-dimethyl-N-phenylbut-2-enamide **1m**, 12 hours at room temperature, then 19.5 ml (140 mmols, 2 eq.) of triethylamine; yield: 11.4 g (82%) (mixture of E and Z isomers); pale yellow liquid; Bp. 70°C (0.2 torr); IR (CH_2Cl_2): 1825 (H_2C=CH); 1630 (C=CCl); ^{1}H NMR (Major): 7.24 (*dd*, *J* = 8.7, 7.3, 2H, H_{meta}); 6.89 (*t*, *J* = 7.3, 1H, H_{para}); 6.79 (*d*, *J* = 8.7, 2H, H_{ortho}); 6.66 (*dd*, *J* = 17.6, 10.9, 1H, =CH); 5.32 (*dd*, *J* = 17.6, 0.95, 1H, *H*CH=); 3.02 (*s*, 3H, NCH_3); 2.01 (*s*, 3H, CCH_3); Minor: 7.24 (*dd*, *J* = 8.7, 7.3, 2H, H_{meta}); 7.01 (*dd*, *J* = 17.4, 10.9, 1H, =CH); 6.89 (*t*, *J* = 7.3, 1H, H_{para}); 6.79 (*d*, *J* = 8.7, 2H, H_{ortho}); 5.40 (*dd*, *J* = 17.4, 1.2, 1H, *H*CH=); 5.31 (*dd*, *J* = 10.9, 1.2, 1H, HC*H*=); 3.03 (*s*, 3H, NCH_3); 1.82 (*s*, 3H, CCH_3); ^{13}C NMR (mixture of E/Z isomers): 146.1 and 145.7 (*S*, CCl); 137.0 (*S*, N*C*C_5H_5); 134.7 and 133.3 (*Dqd*, *J* = 158, 3.5, 3.5, H*C*=CH_2); 131.5 and 129.9 (*S*, *C*CH_3); 129.05 and 129.01 (*D*, *J* = 159, C_{meta}); 119.8 and 119.6 (*D*, *J* = 163, C_{para}); 117.5 and 115.9 (*T*, *J* = 160, CH_2); 114.3 and 114.1 (*D*, *J* = 156, C_{ortho}); 37.6 and 37.1 (*Q*, *J* = 138, NCH_3); 14.4 and 13.6 (*Qd*, *J* = 128, 4.5, *C*CH_3); MS (EI, $C_{12}H_{14}ClN$ (207.7)): m/z = 207 (100%, $M^{+\bullet}$); 192 (51%, $[M\text{-}Me]^+$); 172 (71%, $[M\text{-}Cl]^+$).

5-chloro-1,4-dimethyl-2,3-dihydro-1H-pyrrole (4n)

3.26 ml (35 mmols) of phosphorus oxychloride, 50 µl (0.7 mmol, 0.02 eq.) of N,N-dimethylformamide, 7 ml of dichloromethane, 3.96 g (35 mmols) of 1,3-dimethyl-2-pyrrolidone **1n**, 12 hours at room temperature, then the solution of α-chloromethyleneiminium was added to 44.6 ml (320 mmols, 9 eq.) of triethylamine; yield: 1.46 g (60%) (the product was contaminated with 5% of triethylamine); colourless liquid; Bp. 45°C (15 torr); IR (CH_2Cl_2): 1681 (C=CCl); ^{1}H NMR: 3.07 (*t*, *J* = 8.7, 2H, NCH_2); 2.52 (*s*, 3H, NCH_3); 2.37 (*t*, *J* = 8.7, 2H, NCH_2CH_2); 1.69 (*t*, *J* = 1.2, 3H, CCH_3); ^{13}C NMR: 133.8 (*S*, CCl); 107.8 (*S*, *C*CH_3); 54.2 (*Tqt*, *J* = 139, 4.8, 2.4, NCH_2); 39.5 (*Q*, *J* = 136, NCH_3); 32.4 (*Tq*, *J* = 132, 3.5, NCH_2CH_2); 12.9 (*Q*, *J* = 127, CH_3C); MS (EI, $C_6H_{10}ClN$ (131.6)): m/z = 131 (60%, $M^{+\bullet}$); 130 (100%, $[M\text{-}H]^+$); 116 (32%, $[M\text{-}Me]^+$); 96 (6%, $[M\text{-}Cl]^+$); 95 (18%, $[M\text{-}HCl]^{+\bullet}$).

7-chloro-1,6-dimethyl-2,3,4,5-tetrahydro-1H-azepine (4o)

4.85 ml (52 mmols, 1.1 eq.) of phosphorus oxychloride, 70 µl (0.9 mmol, 0.02 eq.) of N,N-dimethylformamide, 10 ml of dichloromethane, 5.3 g (47 mmols) of 1,3-dimethylcaprolactame **1o**, 12 hours at room temperature, then 19.5 ml (140 mmols, 3 eq.) of triethylamine; yield: 6.1 g (81%); colourless liquid; Bp. 81°C (15 torr); IR (CH_2Cl_2): 1639 (C=CCl); ^{1}H NMR: 2.95 (*dd*, *J* = 5.8, 2H, NCH_2); 2.64 (*s*, 3H, NCH_3); 2.14 (*dd*, *J* = 5.7, 5.7, 2H, $CMeCH_2$); 1.74 (*s*, 3H, CCH_3); 1.68-1.59 (*m*, 2H, CH_2); 1.51-1.42 (*m*, 2H, CH_2); ^{13}C NMR: 137.8 (*S*, CCl); 119.1 (*Ssept*, *J* = 6.4, *C*CH_3); 53.6 (*Tq*, *J* = 135, 3.3, NCH_2); 38.4 (*Qt*, *J* = 135, 3.3, NCH_3); 33.4 (*Tsept*, *J* = 126, 4, 4, $MeCCH_2$); 27.7 (*Tm*, *J* = 127, NCH_2CH_2); 23.3 (*Tquint*, *J* = 127, 4.8, $MeCCH_2CH_2$); MS (EI, $C_8H_{14}ClN$ (159.65)): m/z = 159 (100%, $M^{+\bullet}$); 144 (62%, $[M\text{-}Me]^+$); 131 (9%, $[M\text{-}C_2H_4]^{+\bullet}$); 130 (53%, $[M\text{-}C_2H_5]^+$); 124 (91%, $[M\text{-}Cl]^+$); 116 (32%, $[M\text{-}C_2H_5N]^{\cdot+}$).

Synthesis α-bromoenamines

General procedure

Phosphorus oxybromide, N,N-dimethylformamide and dry dichloromethane were introduced in a three-necked, round-bottomed flask equiped with a magnetic stirring bar, a pressure-equalising dropping funnel and a reflux condenser. After cooling the flask in an ice-water bath, a solution of the amide in dry dichloromethane was dropwise added. The resulting mixture was stirred overnight at room temperature (the reaction was monitored by ^{1}H NMR). The flask was again cooled at 0°C and triethylamine was slowly added. The cooling bath was removed and the mixture was vigorously stirred for 3 hours at room temperature (the reaction was monitored by ^{1}H NMR). Low boiling petroleum ether was then added and the mixture was allowed to stand overnight at 4°C. The precipitate of triethylamine hydrochloride was removed by filtration under argon. The precipitate was washed with petroleum ether. The solvents were removed under reduced pressure and the residue was purified by distillation.

N-(1-bromo-2-methylprop-1-enyl)-N,N-dimethylamine (9a)

100 g (350 mmols, 1.2 eq.) of phosphorus oxybromide, 450 µl (5.81 mmols, 0.02 eq.) of N,N-dimethylformamide, 100 ml of dichloromethane, 37.5 ml (33.5 g, 290 mmols) of N,N,2-trimethylpropionamide **1a**, overnight at room temperature, then 48.5 ml (350 mmols, 1.2 eq.) of triethylamine; yield: 42.5 g (82%); RN 73630-93-0; colourless liquid; Bp. 35°C (15 torr); IR (CH_2Cl_2): 1675 (C=CBr); ^{1}H NMR: 2.31 (*s*, 6H, $N(CH_3)_2$); 1.80 (*s*, 6H, $C(CH_3)_2$); ^{13}C NMR: 140.4 (*Ssept*, *J* = 6.7, CBr); 126 (*Ssept*, *J* =

6.5, $C(CH_3)_2$); 43.7 (*Qq*, *J* = 136, 4.4, $N(CH_3)_2$); 21.6 (*Qq*, *J* = 128, 4.0, $C(CH_3)_2$); MS (EI, $C_6H_{12}BrN$ (178.07)): **m/z = 177** (22%, $M^{+\bullet}$); 162 (trace, **[M-Me]$^+$**); **98 (100%, [M-Br]$^+$)**.

1-(1-bromo-2-methylprop-1-enyl)pyrrolidine (9b)

25 g (87 mmols, 1.25 eq.) of **phosphorus oxybromide**, 100 µl (1.3 mmols, 0.02 eq.) of N,N-dimethylformamide, **20 ml of dichloromethane**, 10 g (47 mmols) of 1-isobutyrylpyrrolidine **1b**, 1 hour at 0°C, then 24 ml (173 mmols, 2.5 eq.) of **triethylamine**; yield: 8.7 g (61%); colourless liquid; **Bp. 42°C** (0.3 torr); IR (CH_2Cl_2): 1675 (C=CBr); ^1H NMR: 2.77 (*m*, 4H, NCH_2); 1.87-1.82 (*m*, 4H, NCH_2CH_2); 1.78 (*s*, 6H, $C(CH_3)_2$); ^{13}C NMR: 135.5 (*S*, CBr); 127.2 (*Ssept*, *J* = 6.4, $C(CH_3)_2$); 51.7 (*T*, *J* = 140, NCH_2); 24.7 (*T*, *J* = 132, NCH_2CH_2); 21.8 (*Qq*, *J* = 124, 4, $C(CH_3)_2$); MS (EI, $C_8H_{14}BrN$ (204.1)): m/z = 203 (16%, $M^{+\bullet}$); 202 (5%, $[M-H]^+$); 124 (100%, $[M-Br]^+$).

4-(1-bromo-2-methylprop-1-enyl)morpholine (9c)

25 g (87.2 mmols, 1.25 eq.) of phosphorus oxybromide, 100 µl (1.3 mmols, 0.02 eq.) of N,N-dimethylformamide, 30 ml of dichloromethane, 11 g (70 mmols) of 4-isobutyrylmorpholine **1c**, 12 hours at room temperature, then 20 ml (143 mmols, 2 eq.) of triethylamine; yield: 11.3 g (74%); pale yellow liquid; Bp. 43°C (15 torr); IR (CH_2Cl_2): 1676 (C=CBr); ^1H NMR: 3.8-3.7 (*m*, 4H, NCH_2); 2.62-2.52 (*m*, 4H, OCH_2); 1.82 (*s*, 6H, $C(CH_3)_2$); ^{13}C NMR: 135.6 (*S*, CBr); 127.6 (*Ssept*, *J* = 6.4, $C(CH_3)_2$); 65.8 (*T*, *J* = 129, OCH_2); 51.1 (*T*, *J* = 136, NCH_2); 21.7 (*Q*, *J* = 127, $C(CH_3)_2$); MS (EI, $C_8H_{14}BrNO$ (220.1)): m/z = 219 (10%, $M^{+\bullet}$); 218 (8%, $[M-H]^+$); 140 (100%, $[M-Br]^+$).

N-(1-bromo-2-methylprop-1-enyl)-N,N-diisopropylamine (9d)

25 g (87.2 mmols, 1.6 eq.) of phosphorus oxybromide, 420 µl (5.4 mmols, 0.1 eq.) of N,N-dimethylformamide, 30 ml of dichloromethane, 9.32 g (54.4 mmols) of 2-methyl-N,N-diisopropylpropionamide **1e**, reflux 3 h, then 16.7 ml (120 mmols, 2.2 eq.) of triethylamine; yield: 9.4 g (74%) ; colourless liquid; Bp. 45°C (0.7 torr); IR (CH_2Cl_2): 2020 ($C=C=N^+$); 1655 (C=CBr); ^1H NMR: 3.32 (*sept*, *J* = 6.5, 2H, NCH); 1.72 (*s*, 6H, $C(CH_3)_2$); 1.06 (*d*, *J* = 6.5, 12H, $CH(CH_3)_2$); ^{13}C NMR: 135.2 (*S*, CBr); 130.3 (*S*, $C(CH_3)_2$); 50.2 (*D*, *J* = 145, $CH(CH_3)_2$); 23.2 (*Q*, *J* = 128, $C(CH_3)_2$); 20.2 (*Q*, *J* = 130, $CH(CH_3)_2$); MS (EI, $C_{10}H_{20}BrN$ (234.17)): m/z = 233 (13%, $M^{+\bullet}$); 232 (7%, $[M-H]^+$); 218 ($[M-Me]^+$); 154 (100%, $[M-Br]^+$).

N-[bromo(cyclohexylidene)methyl]-N,N-dimethylamine (9e)

25 g (87.2 mmols, 1.1 eq.) of **phosphorus oxybromide**, 100 µl (1.3 mmols, 0.02 eq.) of N,N-dimethylformamide, **30 ml of dichloromethane**, 11.9 g (79 mmols) of N,N-dimethylcyclohexanecarboxamide **1i**, 12 hours at room temperature, then 45 ml (320 mmols, 4 eq.) of triethylamine; yield: 10.7 g (62%); pale yellow liquid; Bp. 41°C (0.05 torr); IR (CH_2Cl_2): 1666 (C=CBr); ^1H NMR: 2.3 (*s*, 6H, $N(CH_3)_2$); 2.35-2.25 (*m*, 4H, CCH_2); 1.70-1.45 (*m*, 6H, $CCH_2(CH_2)_3$); ^{13}C NMR: 138.1 (*Ssept*, *J* = 6.5, CBr); 132.7 (*S*, CCH_2); 41.8 (*Qq*, *J* = 135, 4.2, $N(CH_3)_2$); 32.2 (*T*, *J* = 125, CCH_2); 27.2 (*T*, *J* = 127, CCH_2CH_2); 26.5 (*Tquint*, *J* = 127, 4.7, $C(CH_2)_2CH_2$); MS (EI, $C_9H_{16}BrN$ (218.13)): m/z = 217 (20%, $M^{+\bullet}$); 138 (100%, $[M-Br]^+$).

N-(1-bromo-2-methylbuta-1,3-dienyl)-N,N-dimethylamine (9f)

12.5 g (43.6 mmols, 1.1 eq.) of phosphorus oxybromide, 55 µl (0.7 mmol, 0.02 eq.) of N,N-dimethylformamide, 15 ml of dichloromethane, 5 g (39.4 mmols) of N,N-dimethyltiglamide **1k**, 2 hours at 0°C, then 10 ml (72 mmols, 1.8 eq.) of triethylamine; yield: 1.8 g (24%); pale orange liquid; Bp. 30°C (0.1 torr); IR (CH_2Cl_2): 1825 ($H_2C=C$); 1630 (C=CBr); ^1H NMR: 7.15 (*dd*, *J* = 10.9, 17.6, 1H, $CH_2=CH$); 5.29 (*dd*, *J* = 17.6, 3.1, 1H, *H*CH=CH); 5.15 (*d*, *J* = 10.9, 1H, HC*H*=CH); 2.36 (*s*, 6H, $N(CH_3)_2$); 1.90 (*s*, 3H, CCH_3); ^{13}C NMR: 145.1 (*S*, CBr); 134.9 (*D*, *J* = 159, $H_2C=CH$); 127.4 (*S*, CCH_3); 114.6 (*DD*, *J* = 155, 157, $H_2C=CH$); 43.5 (*Qq*, *J* = 136, 4.4, $N(CH_3)_2$); 15.6 (*Qd*, *J* = 128, 4.4, CCH_3); MS (EI, $C_7H_{12}BrN$ (190.08)): m/z = 189 (68%, $M^{+\bullet}$); 174 (32%, $[M-Me]^+$); 110 (100%, $[M-Br]^+$).

Acknowledgements

This work was supported by the "Fonds National de la Recherche Scientifique" (fellowship to LP), Ciba-Geigy (Basel, now Novartis, fellowship to IGK), I.R.S.I.A. (fellowship to MH, PB), the Ministère de l'Education et de la Recherche Scientifique de la Communauté française de Belgique (Action Concertée 96/01-197) and the Fonds de la Recherche Fondamentale Collective. (convention 2.4587.96).

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