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ON THE DIRECT METALATION OF ISOPRENE

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Isoprene has been metalated in tetrahydrofuran with an excess of sterically hindered potassium dialkylamides, prepared by combining equimolar amounts of the corresponding lithium amide and potassium *tert*-butoxide Subsequent reaction with oxirane, alkyl bromides, and pivaldehyde gave the expected coupling products in reasonable yields Coupling with $(CH_3)_2CHCH_2CH{=}O$ and $(CH_3)_2C{=}CHCH{=}O$ afforded the bark beetle pheromones (±)-ipsenol and (±)-ipsdienol in low yields

Introduction

Several articles deal with the metalation of simple olefins with strongly basic reagents *E*-, *Z*-2-Butene, and 1-butene have been deprotonated with BuLi TMEDA to give crotyllithium,[1] while a number of allylic anions have been generated with the BuLi *t*-BuOK[2-4] system [5-8] The metalation of isobutene can be achieved with BuLi TMEDA[9,10] as well as with BuLi *t*-BuOK [11,12] Whereas in the presence of tetrahydrofuran (THF) or TMEDA 1,3-dienes undergo rapid addition,[13] 1,4-dienes (C=C-CH-C=C) are readily metalated with BuLi in THF [14-16] For the metalation of 1,3-dienes (C=C-C=C-CH) BuLi *t*-BuOK is the appropriate base [13,17-20]

Bates *et al* [13,20] metalated 2,3-dimethyl-butadiene (**1**) with the couple BuLi *t*-BuOK in an apolar solvent (Scheme I) Envisaging the intermediate occurrence of monoanion **2** in the dimetalation of **1**, they expected *that isoprene could be metalated by this system to the elusive 2-vinylallyl anion* **5a** [13] However, they observed addition of the base to give (after hydrolysis) 2-methyl-1-octene (**6a**) and 2-methyl-2-octene (**6b**) [13]

The addition of organolithium compounds to olefins is a well-known reaction, which has been applied as initiation in the polymerization of isoprene [21-23] Addition of allyl Grignard reagents to isoprene is a crucial reaction in the synthesis of natural terpenoids [24] Also diethylamine in the presence of sodium naphthalenide,[25,26]

Partly published Klusener, P A A, Hommes, H, Verkruijsse, H D, Brandsma, L *J Chem Soc, Chem Commun* **1985**, 1677 and lithium diethylamide[27] are reported to add to the diene system of isoprene Treatment of isoprene with the radical anion sodium naphthalenide only gives rise to dimerization, giving mainly $[Me_2C=CH-CH_2]_2$ [28]

Scheme I[13]

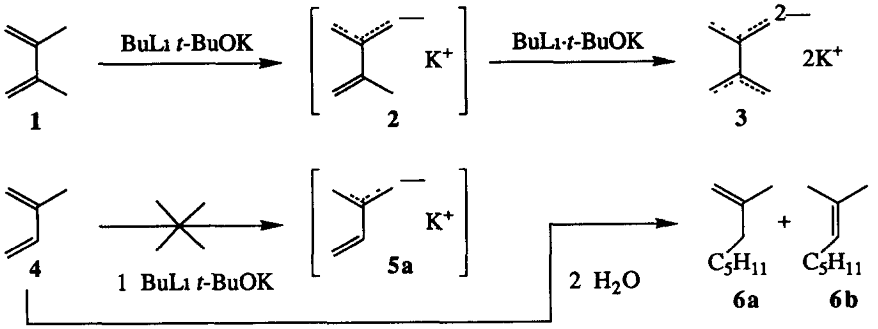
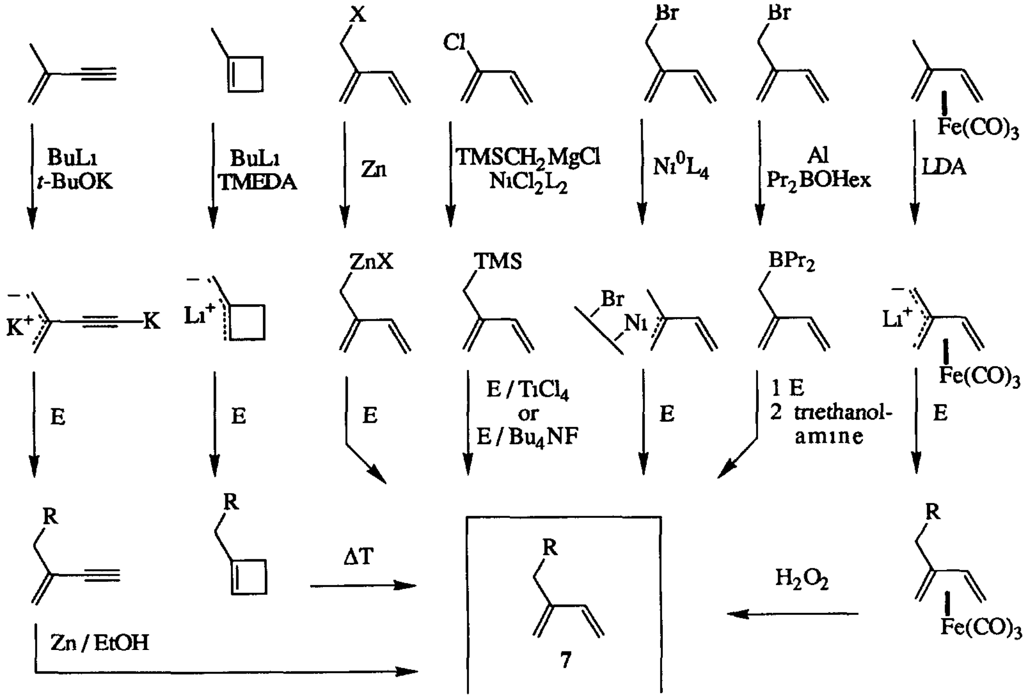


Figure I. Isoprene C-5 Synthons[29-39]

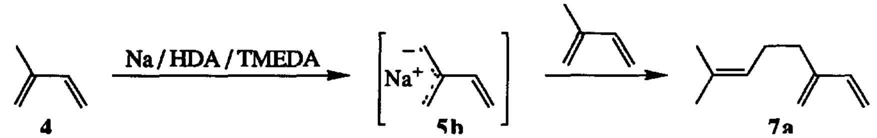


Since the chance of a successful direct metalation of isoprene to afford a building block for the synthesis of terpenoids was considered low, several alternative synthetic routes[29] and "isoprene C-5 synthons" have been developed [29-39] (See Figure I)

In 1977 Takabe *et al*[40] reported the reaction of isoprene with sodium in the presence of diisopropylamine and TMEDA and obtained myrcene (**7a**) in 10% yield (See Scheme II). They assumed that the methyl group of isoprene initially was metalated to form the isoprene-sodium compound (**5b**), which subsequently had reacted with a second molecule of isoprene

This result,[40] and the unsuccessful attempts of Bates *et al*[13,20] led us to investigate the metalation of isoprene with strongly basic non-nucleophilic reagents[41]

Scheme II[40]



Results and Discussion

Metalation of Isoprene. Our experiments were based upon the consideration that a sterically hindered base with a sufficiently high thermodynamic as well as kinetic basicity would be required An extensively exploited property of bases such as lithium diisopropylamide (LDA) is their decreased tendency to add across multiple bond systems[42-44] Reaction at *ca* −70°C of isoprene with a 100% excess of LDA in THF, followed by addition of a corresponding excess of 1-bromoheptane and allowing the temperature to rise to 0°C gave no trace of the desired alkylation product (**7b**), while oligomerization had occurred to a slight extent only The low yield of the desired product thus may largely ascribed to an unfavourable deprotonation equilibrium (Scheme III) Since the pK_a value of secondary amines increases with the bulkyness of the substituents,[45-51] we expected metalation of isoprene with a base like lithium 2,2,6,6-tetramethylpiperidide (LiTMP, derived from the readily available[52] amine with pK_a 37 3[47,48] or 37 0[51]) to be more successful than with LDA, being derived from diisopropylamine with the lower pK_a value 35 7[47,48] or 34 4[51] However, interaction between LiTMP and isoprene in THF, followed by addition of 1-bromoheptane and raising the temperature to 35°C, gave only 1-heptene (as a result of dehydrohalogenation) and unconverted bromoheptane

Lithium amides can be converted into the corresponding potassium amides by addition of potassium *tert*-butoxide,[53-54] which increases the reactivity as well as the basicity[50,51,53-57] Applying this knowledge[58] we attained a significant improvement (42% yield of **7b**) by carrying out the metalation of isoprene with a 50% excess of potassium diisopropylamide (KDA) — prepared *in situ* by adding HDA to the couple BuLi *t*-BuOK in THF —, other conditions being similar to the preceding experiments Also in this case dehydrohalogenation of bromoheptane occurred When the functionalization was carried out with oxirane, the expected alcohol (**7c**) was obtained in *ca* 60% yield The reaction with 50% excess of *isoprene* gave the same result. Reaction of isoprene with *one molar* equivalent of KDA and subsequent functionalization with oxirane resulted in a yield of 50% Since these results suggest a deprotonating equilibrium with K = 1, we repeated the experiments with larger excessses of isoprene or of KDA. However, no higher yields were obtained

Scheme III

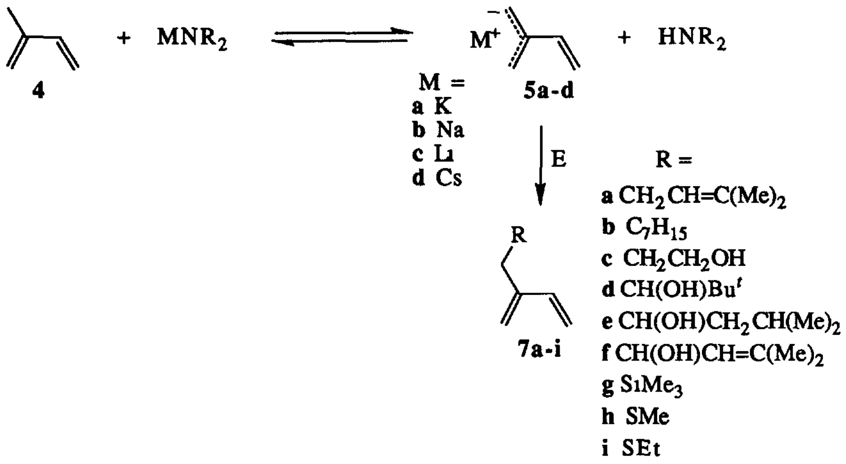


Table I. Variation of the Reaction Conditions.
Metalation of Isoprene with KDA and Subsequent Functionalization with Oxirane

KDA[a]	isoprene[a]	solvent[b]	time (min)	temperature (°C)	yield (%)[c]
1	1	THF/hexane	30	–70	50
1	1 5	"	"	"	60[d,e]
1.5	1	"	"	"	60[d]
1	4	"	"	"	"
2	1	"	"	"	"
1 5	1	"	"	–40	"
1 5	1	"	60	–70	"
1	1 5	"	1	"	"
1 5	1	THF/hexane/TMEDA	30	"	"
1	2	hexane/1 5 eq THF[f]	"	–70	"
1	1 5	hexane/TMEDA	"	–20	52

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[a] Amounts are related to 0 10 mol of KDA [b] Per 0 10 mol of KDA 62 mL of hexane and 62 mL of THF and/or 0 10 mol of TMEDA was used [c] Yields of 7c after subsequent addition of a solution of an excess of oxirane in THF, aqueous workup and distillation [d] Variable yields of 57-62% [e] Slow addition (30 min) of the THF/oxirane solution afforded a similar yield [f] Only 10 6 g of THF (0 15 mol) was present during the metalation

Table II. Variation of the Base. Metalation of Isoprene and Subsequent Functionalization with Oxirane

amide[h]	pK$_a$[a]	KNR$_2$[b] ·	isoprene[b]	solvent[c]	time (min)	temp (°C)	yield (%)[d]
KNEt$_2$	31 7[51]	1 5	1	THF	30	−70	10
KDA[e]	35.7[48], 34 4[51]	1 5	1	THF	1	−70	60
KN(c-C$_6$H$_{11}$)$_2$[59]	35.7[48], 34 7[51]	1	1	THF	30	−70	60
8a	*ca* 36[f]	2	1	TMEDA	10	−25	41[g]
KTMP (**8b**)	37 3[48], 37 0[51]	2	1	THF	20	−70	70
KTMP		2	1	THF	120	−70	82
8c	38 3[48]	1	1 5	THF	115	−50	15[g]
8c		1	2	TMEDA	10	−25	54
8d		1 5	1	THF	90	−70	33
8d		1	2	TMEDA	10	−25	45[g]
8d		1 5	1	THF/TMEDA	30	−70	60
8e	39 1[48]	1	1 5	THF	65	−70	14[g]
8e		1 5	1	THF	45	−70	27[g]
8e		1	2	THF/TMEDA	120	−90→−50	22[g]
8e		1 5	1	THF/TMEDA	180	−90→−70	36[g]
8e		1	1 5	THF/TMEDA	120	−70→−30	46[g]
8e		1	2 5	TMEDA	30	−25	47[g]
8e		1	2	TMEDA	5	−40→−20	64[g]
8e		1 5	1	TMEDA	5	−40→−20	36[g]
8f	> 40[f]	1	1 5	THF	30	−65	28[g]
8f		2	1 5	TMEDA	5	−40→−20	55[g]

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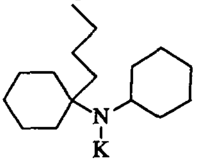
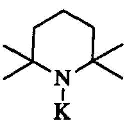
[a] pK$_a$ values of the conjugated amines according to Fraser[48] and/or Ahlbrecht[51] measured with the corresponding *lithium* amides, the pK$_a$ values measured with *potassium* amides are higher[60] pK$_a$(K) = 0 77 pK$_a$(Li) + 15 3 [51] [b] Amounts are related to 0 050 mol of KNR$_2$ [c] Hexane (originating from the used solution of BuLi in hexane) was present too, thus in the case of THF a 1 1 mixture of THF/hexane was applied and in the case of TMEDA 2 molar equivalents related to the base were used [d] Yields of **7c** after subsequent addition of a solution of an excess of oxirane in THF, aqueous workup and distillation [e] More experimental data in Table I [f] Estimated pK$_a$ values of the conjugated amines, based upon the values reported by Fraser[48] and Ahlbrecht [51] [g] A considerable amount of viscous polymeric residue remained after distillation [h] Structures


8a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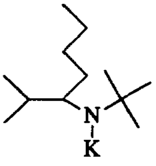
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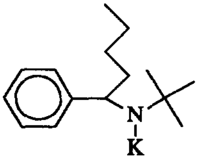
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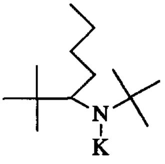
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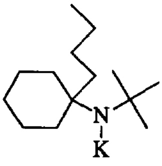
8f

Significantly better results were obtained by using KTMP, which has a greater thermodynamic basicity than KDA [51] Under conditions similar to those in the case of KDA, the reaction with oxirane resulted in yields of the corresponding alcohol up to 80%.(See Table I) It should be pointed out, however, that longer reaction times were necessary for the metalation with this base As expected from the lower pK_a value of diethylamine, a similar experiment with $KNEt_2$ gave the hydroxyalkylation product in 10% yield only

Extrapolation of the results obtained in the series $KNEt_2$ < KDA < KTMP led to the expectation that the use of more bulky amides would lead to a further improvement of the yields after reaction with oxirane However, the yields were even lower than in the reactions with KDA Although these bases are stronger than KDA or KTMP in a thermodynamic sense, the greater steric hindrance makes them less efficient in deprotonations, so that longer reaction times are necessary Unfortunately, oligomerization of isoprene then becomes an important side process

Fraser and Mansour[50] found that the rate of metalation of triphenylmethane with sterically hindered bases (*e g* LiTMP and LDA) in THF were dramatically increased by adding TMEDA We observed a similar accelerating effect upon combining the bases **8d** and **8e** with TMEDA, but the results remained less satisfactory

Table III. Functionalization of metalated isoprene

base[a]	electrophile	product	yield (%)[c]
KDA	$Me_2C{=}CHCH_2Br$[b]	myrcene (**7a**)	30
KDA	1-chloroheptane[b]	**7b**	40
KDA	1-bromoheptane[b]	**7b**	42
KTMP	1-bromoheptane[b]	**7b**	67
KDA	oxirane[b]	**7c**	60
KTMP	oxirane[b]	**7c**	72
KDA	*t*-BuCHO[b]	**7d**	39
KDA	Me_2CHCH_2CHO[b]	ipsenol (**7e**)	19
KDA	$Me_2C{=}CHCHO$[b]	ipsdienol (**7f**)	21
KDA	TMSCl[d]	**7g**	19
KDA	MeSSMe[d]	**7h**	20[e]
KDA	EtSSEt[d]	**7i**	14[e]

[a] Metalation conditions 100% excess of isoprene, 30 min at -70°C in THF, KDA experiments were carried out on 0 10 molar scale, KTMP experiments on 0 05 molar scale [b] The electrophile was added at -70°C [c] Yields after distillation [d] The reaction mixture was poured into a solution of the electrophile in THF at -90°C [e] Chemical yield, the distilled product contained also $(i\text{-}Pr)_2NSR$ and unconverted RSSR

than those obtained with KTMP, oligomerization of isoprene being the principal side reaction Although combinations of **8d-f** with TMEDA in hexane at *ca* –30°C reacted faster with isoprene than they did at –70°C in THF, the yields were lower than that obtained with KTMP in THF-hexane mixtures. Under these conditions oligomerization appeared to be more serious than at low temperatures in THF

Functionalization of Metalated Isoprene. Functionalization experiments with isoprene — metalated under the optimized conditions with KDA and KTMP— were carried out (Table III) The natural products, myrcene, ipsenol, and ipsdienol, the latter two compounds being pheromones of the bark beetle,[29,61] were obtained by direct functionalization of isoprene with prenyl bromide, isovalderaldehyde, and 3-methyl-2-butenal, respectively Yields of the expected derivatives were moderate to low*

Effect of the Metal Counter-ion on the Metalation of Isoprene. The yields of the functionalization products are not as high as those obtained with oxirane This can be ascribed to elimination of hydrogen halides (from alkyl halides), formation of enolates of the carbonyl compounds, metalation of the initial thioalkylated product to $H_2C{=}CHC({=}CH_2)CHKSR$ and subsequent introduction of a second RS group, and the competitive reaction of the electrophile with KDA or KTMP, resulting in an undesired shift of the deprotonation equilibrium (Scheme III) As suchlike processes are generally less serious with lithium compounds, we expected to obtain better results when prior to the functionalization, the potassium in **5a** was exchanged for lithium, to give **5c** This can be done by adding anhydrous lithium bromide to the reaction mixture [11,29,62] However, upon the addition of a solution of anhydrous lithium bromide in THF to the reaction mixture, the red colour of the isoprene anion disappeared instantaneously, and consequently no trace of coupling product could be isolated, not even with oxirane Thus, introduction of lithium as counter-ion causes the deprotonation equilibrium (Scheme III) to shift completely to the left side (see Scheme IV)

Scheme IV

An analogous case is the interaction between diphenylmethane and alkali metal amides [63] Whereas Ph_2CHNa and Ph_2CHK are stable in liquid ammonia, the lithium compound undergoes ammonolysis to give free diphenylmethane and lithiumamide

Electrostatic interaction between the metal and the anionic part may be invoked to explain these phenomena The larger metal ion (K^+) prefers to be associated with the larger anion (in many cases an anion with

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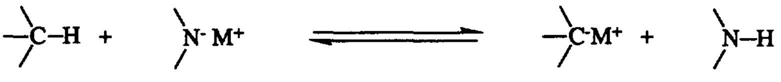
Brown and Randad[87] obtained remarkably good yields of carbinols (~65%) by reacting isoprene with KTMP, then converting the potassiated isoprene into a boron derivative and finally adding the aldehyde delocalized charge, *e.g.* an allylic anion), whereas the smaller cation (Li^+) prefers to combine with the smaller anion (mostly an anion with localized charge, *e.g.* an amide anion). Assuming for the sake of simplicity that the metal cation and anions behave electrostatically as point charges centered on the atoms bearing the charges in their usual structural formulas, one can calculate the change in electrostatic energy for the deprotonation equilibrium (simplified in Scheme V) from the interionic distances (d_{CM} and d_{NM}) of the ion pairs as given in the equation of Scheme V, where $\Delta E_{(CH\rightarrow NH)}$ is the enthalpy difference between isoprene and the amine.

Scheme V



$$\Delta E_M = \frac{-e^2}{4\pi\varepsilon_0}\left(\frac{1}{d_{CM}} - \frac{1}{d_{NM}}\right) + \Delta E_{(CH\rightarrow NH)}$$

According to Grovenstein[60] we took for the radii of carbon in an anion 1.65 Å,[64] of nitrogen in an amide 1.40 Å,[65,66] and Pauling's crystal radii[67] of the alkali metal cations. From our results of the metalation of isoprene with KDA we could estimate an equilibrium constant of about 1, thus $\Delta E_K \approx 0$. With this value we calculated $\Delta E_{(CH\rightarrow NH)}$, which was substituted in the equation with which ΔE_{Li} was calculated to be 8.3 kcal/mol. This energy difference corresponds with an equilibrium constant of 4 10^{-9}, or a pK_a difference of 8.5 between LDA and KDA, and is comparable with the reported[51] difference of 7.1 between LDA (34.4) and KDA (41.5).

In a similar way ΔE_{Cs} was calculated to be −2.2 kcal/mol, corresponding with a pK_a value 2.2 units higher than in the case of potassium. This is in good agreement with the experiment. The yields obtained after metalation of isoprene with CsDA and subsequent functionalization with oxirane were *ca.* 10% higher (Table IV), than those obtained with KDA under similar conditions. ΔE_{Na} was calculated to be +3.4 kcal/mol, which corresponds with a pK_a value 3.5 units less than in the case of potassium, and from which the low extent of metalation of isoprene with NaDA found by subsequent reaction with oxirane was predicted (Table IV).

Table IV. Variation of the Metal Counter-cation on the Metalation of Isoprene[a]

amide	yield (%)[b]	amid	yield (%)[b]
LDA	—	CsDA	72[c]
NaDA	7	LiTMP	—
KDA	60	KTMP	70

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[a] Reaction conditions: 50% excess of isoprene, 30 min at −70°C in THF/hexane (1/1). [b] Yields of oxirane quench product (7c) after distillation. [c] With 50% excess of CsDA a similar yield was obtained.

Thus, the pK_a value of diisopropylamine corresponds with an ion-pair basicity for LDA that is not sufficient for generating any isoprenyllithium from isoprene With KDA, having a higher ion-pair basicity than LDA, isoprenyl potassium is formed in a significant concentration. Attempts to replace potassium by lithium in the presence of HDA by addition of lithium bromide without influencing the equilibrium (are doomed to) fail, because Li^+ combines only with the amide anion

Scheme VI

$$\begin{tikzcd}
PhCH_3 \arrow[r, "BuLi\ t\text{-}BuOK"] \arrow[rr, bend left, "BuLi\ TMEDA"] & PhCH_2K \arrow[r, "LiBr"] & PhCH_2Li
\end{tikzcd}$$

$$PhCH_2Li + HDA \rightleftharpoons \underset{\text{(colourless)}}{PhCH_3} + LDA$$

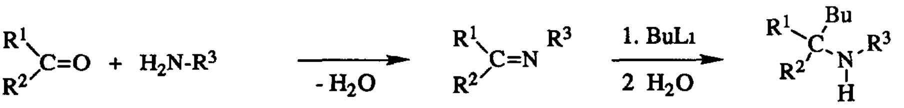
$$t\text{-}BuOK + LDA \longrightarrow t\text{-}BuOLi + KDA$$

$$PhCH_3 + KDA \rightleftharpoons \underset{\text{(red)}}{PhCH_2K} + HDA$$

The phenomena described above may be illustrated by the following experiments with toluene This compound can be quantitatively metalated with BuLi·TMEDA in hexane to give an orange solution of benzyllithium Toluene can also be metalated with BuLi *t*-BuOK, and with *one* equivalent of lithium bromide the formed benzylpotassium can be converted into benzyllithium[11] Upon successive addition of the co-solvent THF and an equivalent amount of diisopropylamine the solution becomes colourless Upon subsequent addition of *t*-BuOK the deep-red colour of benzylpotassium reappears (Scheme VI)

Synthesis of Sterically Hindered Dialkyl Amines. The highly branched amines **10a**, and **c-f** were synthesized as shown in the general Scheme VII

Scheme VII



9a, c-f **10a, c-f**

(Structures in Tables VIII and IX)

The first step is the condensation of a primary amine with a carbonyl compound to give an imine The formation of imines has been reviewed,[68] and convenient procedures are reported for sterically hindered imines containing aryl groups,[69-73] using molecular sieves (0.6 - 3 kg per mol^{-1}) for the condensation of ketones with aryl amines,[70,71] aluminum oxide for the reaction of benzylamines with arylaldehydes[69], and even simply mixing of benzaldehyde with *tert*-alkylamines yields *N*-*t*-alkyl-*N*-benzylideneamines.[72] However, imines derived from *tert*-butylamine and an aldehyde or a ketone are difficult to prepare. Fraser and Mansour[48] reported the synthesis of **9c** and **e**, using molecular sieves for removing the water, in 54 and 34% yields, respectively. Alternative multi-step syntheses of *N*,*N*-di-*t*-alkylamines avoiding the elusive imine step were developed by Rathke[74] and Corey.[75] We decided first to follow the method represented in Scheme VII, however.

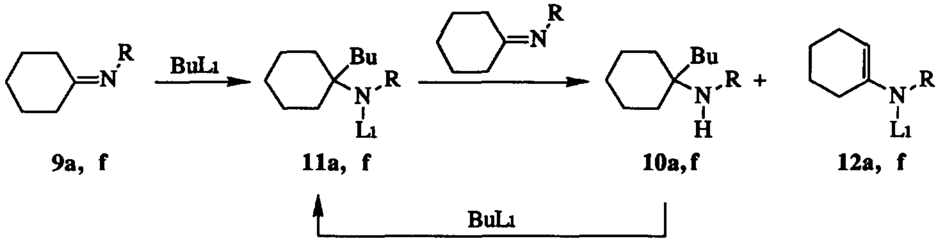
Imines **9a**, **d**, and **f** were synthesized following the conventional methods — refluxing with benzene as azeotroping agent, simple mixing the reactants,[72] and using molecular sieves as drying agent, respectively — in 90, 80, and 33% yield, respectively.

The synthesis of **9c** and **9e** was considerably improved (*ca.* 85% yield!) by using basic aluminum oxide as drying agent and hexane or pentane as solvent. This method differs from that of Texier-Boullet[69] who used aluminum oxide without a solvent. In the case of enolizable ketones or aldehydes dilution of the reactants is necessary to avoid aldol condensation. This side reaction was also observed by Kyba[70] in the condensation of acetone with arylamines on molecular sieves. The impurities in the products, which Texier-Boullet[69] obtained in low yields by the condensation of acetone or phenylmethylketone with benzylamine, may also be due to aldol condensation. An attempt to prepare **9f** from cyclohexanone and *tert*-butylamine according the method of Texier-Boullet[69] afforded after a few days at 20°C the aldol product of cyclohexanone as the only compound in 35% yield. In this case, however, dilution of the reactants did not cause any reaction. Thus, aluminum oxide can be used successfully for the synthesis of imines by condensation of amines with non-enolizable ketones or aldehydes, and, if the latter are enolizable, a solvent is required.

The second step involves the addition of butyllithium to the double bond of the imine. This reaction can be carried out by addition of BuLi to the imine,[48,68] giving after aqueous workup the amines **10c**,[76] **d**, and **e** in high yields (80-90%). Addition of BuLi to the imines **9a** and **f**, however, afforded after aqueous workup mixtures of imine and amine with ratios of *ca.* 1:1 and 3:1, respectively. Treatment of these mixtures with BuLi, in order to convert the recovered imine into the desired adduct, and subsequent hydrolysis gave no purer product. An improvement to 70% and 50% yield, respectively, was attained by addition of imines **9a** and **f** to a 100% excess of BuLi. This result can be explained by the reaction sequence depicted in Scheme VIII.

The addition product of BuLi and the imine is a sterically hindered lithium amide (**11**), which is capable of deprotonating the unreacted starting imine to give the lithiated enamide **12** and amine **10**. The latter can subsequently be deprotonated by BuLi, after which **9** can be deprotonated again. Since the metalation of imines with LDA has been reported, and has been used for the derivatization of imines,[77-80] the sequence of Scheme VIII seems reasonable.

Scheme VIII



Thus, the undesired formation of **12** can be reduced by reverse addition, the imine being added to an excess of BuLi

Experimental Section

a. General Remarks. ^1H and ^{13}C NMR spectra were recorded on a Bruker AC200 apparatus, using deuterio chloroform as solvent and internal standard, unless indicated otherwise Mass spectroscopy was performed on a Kratos MS80 GC-MS combination apparatus THF was distilled from $LiAlH_4$ and stored on sodium lead alloy under nitrogen Butyllithium (*ca* 1.6 M hexane solution), potassium- and sodium *tert*-butoxide are commercially available and were used as such Commercial isoprene was distilled (bp 34°C) in portions of *ca* 100 mL from magnesium sulfate, and stored on molecular sieves (4Å) at –30°C TMEDA and HDA were distilled from $LiALH_4$ and stored under nitrogen All reactions were carried out in an atmosphere of nitrogen in a 500 mL three-necked, round-bottomed flask equipped with a mechanical stirrer, gas-inlet, -outlet, and thermometer

b. Metalation of Isoprene with KDA in THF/hexane and Subsequent Functionalization with Oxirane. (Typical procedure for Table I). Preparation of 4-Methylene-5-hexen-1-ol (7c). A mixture of 0 105 mol of *t*-BuOK, 0.105 mol of HDA, and 60 mL of THF was placed in the flask (in *one* reaction also 0 105 mol of TMEDA was added) The resulting solution was cooled to –100°C, after which a solution of 0 100 mol of BuLi in 62 mL of hexane was added from a syringe over 2 min During this addition the mixture was efficiently stirred and the temperature kept between –100 and –90°C After the addition the temperature was allowed to rise to –70°C and isoprene (amounts are listed in Table I) was added in one portion The colour of the solution changed immediately into red The reaction was complete (*in casu* the equilibrium was established) within 1 min. (This was shown by quenching aliquots with oxirane, subsequent hydrolysis and GC analysis) After 1 min (or a longer period, see Table I) a solution of 0.150 mol of oxirane in 20 mL of THF was added in one portion at –70°C, allowing the temperature to rise (to *ca* –20°C in a few seconds, without external cooling) After the red colour has changed to light-yellow, 100 mL of water was added, and the pH of the aqueous layer was lowered to *ca* 4 by adding a 10% aqueous solution of sulfuric acid, while keeping the temperature below 20°C (Hydrochloric acid cannot be used, since it reacts with the excess of oxirane to give chloroethanol, which is difficult to separate from the product). The aqueous layer was extracted four times with ether and the combined organic solutions dried over magnesium sulfate. Removal of the solvent *in vacuo* and distillation afforded **7c** in 57-62% yield, bp 77°C (12 mm Hg) or 40°C (0 1 mm Hg), $n^{20}{}_D$ 1 4780, for spectroscopic data see Tables V-VII

Raising the pH of the aqueous layer to >10, by adding potassium hydroxide, subsequent extraction with ether, drying over potassium carbonate, removal of the solvent *in vacuo*, and distillation afforded $(i\text{-}C_3H_7)_2NCH_2CH_2OH$ in 35-40% yields, bp 50°C (2 mm Hg), $n^{20}{}_D$ 1 4427, mass spectrum *m/e* (% of base peak) 145 (M^+, 6), 130 (16), 114 (100), 102 (8), 88 (35), 72 (68), 56 (14), 43 (28), 30 (67), ^1H NMR δ 3 34 (CH_2O, t, J = 5 8 Hz), 3 20-3 30 (OH), 2 92 (2 CH, septet, J = 6 7 Hz), 2 50 (CH_2N, t, J = 5 8 Hz), 0 91 (4 CH_3, d, J = 6 7 Hz), ^{13}C NMR δ 58.4 (CH_2O), 47 4 (2 CH), 45 1 (CH_2N), 20 6 (4 CH_3)

c. Metalation of Isoprene with KDA/TMEDA in Hexane and Subsequent Functionalization with Oxirane. (Table I). A mixture of 0 105 mol of *t*-BuOK, 0 105 mol of HDA, 60 mL of hexane, and 0 105 mol of TMEDA was cooled to –50°C, after which a solution of 0 100 mol of BuLi in 62 mL of hexane was introduced from a syringe over 2 min During this addition the mixture was efficiently stirred and the temperature kept between –50 and –30°C After an additional 10 min of stirring at –30 °C 0 150 mol of isoprene was added in one portion The colour of the mixture turned immediately into red After 30 min at –20°C the mixture was cooled to –60°C, and a solution of 0 15 mol of oxirane in 30 mL of THF was added The temperature was allowed to rise, and subsequent workup, performed as described in section b, afforded **7c** in *ca* 60% yield

d. Metalation of Isoprene with $KNEt_2$, $KN(c\text{-}C_6H_{11})_2$, or 8a-f in THF or THF/TMEDA. (Table II). A solution of 0 055 mol of *t*-BuOK and 0 051 mol of the amine ($HNEt_2$, $HN(c\text{-}C_6H_{11})_2$, or **10a-f**, respectively) in 30 mL of THF (and, if mentioned in Table II, 0 055 mol of TMEDA) was placed in the flask The resulting solution was cooled to –100 °C, after which a solution of 0.050 mol of BuLi in 31 mL of hexane was introduced from a syringe over 1 min During this addition the mixture was efficiently stirred and the temperature kept between –100 and –90°C After the addition the temperature was allowed to rise to –70°C Stirring at this temperature was continued for 20 min in the case of the starting amines **10a-f** to ensure complete formation of the amides **8a-f** Isoprene (amounts are listed in Table II) was added in one portion at the temperature given in Table II Quenching with a solution of 0 10 mol of oxirane in 20 mL of THF after the given reaction time, and subsequent workup was performed as described in section b Yields of **7c** are reported in Table II

The sterically hindered amines were recovered in 80-97% by adding potassium hydroxide to the aqueous layer (pH > 10), followed by two extractions with ether, drying over potassium carbonate, removal of the solvent *in vacuo*, and subsequent distillation.

e. Metalation of Isoprene with the Amides 8a, or c-e and TMEDA as co-Solvent. (Table II). A mixture of 0.055 mol of *t*-BuOK, 0.051 mol of the amine (**10a**, or **c-e**, respectively), 30 mL of hexane, and 0.055 mol of TMEDA was cooled to –50°C, after which a solution of 0.050 mol of BuLi in 31 mL of hexane was introduced with a syringe over 1 min. During this addition the mixture was efficiently stirred and the temperature kept between –50 and –30°C. Thick yellow suspensions of the amides were formed. After an additional 10 min stirring at –30°C isoprene (amounts in Table II) was added in one portion at the temperatures given in Table II. After the given reaction time, quenching with oxirane (0.10 mol in 20 mL of THF) and subsequent workup were performed as described in section b. Yields of **7c** are reported in Table II. Recovery of the amines was carried out as described in section e.

f. Metalation of Isoprene with KDA in THF/hexane and Subsequent Functionalization with 1-Chloroheptane, 1-Bromoheptane, Prenylbromide, Pivaldehyde, Isovalderaldehyde, or Senecio-aldehyde. (Table III). Preparation of 7a, b, d-f. A solution of 0.055 mol of *t*-BuOK and 0.051 mol of HDA in 60 mL of THF was cooled to –100°C, after which a solution of 0.050 mol of BuLi in 31 mL of hexane was introduced from a syringe over 1 min. During this addition the mixture was efficiently stirred and the temperature kept between –100 and –90°C. After the addition, the temperature was allowed to rise to –70°C and 0.010 mol of isoprene was added in one portion. After an additional 5 min of stirring at this temperature, 0.058 mol of the electrophile was added without external cooling. Workup carried out as described in section b (however, in the case of **7a** and **b** washings with water were performed too) afforded:

myrcene (7a) in 30% yield, bp 50-55°C (12 mm Hg), [Lit. 56.5-58°C (15 torr),[40] 64-65°C (14 mm Hg),[81,82] 60-62°C (19 mm Hg),[83]], n^{20}_{D} 1.4690, [Lit. 1.4697,[81] 1.4700,[82] 1.4686,[83]],

3-methylene-1-undecene (7b) in 40% yield, bp 87°C (12 mm Hg), n^{20}_{D} 1.4512,

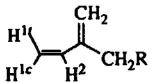
5-methylene-2,2-dimethyl-6-hepten-3-ol (7d) in 39% yield, bp 60°C (2 mm Hg), n^{20}_{D} 1.4632,

ipsenol (7e) in 19% yield, bp 45 (0.1 mm Hg), n^{20}_{D} 1.4633,

ipsdienol (7f) in 21% yield, bp 32-37°C (0.02 mm Hg),n^{20}_{D} 1.4854,

For spectroscopic data of **7a-f** see Tables V-VII.

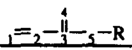
Table V. ^1H NMR Data of 7



no	R	H^{1t}	H^{1c}	H^2	$C=CH_2$	CH_2 (*J*)	J_{trans}	J_{cis}	R (H)
7a	$CH_2CH=C(CH_3)^a$	5 25	5 07	6 39	5 00-5 04	2 28-2 13 (m)	17 6	10 8	5 17 (HC=, tsept, ^3J = 6 7 Hz, ^4J = 1 5 Hz), 2 28-2 13 (CH_2, m), 1 70-1 72 (CH_3, m), 1 62-1 64 (CH_3, m)
7b	$(CH_2)_6CH_3$	5 23	5 04	6 38	4 97-5 02	2 21 (t, 6 7)	17 6	10 6	1 40-1 55 (CH_2CH_2C=, m), 1 20-1 40 ($(CH_2)_5CH_3$, b), 0 90 (CH_3, t, *J* = 6 4 Hz)
7c	CH_2CH_2OH	5 20	5 02	6 33	4 95-5 00	2 24 (t, 7 5)	17 6	10 8	3 62 (CH_2O, t, *J* = 6 5 Hz), 3 16 (OH, b), 1 70 (CH_2CH_2O, tt, *J* = 6 5, 7 5 Hz)
7d	CH(OH)Bu^t	5 20	5 07	6 37	5 11-5 14 5 06-5 09	2 61 (dt, 13 8, 1 8) 2 03 (dd, 13 8, 10 7)	17 6	11 0	3 35 (CH, dd,*J* = 10 7, 1 8 Hz), 1 8-2 1 (OH, b), 0 95, ($C(CH_3)_3$, s)
7e	$CH(OH)CH_2CH(CH_3)_2^{a\,b}$	5 21	5 02	6 34	5 02-5 15	2 21-2 36 (m)	17 7	10 5	3 76(CHO, dddd, *J* =7 4,5 6,8 5,4 4 Hz), 2 77(OH, s), 1 60-2 05 ($CHCH_3$, m), 1 20-1 40 (CH_2, m), 0 92 (CH_3, d, *J* = 6 6 Hz), 0 96 (CH_3, d, *J* = 6 6 Hz)
7f	$CH(OH)CH=C(CH_3)_2^{a,b}$	5 30	5 04	6 43	5 02-5 17	2 58 (dd, 13 5, 6 7) 2 30 (dd, 13 5, 6 7)	18 0	11 3	5 02-5 17 (CH=, m), 4 95 (CHO, ddd, *J* = 9 2, 6 7, 6 7 Hz), 1 72 (CH_3, s), 1 65 (CH_3, s)
7g	$Si(CH_3)_3^a$	5 09	5 02	6 35	4 86-4 89 4 76-4 78	1 69 (d, 1 0)	17 5	10 6	0 03 ($Si(CH_3)_3$, s)
7h	SCH_3	5 32	5 13	6 32	5 07-5 11	3 25 (d, 1 0)	17 6	10 9	2 00 (SCH_3, s)
7i	SCH_2CH_3	5 32	5 12	6 32	5 07-5 10	3 29 (d, 0 9)	17 7	10 7	2 50 (CH_2S, q, *J* = 7 5 Hz), 1 08 (CH_3, t, *J* = 7 5 Hz)

[a] These data correspond with those reported in literature **7a**,[40,83] **7e**,[30,33] **7f**,[31] **7g**[34] [b] Spectra of **7e** and **f** were recorded on a Varian EM390 (90 MHz) apparatus with CCl_4 as solvent and $SiMe_4$ as internal standard

Table VI. ^{13}C NMR Data of 7



$\overset{}{_1}{=}{_2}{-}\overset{4}{\overset{\|}{_3}}{-}{_5}{-}R$

no	R	C^1	C^2	C^3	C^4	C^5	R(C)
7a	$CH_2CH{=}C(CH_3)$	115 6	139 0	146 1	113 0	31 4	131 7 (*C*=CH), 124 2 (CH=), 26 7 (CH_2), 25 6 (CH_3), 17 6 (CH_3)
7b	$(CH_2)_6CH_3$	115 3	139 0	146 6	112 9	31 4[a]	31 9[a] ($CH_2CH_2CH_3$), 29 7, 29 5, 29.3 ($CH_2CH_2CH_2$), 28 2 ($CH_2CH_2C{=}$), 22 7 (CH_2CH_3), 14 0 (CH_3)
7c	CH_2CH_2OH	115 7	138 6	145 7	113 2	30 8	62 1 (CH_2OH), 27 3 (CH_2CH_2OH)
7d	CH(OH)Bu^t	118 4	138 3	143 9	114 2	34 4	76 5 (CHOH), 34 7 (*C*CH), 25 7 (3 CH_3)
7e	$CH(OH)CH_2CH(CH_3)_2$[b]	117 7	138 3	142 8	113 3	46 0	67 1 (CHOH), 40 2 (CH_2), 24 1 ($CHCH_3$), 23 1 (CH_3), 21 5 (CH_3)
7f	$CH(OH)CH{=}C(CH_3)_2$[b]	118 6	138 4	142 1	113 8	39 7	126 6 (CH=), 125 9 (*C*=CH), 67 5 (CHOH), 25 5 (CH_3), 18 2 (CH_3)
7g	$Si(CH_3)_3$	114 1	139 9	144 1	113 5	21 2	-1 3 (3 CH_3)
7h	SCH_3	117 6	136 8	141 1	114 7	35 1	15 1 (CH_3)
7i	SCH_2CH_3	117 4	136 6	141 7	114 7	35 5	25 5 (CH_2), 12 0 (CH_3)

[a] These values may be interchanged [b] Spectra recorded on a Bruker WP200 (50 MHz) apparatus

Table VII. Mass Spectral Data of 7

no	formula	molecular ion		base peak	other peaks
		M^+, *m/e*	%	*m/e*	*m/e* (%)
7a	$C_{10}H_{16}$	136	5	93	121 (4), 107 (3), 79 (14), 69 (86), 53 (12), 41 (98), 27 (8)
7b	$C_{12}H_{22}$	166	2	68	151 (1), 138 (2), 123 (2), 110 (10), 95 (20), 81 (20), 55 (15), 41 (15), 29 (4)
7c	$C_7H_{12}O$	112	3 5	68	94 (32), 79 (45), 67 (65), 53 (42), 41 (43), 27 (18)
7d	$C_{10}H_{18}O$	154	2	69	136 (4), 121 (6), 87 (80), 57 (73), 41 (72), 29 (14)
7e	$C_{10}H_{18}O$	154	—	68	136 (M^+-H_2O, 2 4), 121 (2), 93 (9), 85 (19), 79 (12), 53 (15), 43 (30)
7f	$C_{10}H_{16}O$	152	0 13	119	150 (0 4), 134 (55), 105 (32), 91 (95), 79 (80), 65 (11), 53 (15), 41 (23)
7g	$C_8H_{16}Si$	140	8	73	125 (5), 109 (2), 97 (8), 85 (3), 59 (13), 45 (11)
7h	$C_6H_{10}S$	114	100	114	99 (40), 68 (58), 61 (67), 53 (14), 45 (16), 41 (42), 39 (34)
7i	$C_7H_{12}S$	128	50	68	113 (14), 99 (32), 85 (15), 75 (50), 41 (98)

g. Metalation of Isoprene with KDA in THF/hexane and Subsequent Functionalization with Trimethylchlorosilane, Dimethyl Disulfide, or Diethyl Disulfide. (Table III). Preparation of 7g-i. The metalation of isoprene was carried out as described in section f. The cold reaction mixture (–70°C) was poured over 1 min into a solution of 0.050 mol of the electrophile, with vigorous stirring and cooling at –90°C in a bath with liquid nitrogen. The red colour disappeared immediately. Workup carried out as described in section b (however, washings with water were performed too) afforded

2-methylene-1-trimethylsilyl-3-butene (7g) in 19% yield, bp 60°C (75 mm Hg), [Lit. 69-70°C (80 mm Hg)[34]],

2-methylene-1-methylthio-3-butene (7h) in 20% yield (according to GC and NMR), bp 40°C (12 mm Hg), the product was contaminated with dimethyl disulfide and $(i\text{-}C_3H_7)_2NSCH_3$: mass spectrum *m/e* (% of base peak) 147 (M^+, 33), 132 (29), 90 (100), 43 (14), ^1H NMR δ 3.17 (CH, septet, J = 6.5 Hz), 2.13 (SCH_3, s), 1.09 (CH_3CH, d, J = 6.5 Hz), ^{13}C NMR δ 55.5 (CH), 26.4 (SCH_3), 22.3 (CH_3CH),

2-methylene-1-ethylthio-3-butene (7i) in 14% yield (according to GC and NMR), bp 45°C (12 mm Hg), the product was contaminated with diethyl disulfide and $(i\text{-}C_3H_7)_2NSCH_2CH_3$: mass spectrum *m/e* (% of base peak) 161 (M^+, 24), 146 (35), 104 (100), 90 (15), 76 (30), 58 (30), 44 (42), 27 (18), ^1H NMR δ 3.16 (CH, septet, J = 6.5 Hz), 2.45 (SCH_2, q, J = 7.4 Hz), 1.20 (CH_3CH_2, d, J = 7.4 Hz), 1.06 (CH_3CH, d, J = 6.5 Hz), ^{13}C NMR δ 55.3 (CH), 32.6 (SCH_2), 22.3 (CH_3CH), 14.4 (CH_3CH_2).

For spectroscopic data of **7g-i** see Tables V-VII.

h. Metalation of Isoprene with CsDA and Subsequent Functionalization with Oxirane. (Table IV). A solution of *t*-BuOCs in THF was prepared by reaction of 0.32 mol Cs (43 g) with 0.30 mol of *t*-BuOH in 600 mL of THF at 40°C until the colour turned into blue.[84] A mixture of 110 mL of this solution, containing 0.055 mol of *t*-BuOCs, and 0.051 mol of HDA (5.15 g) was cooled to –100°C, after which a solution of 0.050 mol of BuLi in 31 mL of hexane was introduced from a syringe over 1 min. During this addition the mixture was efficiently stirred and the temperature kept between –100 and –90°C. After the addition the temperature was allowed to rise to –80°C and 0.075 mol of isoprene was added in one portion. The colour of the solution changed immediately into red. After an additional 30 min stirring at –70°C, a solution of 0.10 mol of oxirane in 20 mL was added. The temperature was allowed to rise, and workup was performed as described in section b. This gave **7c** in 71-73% yields.

i. Metalation of Isoprene with NaDA and Subsequent Functionalization with Oxirane. (Table IV). Exactly the same procedure as with KDA was followed (described in section b), using *t*-BuONa instead of *t*-BuOK, and 50% excess of isoprene. **7c** was obtained in 7% yield.

j. Preparation of the Imines. *N*-Cyclohexylidene-*N*-cyclohexylamine (9a). A mixture of 0 5 mol of cyclohexanone, 0.5 mol of cyclohexyl-amine and 300 mL of benzene was heated under reflux, using a Dean-Stark apparatus, until the formation of water has ceased. Removal of the solvent *in vacuo* and subsequent distillation gave **9a** in >90% yields

***N*-Isobutylidene-*N*-*tert*-butylamine (9c).**[87] A round-bottomed flask was charged with 75 g of basic aluminum oxide (dried for 2 days at 200°C), 150 mL of anhydrous pentane, 0 20 mol of 2-methylpropanal and 0.37 mol of *tert*-butylamine After 18 hours at room temperature, the aluminum oxide was filtered off and rinsed thoroughly with pentane The pentane was distilled off through a Widmer column Distillation gave **9c** in 84% yield

***N*-Benzylidene-*N*-*t*-butylamine (9d).**[87] This compound was prepared following the procedure described in literature [72,86] A mixture of 0 50 mol of benzaldehyde and 0 55 mol of *tert*-butylamine was kept several hours at room temperature, subsequent separation of the water, followed by distillation gave **9d** in yields >90%

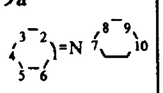
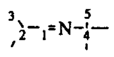
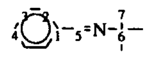
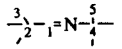
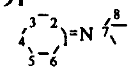
***N*-(2,2-Dimethylpropylidene)-*N*-*tert*-butylamine (9e).**[87] A similar procedure was followed as described in for **9c**, using 120 g of basic aluminum oxide, 140 mL of anhydrous pentane, 0 16 mol of 2,2-dimethylpropanal and 0 30 mol of *tert*-butylamine Workup after 29 h at room temperature gave **9e** in 85% yield

***N*-Cyclohexylidene-*N*-*tert*-butylamine (9f).** Molecular sieves (250 g, 4 Å, dried *in vacuo* at 150°C, 3 h) were placed in a flask, which equipped with a dropping funnel (without a side-tube) and a gas-outlet/inlet The flask was evacuated, and 0 50 mol of cyclohexanone, 250 mL of anhydrous hexane, and 0 68 mol of *tert*-butylamine were subsequently added Nitrogen was admitted, and the flask was swirled After heating under reflux for 3 h, and standing for one night at room temperature, the liquid was decanted and the molecular sieves were thoroughly rinsed with ether Removal of the solvents and subsequent distillation gave **9f** in 33% yield (according to GC and NMR), the product was contaminated with cyclohexanone

Physical and spectroscopic properties of the imines **9a**, **c-f** are listed in Table VIII

Attempt to Prepare 9f from *tert*-Butylamine and Cyclohexanone over Aluminum Oxide. Basic aluminum oxide (250 g, dried for 2 days at 200°C) and 0 50 mol of cyclohexanone was placed in the flask The mixture was swirled by hand until the cyclohexanone homogeneously was dispersed on the alumina A reflux condenser was placed on the flask and 0 68 mol of *tert*-butylamine was added through the condenser After swirling for 1 min the flask was placed in a heating bath and the mixture heated under reflux for 6 h After this period the mixture was allowed to stand at room temperature for 5 days The alumina was rinsed well with ether, and the rinsings concentrated *in vacuo* Subsequent distillation of the remaining liquid gave 2-(1-cyclohexenyl)cyclohexanon in 35% yield, bp 110°C (2 mm Hg), in 35% yield, $n^{20}{}_D$ 1 5055 ^{1}H NMR (acetone-d_6, 2 05 ppm) δ 5 34-5 40 (1 H, m, CH=), 2.89-3 00 (1 H, m, CHC=O), 2 16-2 45 (2 H, m,

Table VIII. Physical and Spectroscopic Properties of Imines (9)

compound	bp °C (mmHg) n^{20}_D or mp formula	^1H NMR δ (ppm)	^{13}C NMR δ (ppm)	mass spectrum *m/e* (% of base peak)
9a 	120 (12) *ca* 25 °C $C_{12}H_{21}N$	3 00-3 20 (H^7, m), 2 00-2 15 ($4H^{2,4}$, m), 1 35-1 60 (11H, m), 0 90-1 35 (5H, m)	170 2 (C^1), 57 4 (C^7), 39 8 (C^2), 33 7 ($2C^8$), 28 6 (C^6), 27 5, 27 2 ($C^{3,5}$), 24 7 ($2C^9$), 25 8, 25 4 ($C^{4,10}$)	179 (M^+, 44), 150 (13), 136 (63), 124 (12), 98 (100), 83 (32), 69 (20), 55 (48), 41(29)
9c 	115 (760)^a 1 4055 $C_8H_{17}N$	7 41 (H^1, d), 2 41 (H^2, dsept), 1 16 ($9H^5$, s) 1 05 ($6H^3$, d), J_{12} = 6 8Hz, J_{23} = 5 9Hz$^{a\ b}$	163 1 (C^1), 55 6 (C^4), 34 1 (C^2), 29 2 ($3C^5$) 19 2 ($2C^3$)^a	127 (M^+, 23), 112 (77), 99 (6), 84 (10), 72 (25), 75 (100), 41 (18)^a
9d 	87-88 (12)^a 1 5195 $C_{11}H_{15}N$	8 32 (H^5, s), 7 78-7 84 ($2H^2$, m), 7 40-7 45 ($3H^{3,4}$, m), 1 36 ($9H^7$, s)^a	154 8 (C^5), 137 0 (C^1), 129 9 (C^4), 128 3 ($2C^3$), 127 7 ($2C^2$), 57 0 (C^6), 29 5 ($3C^7$)	161 (M^+, 10), 146 (100), 106 (25), 104 (23), 89 (7), 77 (8), 57 (25)
9e 	122 (760)^a 1 4011 $C_9H_{19}N$	7 47 (H^1, s), 1 16 ($9H^5$, s), 1 06 ($9H^3$, s)$^{a\ b}$	164 9 (C^3), 55 8 (C^4), 35 6 (C^2), 29 7 ($3C^5$), 27 0 ($3C^1$)^a	141 (M^+, 24), 126 (63), 86 (20), 84 (22), 70 (21), 57 (100), 41 (22)^a
9f 	77 (12) 1 4692 $C_{10}H_{19}N$	2 22-230 ($2H^2$, m), 2 02-2 10 ($2H^6$, m), 1 40-1 65 ($6H^{3,4,5}$, m), 1 12 ($9H^8$, s)	171 2 (C^1), 53 6 (C^7), 41 6 (C^2), 33 1 (C^6), 30 5 ($3C^8$), 28 0 (C^3), 27 0 (C^5), 25 7 (C^4)	153 (M^+, 34), 138 (65), 110 (31), 96(35), 82(18), 69(54), 57 (100), 41 (37), 29 (16)

^{a} These data correspond with those reported in literature 9c,e,[48] 9d [72] ^{b} $CDCl_3$ as solvent and CH_2Cl_2 as internal standard (5 32 ppm)

$CH_2C=O$), 1.50-2 10 (14 H, m, 7 CH_2); ^{13}C NMR (acetone[D_6], 29.85 ppm) δ 209 8 (C=O), 137 2 (*C*=CH), 123.4 (*C*H=C), 59 1 (*C*HC=O), 42.6 (*C*H_2C=O), 32 6 (*C*H_2C=O), 28.3, 27.7, 25 9, 25 6, 23 6, 23 2 (6 CH_2)

k. Preparation of the Sterically Hindered Amines. *N*-Cyclohexyl-*N*-(1-butyl-cyclohexyl)amine (10a). A solution of 0.10 mol of **9a** in 20 mL of hexane was added over 15 min to an efficiently stirred solution of 0 20 mol of butyllithium in 124 mL of hexane During this addition the reaction mixture was kept at 20°C by cooling in an ice-bath and efficient stirring The resulting clear solution was poured over 1 min into 0 5 kg of finely crushed ice, while continuously swirling The aqueous layer was extracted twice with ether After concentration of the combined organic solutions *in vacuo* a sufficient amount of 9% aqueous hydrochloric acid was added, to bring the pH below 1 under these conditions **9a**, present fir 10%, was hydrolized After swirling for 5 min, potassium hydroxide was added to bring the pH above 11 During this addition the mixture was efficiently swirled and the temperature kept below 20°C by adding ice Two extractions with ether, removal of the solvent *in vacuo*, and subsequent distillation gave **10a** in 75-80% yields

***N*-*tert*-Butyl-*N*-(1-isopropyl-pentyl)amine (10c).** 0 19 Mol of **9c** was added over 15 min to a solution of 0 20 mol of BuLi in 125 mL of hexane, with efficient stirring and cooling at 20°C After the addition the reaction mixture was poured into 200 mL of ice-water, and the aqueous layer was extracted one time with pentane The combined organic solutions were dried over potassium carbonate Removal of the solvent and distillation gave **10c** in 82% yield

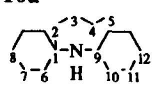
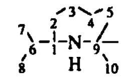
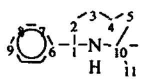
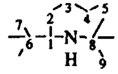
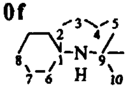
***N*-*tert*-Butyl-*N*-(1-phenylpentyl)amine (10d).** This compound was prepared in 80% yield following the procedure described in literature [72]

***N*-*tert*-Butyl-*N*-(1-*tert*-butylpentyl)amine (10e).** **9e** (0 07 mol) was added in one portion to an efficiently stirred solution of 0 096 mol of BuLi in 59 mL of hexane and 55 mL ether with cooling at 8 °C After an additional 2 25 h without cooling, the mixture was quenched with water Extractions with ether, drying over potassium carbonate, removal of the solvents *in vacuo*, and subsequent distillation gave **10e** in 74% yield

***N*-*tert*-Butyl-*N*-(1-cyclohexylpentyl)amine (10f).** Following the procedure as described for **10a** (see above), imine **9f** was added to a 100% excess of butyllithium in hexane at 20°C Subsequent similar workup afforded **10f** in 50% yield

Physical and spectroscopic properties of the amines **10a**, **c-f** are listed in Table IX

Table IX. Physical and Spectroscopic Properties of the Sterically Hindered Amines (10)

compound	bp °C (mmHg) n^{20}_D formula	^{1}H NMR δ (ppm)	^{13}C NMR δ (ppm)	mass spectrum *m/e* (% of base peak)
10a 	135 (2) 1 4850 $C_{16}H_{31}N$	2 27-2 43 (H^9, m), 1 53-1 71 (4H^6, m),^{a} 1 39-1 53 (2H^2, m), 0 89-1 39 (20H, m), 0 82 (3H^5, t, J = 6 6 Hz), 0 60-0 70 (NH, b)	54 1 (C^1), 49 5 (C^9), 36 9 (3C^{2,6}), 36 4 (2C^{10}), 26 1 (C^8), 25 7 (3C^{11,12}), 24 8 (C^3), 23 3 (C^4), 22 0 (2C^7), 14 0 (C^5)	237 (M$^+$,4), 208(7), 194(34), 180 (100), 152 (5), 139(18), 124 (4), 112 (8), 98 (24)
10c 	77 (12)^b 1 4303 $C_{12}H_{27}N$	2 27-2 35 (H^1, m), 1 68 (H^6, dsept), 1 10- 1 40 (6H$^{2\text{-}4}$,m), 1 02 (9H^{10},s), 0 85 (3H^5,t), 0 81 (3H^7,d), 0 78 (3H^8,d), 0 4-0 7 (NH,b) J_{16} = 3 5 Hz, J_{45} = J_{67} = J_{68} = 6 8 Hz^b	56 3 (C^1), 50 4 (C^9), 33 1 (C^2), 31.6 (C^6), 30 3 (3C^{10}), 29 0 (C^3), 23 0 (C^4), 18 3 (C^7), 17 9 (C^8), 14 1 (C^5)^b	186 (M+H$^+$, 3), 170 (5), 142 (60), 128 (13), 86 (100), 72 (34), 58 (13)^b
10d 	70-75 (0 1) 1 4866 $C_{15}H_{25}N$	7 15-7 39 (5H^{7,8,9}), 3 72 (H^1, t), 1 61 (2H^2, dt), 1 00-1 42 (4H^{3,4}, m), 1 02 (9H^{11}, s),^{b} 0 87 (3H^5, t), J_{12} = J_{45} = 7 0 Hz, J_{23} = 7 4 Hz	148 0 (C^6), 127 9 (2C^8), 126 9 (2C^7), 126 1 (C^9), 57 4 (C^1), 51 1 (C^{10}), 40 3 (C^2), 30 1 (3C^{11}), 28 8 (C^3), 22 5 (C^4), 13 9 (C^5)	220 (M+H$^+$, 2), 219 (M$^+$, 2), 204(4), 162(88), 147(7), 106 (100), 91(42), 79(7), 58(11)
10e 	88 (12)^b 1 4340 $C_{13}H_{29}N$	2 13-2 18 (H^1, m), 1 62-1 77 (2H^2, m),^{b,c} 1 23-1 50 (4H^{3,4}, m), 1 11 (9H^6, s), 0 91 (9H^9, s), 0 96 (3H^5, t), 0 5-0 7 (NH,b)	60 4 (C^1), 50 4 (C^8), 35 9 (C^2), 35 3 (C^6), 31 7 (C^3), 30 3 (3C^9), 27 1 (3C^7), 23 5 (C^4), 13.8 (C^5)^b	200 (M+H$^+$, 3), 184 (4), 142 (63), 128 (5), 112 (2), 86 (100)^b
10f 	115-120 (12) 1 4646 $C_{14}H_{29}N$	1 10-1 60 (16H, m), 1 15 (9H^{10}, s), 0 89 (3H^5, t, J = 6 7 Hz), 0 45-0 80 (NH, b)	55 6 (C^1), 51.4 (C^9), 38 7 (2C^6), 37 6 (C^2), 33 1 (3C^{10}), 26 2 (C^8), 25.2 (C^3), 23 3 (C^4), 22.4 (2C^7), 14 3 (C^5)	211(M$^+$,7),186(24), 154(62), 138 (5), 126 (15), 112 (47), 98 (100), 81 (12), 58 (22)

^{a} $CDCl_3$ as solvent and $SiMe_4$ as internal standard (0 00 ppm) ^{b} These data correspond with those reported in literature **10c,e**,[48] **10d** [72] ^{c} $CDCl_3$ as solvent and CH_2Cl_2 as internal standard (5 32 ppm)

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