# Synthesis of *N*-(Triisopropylsilyl)- and *N*-(*tert*-Butyldimethylsilyl)aldimines and Their Application in the Synthesis of β-Lactams

Gianfranco Cainelli,* Daria Giacomini,* Paola Galletti
Dipartimento di Chimica "G:Ciamician", Via Selmi, 2, I-40126 Bologna, Italy
Fax +39(51)259456; E-mail: cainelli@ciam.unibo.it
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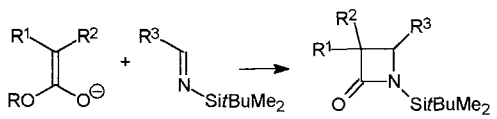
A new and efficient synthesis of *N*-(TIPS)imines and *N*-(TBDMS)-imines starting from enolizable and non-enolizable aldehydes is described. We tested the reactivity of these imines in the preparation of β-lactams. *N*-(TBDMS)imines effectively give *N*-(TBDMS)azetidinones with a *trans* stereochemistry of the ring substituents, complementing *N*-(TMS)imines which instead afford *cis* β-lactams. In contrast, *N*-(TIPS)imines react with ester enolates in few cases because of the extremely low rate of the ring-closure step, so that a decomposition of enolates occurred.

The azomethine group has found widespread application in organic synthesis. Its use has been generally restricted to *N*-substituted imines since imines of ammonia (C=NH) easily undergo self-condensation reactions.[1] *N*-Trimethylsilyl and related *N*-metallo imines have been used as masked imine derivatives of ammonia, in the synthesis of β-lactam antibiotics,[2] diamines,[3] aminols,[4] amines[5] and aziridines.[6] The continuous interest and contribution in this area from our[7] and other laboratories have resulted in developing new routes to *N*-metallo imines and in evaluating their applications in organic synthesis.

An interesting aspect in imine chemistry is represented by the ester enolate–imine condensation. This reaction, first reported in 1943 by Gilman and Speeter[8] using Reformatsky reagents, has become one of the most important methods for the preparation of β-lactams.[9] In this approach, *N*-(trimethylsilyl)imines have been used as the azomethine component to obtain *N*-unsubstituted β-lactams.

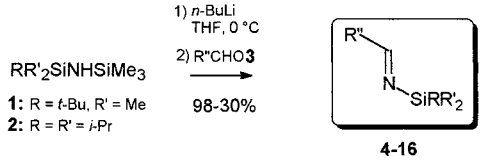
However, the protection of functional groups in β-lactam derivatives presents special problems for the synthetic chemist because of the high reactivity of these substrates.[10] The main group used for temporary protection of the β-lactam nitrogen is the *tert*-butyldimethylsilyl group (TBDMS). The ester enolate–imine condensation route to β-lactams could be improved by the use of *N*-(*tert*-butyldimethylsilyl)imines which should directly give the *N*-(TBDMS)azetidinones (Scheme 1).[11]




**Scheme 1**

As part of an ongoing project concerning the synthesis of β-lactam antibiotics, in this paper we give full details for the synthesis of *N*-(triisopropylsilyl)- and *N*-(*tert*-butyldimethylsilyl)imines and explore their reactivity with ester enolates.

*N*-(TBDMS)- and *N*-(TIPS)imines were obtained in two steps starting from *N*-(*tert*-butyldimethylsilyl)- and *N*-(triisopropylsilyl)amines. Treatment of these amines with butyllithium in THF followed by reaction with chlorotrimethylsilane, gave unsymmetrical disilylamines (**1** and **2**) purified by vacuum distillation.[12] The corresponding lithiated derivatives have been treated with a series of aldehydes **3** at 0 °C or −40 °C; evaporation of the THF afforded the corresponding imines **(4–16)** and $Me_3SiOLi$ (Scheme 2) in good yields.[13]




**4**: R" = Ph, $SiRR_2'$ = TBDMS
**5**: R" = CH=CHPh, $SiRR_2'$ = TBDMS
**6**: R" = $CH(CH_3)_2$, $SiRR_2'$ = TBDMS
**7**: R" = $C_7H_{15}$, $SiRR_2'$ = TBDMS
**8**: R" = cyclohexyl, $SiRR_2'$ = TBDMS
**9**: R" = $CH(OTBDMS)CH_3$, $SiRR_2'$ = TBDMS

**10**: R" = Ph, $SiRR_2'$ = TIPS
**11**: R" = CH=CHPh, $SiRR_2'$ = TIPS
**12**: R" = $CH(CH_3)_2$, $SiRR_2'$ = TIPS
**13**: R" = $C_7H_{15}$, $SiRR_2'$ = TIPS
**14**: R" = cyclohexyl, $SiRR_2'$ = TIPS
**15**: R" = $CH(OTBDMS)CH_3$, $SiRR_2'$ = TIPS
**16**: R" = $CH(OTIPS)CH_3$, $SiRR_2'$ = TIPS

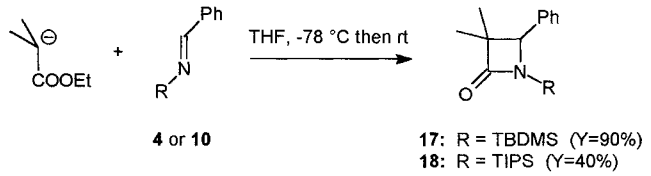
**Scheme 2**

Various aromatic as well as aliphatic aldehydes were quantitatively converted into the new silylimines[7] as determined through $^1H$ NMR by the complete consumption of the starting aldehyde. For example, benzaldehyde was converted into the corresponding *N*-(*tert*-butyldimethylsilyl)imine **4** and *N*-(triisopropylsilyl)imine **10**; starting from the *O*-protected (2*S*)-lactal we were able to prepare the enantiopure imines **9,15** and **16**. Products **4,9,10** and **16** have been purified by vacuum distillation obtaining imines free from the lithiated trimethylsilanol. Even α-branched enolizable imines could be obtained **(6,12)** and $^1H$ NMR spectra of the crude THF solution showed good conversion of the starting aldehydes, however they proved less stable than lactaldimines because attempting to evaporate the solvent we obtained partial oligomerization.[14]

The only imine isomer observed had (*E*)-configuration in analogy with substituted aldimines.[13,15] This fact suggested a *syn* elimination of $Me_3SiOLi$, as occurs in the Peterson[16] olefination, leading to a *trans* arrangement of the substituents. Between the two possibilities (elimination of $Me_3SiOLi$ or $RR_2'SiOLi$), the substitution pattern

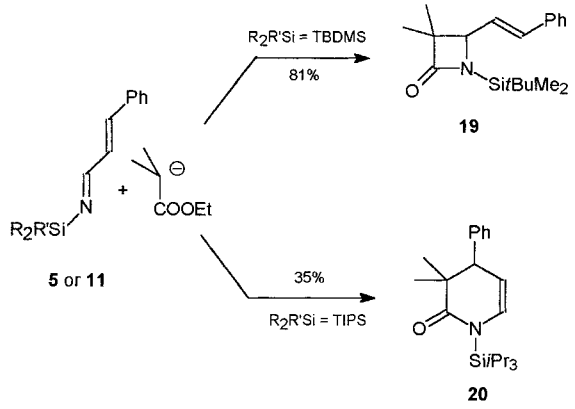
on silicon guided the chemoselectivity of this step[17] so that a selective elimination of TMSOLi instead of TIPSOLi of TBDMSOLi occurred in all our cases.

Preliminary experiments in the ester enolate–imine condensation were performed with the lithium enolate of ethyl isobutyrate and *N*-(TBDMS)imine or *N*-(TIPS)-imine of benzaldehyde (**4**, **10**) (Scheme 3). As expected the reaction directly afforded *N*-trialkylsilylazetidinones (**17** and **18**). Both derivatives showed good stability toward aqueous workup and silica-gel flash chromatography.




**Scheme 3**

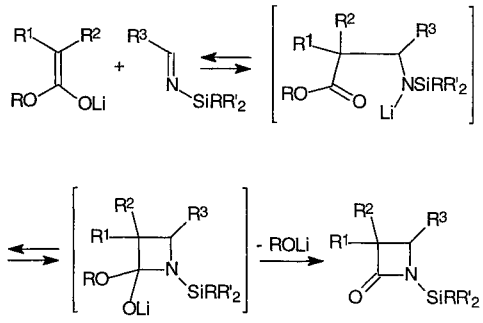
The β-lactam yields are strictly dependent on the imine moiety: *N*-(TBDMS)imine **4** afforded the expected product **17** in 90% yield while *N*-(TIPS)imine **10** gave **18** in 40% yield and the remaining starting imine was recovered unreacted.[18] When imine **5** and **11**, derived from cinnamaldehyde, were used in the cycloaddition reaction, we observed a different regiochemistry: **5** gave the 1,2- while **11** gave the 1,4-adduct, so that in the case of **11** we obtained the six-membered unsaturated δ-lactam instead of the β-lactam (Scheme 4).[19]




**Scheme 4**

These results can be understood considering the mechanism of the reaction (Scheme 5).

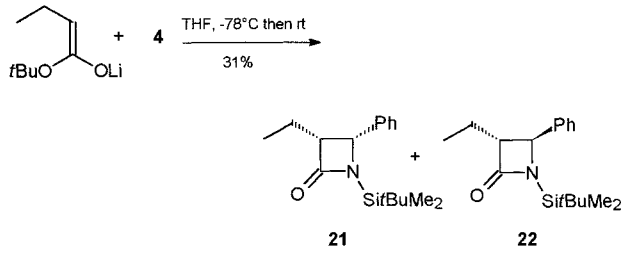
The enolate anion attacks the electrophilic carbon of the imine leading to an acyclic amino ester intermediate in equilibrium with the corresponding four-membered cyclic structure. Elimination of the metal alkoxide finally leads to the end product.[9] This latter step is rate determining and a steric hindrance on nitrogen could slow down the ring-closure reaction, so that in the case of the *N*-(TIPS)benzaldimine **10** a decomposition of the ester enolate works in favor of a low yielding process. In the




**Scheme 5**

case of the *N*-(TIPS) cinnamaldimine **11**, the equilibrating conditions favor the 1,4-addition leading to the formation of the 3,4-dihydropyridin-2-one **20**.

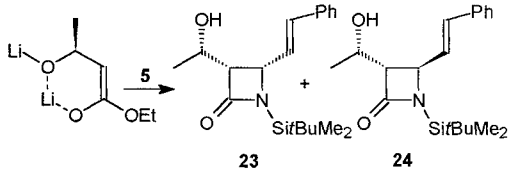
The reaction of the lithium enolate of *tert*-butyl butyrate with imine **4** gave azetidinones **21** and **22** in 31% yield (Scheme 6). Surprisingly, the simple diastereoselectivity resulted in favor of the *trans* isomer (11/89 *cis*/*trans* ratio).




**Scheme 6**

This result opposed those obtained with *N*-(trimethylsilyl)imines where *cis* β-lactams are preferred.[2] The same inversion in the *cis*/*trans* ratio was observed in *N*-aryl imines due to a change in the enolate geometry.[9] In our case, we attribute our result to a thermodynamic control in the ring-closure step of the reaction which favors the *trans* isomer.

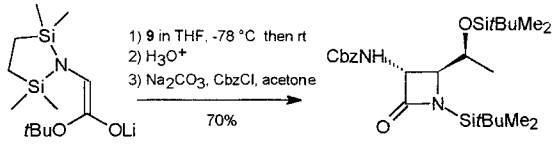
As an enantioselective access to carbapenem antibiotics,[20] we examined the reaction of the *N*-(TBDMS)imine of cinnamaldehyde with the dianion derived from (*S*)-3-hydroxybutyrate. The optically active β-lactams **23** and **24** in a 35/65 *cis*/*trans* ratio were obtained (Scheme 7). The original stereocenter in the nucleophilic partner of the cycloaddition exclusively induced in a 1,2 *lk* manner the $C_3$ stereogenic center whereas the simple diastereoselectivity prefers the *trans* isomer as in the case of *tert*-butyl butyrate.[21]




**Scheme 7**

Again, this fact can be attributed to a thermodynamic control of the cyclization. These compounds were characterized by $^1$H NMR spectroscopy from the coupling constants between H-3, H-4 and H-3, H-1'. The assignment of the relative stereochemistry of the $\beta$-lactams was made by correlation with those obtained in ref. 22.

Treatment of the *N*-(TBDMS)imine of (2*S*)-*O*-(*tert*-butyldimethylsilyl)propanal **9** with an equimolar solution of the lithium enolate of 1-(ethoxycarbonylmethyl)-2,2,5,5-tetramethyl-1-aza-2,5-disilacyclopentane (STABASE), after quenching the reaction mixture as described in the experimental section, afforded the $\beta$-lactam **25** as the *N*-carbobenzoyloxy derivative in 70% yield as the sole isomer (Scheme 8). Very high 1,2-*lk* induction of the stereocenter present in the side chain of the imine upon the $C_4$ stereocenter of the azetidinone was observed and the simple diastereoselectivity resembled that of silylimines of lactic and mandelic aldehydes in reaction with the lithium enolate of STABASE which invariably led to the exclusive formation of *trans* azetidinones.[2,23]




**25**

**Scheme 8**

Attempts to obtain *N*-(TIPS)azetidinones from the enolate of *tert*-butyl butyrate or from the dianion derived from (*S*)-3-hydroxybutyrate or from STABASE failed, probably because the ring-closure step required so high a reaction temperature that decomposition of the enolate occurred.

**Table 1.** Yields, Properties and Spectroscopic Data for Imines **4–16**

| Product | Yield[a] (%) | IR (solvent) $\nu$ (cm$^{-1}$) | $^1$H NMR ($CDCl_3$) $\delta$, $J$ (Hz) | $^{13}$C NMR ($CDCl_3$) $\delta$ | MS (70 eV) *m/z* (%) |
|---|---|---|---|---|---|
| **4** | 98 (43) | 1651, 1250 (film) | (300 MHz) 0.20 (s, 6H), 1.00 (s, 9H), 7.40–7.90 (m, 5H), 9.04 (s, 1H) | (50.3 MHz) 168.6, 139.0, 131.1, 128.4, 26.1, 17.4, −6.2 | 219 (2, M$^+$), 204 (10), 162 (100), 135 (30), 105 (12), 75 (20), 59 (56) |
| **5** | 95 | 1640, 1250 (film) | (200 MHz) 0.02 (s, 6H), 0.90 (s, 9H), 6.85 (dd, 1H, $J$ = 8.1, 16.0), 7.12 (d, 1H, $J$ = 16.0), 7.3–7.6 (m, 5H), 8.73 (d, 1H, $J$ = 8.1) | (50.3 MHz) 171.2, 144.8, 132.1, 129.4, 128.8, 127.5, 26.1, 18.8, −6.1 | 245 (10, M$^+$), 188 (73), 161 (100), 130 (21), 59 (25) |
| **6** | 85 | 1677, 1249 (film) | (200 MHz) 0.70 (s, 9H), 0.89 (d, 6H, $J$ = 6.4), 2.17 (m, 1H), 8.15 (d, 1H, $J$ = 4.3) | (50.3 MHz) 179.5, 41.1, 25.2, 22.3, 18.3, 13.6, −6.8 | 185 (15, M$^+$), 128 (100), 112 (6), 85 (5), 73 (46), 59 (24) |
| **7** | 98 | 1677, 1240 (film) | (200 MHz) 0.02 (s, 6H), 0.88 (t, 3H, $J$ = 6.8), 0.90 (s, 9H), 1.25–1.70 (m, 10H), 2.31 (dt, 2H, $J$ = 7.9, 4.4), 8.45 (t, 1H, $J$ = 4.4) | (75.5 MHz) 176.4, 41.7, 31.7, 29.5, 29.3, 26.1, 25.8, 25.5, 23.0, 18.7, 14.0, −6.3 | 241 (5, M$^+$), 184 (100), 170 (51), 114 (18), 98 (8), 73 (60), 59 (34) |
| **8** | 98 | 1674, 1249 (film) | (300 MHz) 0.02 (s, 6H), 0.90 (s, 9H), 1.20–2.20 (m, 11H), 8.25 (d, 1H, $J$ = 4.6) | (75.5 MHz) 179.6, 48.4, 29.1, 26.3, 26.1, 25.9, 25.7, 25.3, 18.0, −6.3 | 225 (17, M$^+$), 160 (100), 130 (9), 100 (4), 79 (6), 73 (29), 59 (26) |
| **9** | 90 (45) | 1689 (film) | (200 MHz) 0.05–0.15 (12H), 0.90 (s, 18H), 1.27 (d, 2H, $J$ = 6.6), 4.17 (dq, 1H, $J$ = 3.9, 6.6), 8.31 (d, 1H, $J$ = 3.9) | (50.3 MHz) 178.9, 74.2, 25.9, 21.3, 18.3, 17.0, −4.6, −6.2, −6.5 | 301 (41, M$^+$), 244 (3), 147 (100), 133 (11), 114 (10), 73 (95), 59 (10) |
| **10** | 98 (40) | 1650, 1100 (film) | (300 MHz) 1.18 (m, 18H), 1.35 (m, 3H), 7.5–7.9 (m, 5H), 9.20 (s, 1H) | (75.5 MHz) 168.0, 130.9, 128.4, 128.3, 18.2, 11.4 | 261 (2, M$^+$), 218 (100), 105 (18), 59 (19) |
| **11** | 96 | 1640, 1090 (film) | (200 MHz) 1.0–1.1 (18H), 1.25 (m, 3H), 6.84 (dd, 1H, $J$ = 8.1, 15.9), 7.10 (d, 1H, $J$ = 15.9), 7.3–7.6 (m, 5H), 8.83 (d, 1H, $J$ = 8.1) | (75.5 MHz) 171.3, 144.5, 132.4, 129.3, 128.7, 127.4, 25.5, 18.1, 11.2 | 287 (5, M$^+$), 244 (100), 175 (20), 130 (50), 115 (9), 59 (19) |
| **12** | 95 | 1684, 1100 (film) | (300 MHz) 0.9–1.3 (m, 27H), 2.36 (m, 1H), 8.44 (d, 1H, $J$ = 4.3) | (75.5 MHz) 179.9, 39.1, 18.7, 18.5, 18.4, 18.1, 12.7, 11.1 | 227 (30, M$^+$), 184 (100), 142 (18), 114 (11), 98 (5), 59 (18) |
| **13** | 94 | 1678, 1090 (film) | (200 MHz) 0.9–1.4 (m, 34H), 2.31 (dt, 2H, $J$ = 4.2, 7.7), 8.58 (t, 1H, $J$ = 4.2) | (75.5 MHz) 176.2, 41.6, 31.8, 29.3, 22.6, 18.4, 18.1, 14.1, 12.7, 11.1 | 283 (4, M$^+$), 240 (100), 212 (18), 198 (31), 156 (3), 115 (7), 87 (11), 73 (19), 59 (28) |
| **14** | 95 | 1675 (film) | (300 MHz) 0.9–1.10 (m, 21H), 1.2–1.9 (m, 10H), 2.12 (m, 1H), 8.41 (d, 1H, $J$ = 4.4) | (75.5 MHz) 179.4, 48.8, 29.1, 26.1, 25.3, 18.4, 18.1, 11.1 | 267 (21, M$^+$), 224 (100), 207 (8), 115 (4), 87 (7), 73 (15), 59 (24) |
| **15** | 90 | 1685, 1090 (film) | (300 MHz) 0.1 (s, 6H), 0.9–1.1 (27H), 1.20 (m, 3H), 1.28 (d, 3H, $J$ = 6.6), 4.15 (dq, 1H, $J$ = 4.0, 6.6), 8.43 (d, 1H, $J$ = 4.0) | (75.5 MHz) 178.7, 74.4, 25.9, 21.4, 18.4, 18.0, 11.1, −1.4, −4.6 | 343 (23, M$^+$), 300 (19), 203 (14), 184 (90), 157 (87), 115 (57), 73 (100), 59 (60) |
| **16** | 90 (30) | 1685, 1090 (film) | (300 MHz) 1.00–1.30 (42H), 1.32 (d, 3H, $J$ = 6.5), 4.25 (dq, 1H, $J$ = 4.0, 6.5), 8.50 (d, 1H, $J$ = 4.0) | (75.5 MHz) 179.6, 74.4, 22.0, 18.0, 12.2, 11.1 | 385 (15, M$^+$), 184 (36), 157 (100), 115 (40), 59 (40) |

[a] Yields in % based on starting aldehydes via $^1$H NMR and GC. Numbers in parentheses are yields after vacuum distillation.

**Table 2.** Yields, Properties and Spectroscopic Data for Azetidinones **17**–**19**, **21**–**25** and 3,4-Dihydropyridin-2-one **20**

| Product | Yield (%) | IR (solvent) $\nu$ ($cm^{-1}$) | $^1H$ NMR ($CDCl_3$) $\delta$, $J$ (Hz) | $^{13}C$ NMR ($CDCl_3$) $\delta$ | HRMS | MS (70 eV) m/z (%) |
|---|---|---|---|---|---|---|
| **17** | 90 | 1748, 1250 (film) | (200 MHz), −0.17 (s, 3H, SiMe), 0.32 (s, 3H, SiMe), 0.72 (s, 3H, Me), 0.98 (s, 9H, *t*-Bu), 1.45 (s, 3H, Me), 4.31 (s, 1H, HC-4), 7.19–7.40 (m, 5H, arom) | (75.5 MHz) 180.1, 139.0, 128.1, 127.7, 126.0, 65.9, 56.8, 26.3, 24.0, 19.0, 18.0, −5.0, −5.1 | calc. for $C_{17}H_{27}NSiO$ 289.1862 found: 289.1859 | 289 ($M^+$, 5), 274 (4), 232 (5), 162 (8), 135 (3), 132 (100), 117 (36), 91 (8), 73 (4), 59 (5) |
| **18** | 40 | 1750, 1250 (film) | (300 MHz), 0.78 (s, 3H, Me), 1.11 (m, 18H), 1.29 (m, 3H, SiCH), 1.48 (s, 3H, Me), 4.41 (s, 1H, HC-4), 7.21–7.93 (m, 5H, arom) | (75.5 MHz) 180.9, 140.0, 128.1, 127.7, 126.6, 66.4, 56.4, 18.3, 18.2, 18.1, 12.7, 11.8, 11.3 | calc. for $C_{20}H_{33}NSiO$ 331.2331 found: 331.2335 | 331 ($M^+$, 4), 288 (13), 218 (10), 132 (100), 117 (29), 100 (8), 91 (9), 86 (5), 73 (4), 59 (7) |
| **19** | 81 | 1739, 1255 (film) | (200 MHz), 0.18 (s, 3H, Me), 0.26 (s, 3H, Me), 0.97 (s, 9H, *t*-Bu), 1.14 (s, 3H, Me), 1.36 (s, 3H, Me), 3.87 (d, 1H, $J$ = 9.0, HC-3), 6.16 (dd, 1H, $J$ = 9.1, 15.9, PhCH = C*H*), 6.57 (d, 1H, $J$ = 15.9, PhCH), 7.23–7.42 (m, 5H, arom) | (50.3 MHz) 179.6, 136.3, 133.6, 128.8, 128.3, 128.2, 127.9, 126.4, 64.3, 56.6, 26.3, 23.1, 18.4, 17.9, −5.2, −5.4 | calc. for $C_{19}H_{29}NSiO$ 315.2018 found: 315.2021 | 315 ($M^+$, 3), 258 (10), 158 (68), 143 (43), 75 (100) |
| **20** | 35 | 1710, 1651 (film) | (200 MHz), 0.91 (s, 3H, Me), 1.15 (m, 18H), 1.29 (s, 3H, Me), 1.48 (m, 3H, SiCH), 3.3 (d, 1H, $J$ = 4.8, PhCH), 5.22 (dd, 1H, $J$ = 4.8, 7.9, C*H*=CHN), 6.32 (d, 1H, $J$ = 7.9, NCH=), 7.13–7.32 (m, 5H, arom) | (50.3 MHz) 181.6, 140.5, 128.8, 128.2, 128.0, 127.4, 126.8, 109.4, 50.5, 42.3, 26.3, 21.2, 18.3, 18.1, 12.8 | calc. for $C_{22}H_{35}NSiO$ 357.2488 found: 357.2491 | 357 ($M^+$, 5), 201 (5), 174 (10), 132 (16), 131 (98), 103 (81), 75 (100), 45 (35) |
| **21** | 31[a] | 1734, 1250 ($CDCl_3$) | (200 MHz), −0.16 (s, 3H, SiMe), 0.29 (s, 3H, SiMe), 0.7 (t, 3H, $J$ = 7.4, C*H*$_3$CH$_2$), 0.95 (s, 9H, *t*-Bu), 1.45 (m, 2H, CH$_3$C*H*$_2$), 3.45 (m, 1H, HC-3), 4.73 (d, 1H, $J$ = 5.7, PhCH), 7.3 (m, 1H, $J$ = 5.7, PhCH), 7.3 (m, 5H, arom) | (75.5 MHz) 177.0, 138.3, 128.6, 128.0, 127.4, 58.1, 57.3, 29.7, 26.3, 18.8, 11.6, −5.2, −6.0 | calc. for $C_{17}H_{27}NSiO$ 289.1862 found: 289.1858 | 289 ($M^+$, 3), 232 (5), 158 (18), 132 (48), 117 (25), 88 (10), 71 (100), 57 (99) |
| **22** | | 1734, 1250 ($CDCl_3$) | (200 MHz), −0.19 (s, 3H, SiMe), 0.23 (s, 3H, SiMe), 0.93 (s, 9H, *t*-Bu), 1.04 (t, 3H, $J$ = 7.4, C*H*$_3$CH$_2$), 1.82 (m, 2H, CH$_3$C*H*$_2$), 3.04 (dt, 1H, $J$ = 2.4, 6.0, HC-3), 4.20 (d, 1H, $J$ = 2.4, HC-4), 7.3 (m, 5H, arom) | (75.5 MHz) 176.4, 141.7, 128.7, 128.1, 127.9, 127.8, 63.6, 59.3, 26.2, 22.4, 18.6, 11.3, −5.3, −6.1 | calc. for $C_{17}H_{27}NSiO$ 289.1862 found: 289.1855 | 289 ($M^+$, 3), 232 (5), 158 (18), 132 (48), 117 (25), 88 (10), 71 (100), 57 (99) |
| **23** | 70[a] | 3400, 1724, 1265 ($CH_2Cl_2$) | (300 MHz), 0.20 (s, 3H, SiMe), 0.25 (s, 3H, SiMe), 0.97 (s, 9H, *t*-Bu), 1.23 (d, 3H, $J$ = 6.3, CH$_3$), 2.5 (br s, 1H, OH), 3.40 (dd, 1H, $J$ = 6.0, 7.2, HC-3), 4.13 (quintet, 1H, $J$ = 6.7, CHOH), 4.32 (dd, 1H, $J$ = 5.8, 9.4 Hz, HC-4), 6.35 (dd, 1H, $J$ = 15.6, 9.6, PhCH=C*H*), 6.62 (d, 1H, $J$ = 15.8, PhCH=), 7.4 (m, 5H, arom) | (75.5 MHz) 174.5, 136.1, 134.5, 128.7, 128.2, 127.3, 126.5, 77.2, 65.0, 61.2, 55.8, 26.2, 21.6, 18.3, −5.3, −5.5 | calc. for $C_{19}H_{29}NSiO_2$ 331.1968 found: 331.1982 | 331 ($M^+$, 6), 230 (24), 174 (62), 157 (58), 131 (38), 129 (22), 117 (30), 104 (36), 91 (53), 75 (54), 43 (100) |
| **24** | | 3400, 1730, 1265 ($CDCl_3$) | (300 MHz), 0.19 (s, 3H, SiMe), 0.26 (s, 3H, SiMe), 0.97 (s, 9H, *t*-Bu), 1.33 (d, 3H, $J$ = 6.4, Me), 1.7 (bs, 1H, OH), 3.03 (dd, 1H, $J$ = 2.6, 6.5, HC-3), 4.04 (dd, 1H, $J$ = 2.7, 9.3, HC-4), 4.12 (quintet, $J$ = 6.4, 1H, CHOH), 6.19 (dd, 1H, $J$ = 9.1, 15.7, PhCH=C*H*), 6.60 (d, 1H, $J$ = 15.7, PhCH=), 7.35 (m, 5H, arom) | (75.5 MHz) 173.8, 136.0, 132.7, 129.7, 128.7, 128.1, 128.0, 126.4, 77.2, 66.5, 64.9, 55.3, 26.2, 21.2, 18.3, −5.3, −5.6 | calc. for $C_{19}H_{29}NSiO_2$ 331.1968 found: 331.1970 | 331 ($M^+$, 4), 230 (14), 174 (67), 157 (46), 131 (30), 129 (23), 117 (22), 104 (26), 91 (35), 75 (25), 43 (100) |
| **25** | 70 | 3350, 1740, 1710, 1250, 1255 ($CDCl_3$) | (200 MHz), 0.1 (s, 6H, SiMe$_2$), 0.22 (s, 3H, SiMe), 0.28 (s, 3H, SiMe), 0.86 (s, 9H, *t*-Bu), 1.18 (d, 3H, $J$ = 6.2, CH$_3$), 3.7 (m, 1H, C-4H), 4.14 (m, 1H, CHOSi), 4.53 (dd, $J$ = 2.84, 8.06, C-3H), 5.1 (m, 2H, CH$_2$Ph), 5.35 (d, 1H, $J$ = 8.1, NH), m, 5H, arom) | (50.3 MHz) 172.8, 155.2, 136.1, 128.4, 128.0, 67.1, 67.0, 62.0, 58.9, 26.2, 25.6, 18.7, 17.9, 17.4, −4.6, −5.0, −5.3, −5.4 | calc. for $C_{25}H_{44}N_2Si_2O_4$ 492.2840 found: 492.2849 | 492 ($M^+$, 3), 435 (5), 235 (35), 161 (11), 149 (11), 108 (34), 107 (26), 91 (100), 75 (18), 73 (29) |

[a] Yields referred to are *cis* + *trans* azetidinones.

In conclusion, we describe a new efficient synthesis of *N*-(TIPS)- and *N*-(TBDMS)imines starting from enolizable and non-enolizable aldehydes. We have also explored their reactivity against ester enolates that directly afford barely accessible *N*-(TBDMS)azetidin-2-ones. *N*-(TBDMS)imines predominantly give *trans* azetidinones complementing the corresponding *N*-(TMS)imines that instead afford *cis* derivatives.

Commercially available compounds were used without further purification. THF was freshly distilled from sodium benzophenone ketyl. IR spectra were recorded on a FTIR Nicolet 205. NMR spectra were performed on a Varian Gemini 200 and Gemini 300 instruments. Exact masses were recorded with a VG 7070 E mass spectrometer. TLC was performed on silica gel 60 F-254 plates and column chromatography on Merck Kieselgel 60 (230–400 mesh). *N*-(*tert*-Butyldimethylsilyl)- and *N*-(triisopropylsilyl)amine were prepared as described in the literature.[12]

**N-(Triisopropylsilyl)- and N-(*tert*-Butyldimethylsilyl)imines; General Procedure:**

At 0 °C under inert atmosphere, BuLi in hexane (2.5 M, 1.2 mmol) was dropped into a THF (5 mL) solution of the amine **1** or **2** (1 mmol) and the mixture was stirred for 1 h at r.t. The aldehyde **3** (1 mmol) was then added at low temperature (0 °C for aromatic and −40 °C for aliphatic substrates) to the lithium amide solution and the mixture was stirred for 1 h. The reaction was warmed to r.t. and the solvent removed under vacuum. Imines **4**, **9**, **10** and **16** could be purified by vacuum distillation (**4**: bp = 72 °C, $5 \times 10^{-5}$ mbar; **9**; bp = 57 °C, $1.2 \times 10^{-5}$ mbar; **10**: bp = 90 °C, 0.7 mbar; **16**: bp = 110 °C, $2.5 \times 10^{-5}$ mbar).

**Azetidinones: General Procedure:**

To a solution of LHMDSA (1 M in THF, 1.2 mL, 1.2 mmol) in THF (5 mL) at −78 °C, was added the appropriate ester (1 mmol) at a rate such that the temperature did not exceed −70 °C. The mixture was stirred for 1 h at −78 °C and after that the selected silylimine (1 mmol) (obtained by the general procedure as a crude THF solution) was added dropwise over a period of 5 min. The mixture was allowed to warm to r.t. and stirred overnight. The resulting solution was diluted with EtOAc (10 mL) and washed with dil. HCl (1 M, 20 mL). The aqueous washes were re-extracted with EtOAc (2 × 20 mL) and the combined organic layers were dried and concentrated in vacuo. The residue was purified by chromatography over silica gel (cyclohexane/EtOAc = 8/2).

**3-(Benzyloxycarbonylamino)azetidin-2-one 25 from STABASE:**

To a solution of LHMDSA (1 M in THF, 1.2 mL, 1.2 mmol) in THF (5 mL), at −78 °C, was added the STABASE (1 mmol) at a rate such that the temperature did not exceed −70 °C. The mixture was stirred for 1 h at −78 °C and after that the selected silylimine **4** or **9** (1 mmol) (obtained by the general procedure as a crude THF solution), was added dropwise over a period of 5 min. The mixture was allowed to warm to r.t. and stirred overnight. To the resulting brown solution, at 0 °C, sat. aq $NH_4Cl$ (2 mL) was added and the pH was adjusted to 4 with 1 M HCl followed by addition of $NaHCO_3$ till pH 8 was reached. Benzyl chloroformate (2 mmol) dissolved in acetone (2 mL), was added dropwise. After stirring 3 h at r.t., the mixture was extracted with EtOAc (20 mL) and the organic layers were washed with brine, dried and concentrated. The residue was purified by chromatography over silica gel (cyclohexane/EtOAc = 8/2).

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