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The synthesis, structure, and some reactions of sterically hindered α-silylisoxazoles

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Abstract

4-(4,5-Dihydro-4,4-dimethyl-2-isoxazolyl)-3-phenyl-5-silylmethylisoxazole and 3-phenyl-5-silylmethyl-4-isoxazole-t-carboxamide derivatives were synthesized in synthetically useful yields from the corresponding oxazolyl-isoxazole or t-carboxamide by metalation of the isoxazole systems at the C(5) alkyl group followed by electrophilic quenching with either t-butylchlorodiphenylsilane or t-butylchlorodimethylsilane. The silylisoxazole systems were metalated at the C(5) position, producing the corresponding α-silyl carbanion, which upon quenching with MeOD produced C(5) deuterium incorporation. The reaction of silyloxazolylisoxazoles with titanium tetrachloride caused the oxazoline ring to open forming chloro-substituted carboxamide. The X-ray structure of a silyloxazolylisoxazole was obtained and indicates an "*s-trans*" ring juncture with respect to the heterocyclic rings.

Introduction

The chemistry of α-silyl carbanions is a rich and fertile field [1a]. A recent observation by Larson of C-silylation using chlorodiphenylmethylsilane has led to an important extension in the versatility of α-silyl carboxylates [1b,1c]. Isoxazoles are versatile synthetic equivalents, yet there exist only a few reports of silyl derivatives of this heterocycle. Silyl derivatives of simple alkylisoxazoles have been reported [2], but isoxazoles with electron-withdrawing groups in the C(4) position are known to undergo Michael addition with alkyllithium reagents [3] (Fig. 1). Our interest in the study of functionally complex isoxazoles has led us to examine the synthesis, structure and reactions of α-silylalkylisoxazoles with C(4) carboxyl equivalents [4]. We had reported earlier [5] that the reaction of alkyllithioisoxazoles derived from I with chlorotrimethylsilane gave rise to multiple electrophilic incorporation at the C(5) position (Fig. 2). We have now found that this problem can be circumvented by the use of bulky alkyl- and aryl-silanes.

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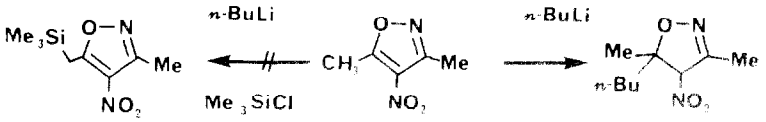

Fig. 1. Nucleophilic addition to the isoxazole ring.

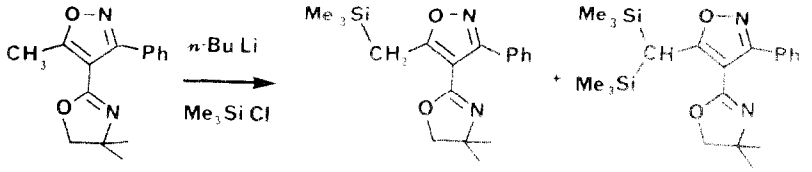

Fig. 2. Multiple electrophilic incorporation at the C(5) position.

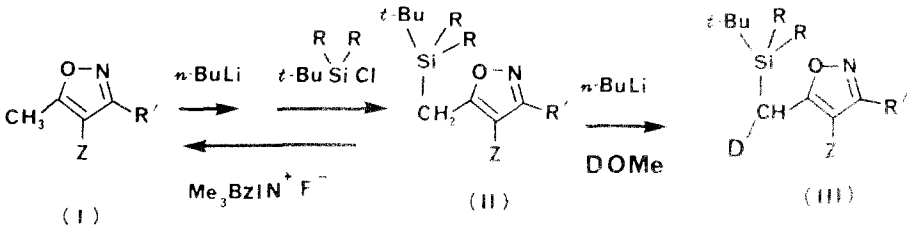

Fig. 3. General reaction scheme: Synthesis, generation and electrophilic quenching of 5-α-silylmethylisoxazolyl carbanions.

The silyl derivatives provide readily isolable compounds for study of the structure and chemical reactivity of these ambident C-silyl vinylogous carbanions. In addition, the α-silyl carbanions described in this paper represent the synthetic equivalent of highly functionalized geminal carbanions and, as such, present numerous possibilities to the organic chemist.

The reaction of I with n-butyllithium at −78 °C, THF, 2 h, followed by addition of an organosilyl chloride, yielded II, with clean silylation (Fig. 3), in moderate to good yields after isolation and purification (Table 1). II represents a highly substituted allylsilane, and we hoped that it would react as such [1]. However,

Table 1

Metalation and electrophilic quenching of I to produce II

Entry	R	R′	Z	% II	m.p.(°C)	Formula	MS. *m/z* (rel.int.)
1	Me	Ph	[a]	78.3	50–53	$C_{21}H_{30}N_2O_2Si$	371, (18)
2	Me	Ph	[b]	63.0	89–91	$C_{31}H_{36}N_2O_2Si$	497, (4.4)
3	Me	Ph	[c]	40.8	96–99	$C_{23}H_{36}N_2O_2Si$	401, (7.4)
4	Ph	Me	[a]	34.0	84–85	$C_{26}H_{32}N_2O_2Si$	432, (1.1)
5	Me	Me	[d]	32.0	oil	$C_{18}H_{32}N_2O_2Si$	353, (5.2)

[a] Z = 2-(4,4-dimethyl)-Δ^2-oxazoline. [b] Z = *N*,*N*-dibenzyl carboxamide. [c] *N*,*N*-diisopropyl carboxamide. [d] Z = (*S*)-2′-methoxymethylpyrrolidinyl carboxamide.

Table 2

Generation and electrophilic quenching of 5-silylmethylisoxazolyl carbanions

Entry	R	R′ [a]	Time (h)	T (°C)	Electrophile	Deuterium incorporation (%) [b]
1	Me	Ph	2	−78	MeOD	56
2	Me	Ph	4	−78	MeOD	86–72
3	Ph	Me	2	−78	MeOD	73

[a] Z = 2-(4,4-dimethyl)-Δ^2-oxazoline. [b] Determined by mass spectrometry.

treating IIa with benzaldehyde dimethylacetal in the presence of a Lewis acid, $TiCl_4$ [11] produced a ring opened isoxazole-4-yl-chlorocarboxamide (IV, Fig. 4) when Z was oxazoline. It has previously been reported [12] that trialkylallylsilanes react with acetals in the presence of catalytic amounts of trimethylsilyl trifluoromethanesulfonate, yielding an allyl ether. IIa produced no such results, which we again attribute to the basicity of the oxazoline nitrogen.

Formation of the α-silyl carbanion was observed under standard thermodynamic metalation conditions, that is, a solution of butyllithium was added dropwise to a cold THF solution of the organic acid II. Deuterium incorporation occurred exclusively at the C(5) substituent on the isoxazole ring to give III (Table 2) (Fig. 3).

Discussion

Silylation with bulky silyl groups produces clean monoincorporation, and subsequent metalation of the silylisoxazoles followed by electrophilic quenching with MeOD showed that deprotonation again occurs at the C(5) alkyl group of the isoxazole ring.

Lewis acid catalyzed reaction of the silyloxazolylisoxazole systems revealed that the lone pair electrons on the oxazoline nitrogen appear to be sufficiently basic to complete the Lewis acid (in this case, $TiCl_4$) yielding the chlorosilylisoxazoleamide (Fig. 4).

This titanium mediated ring opening of oxazolines could prove to be of general usefulness as an ethyleneimine synthetic equivalent.

Crystal structure of 4-(4,5-dihydro-4,4-dimethyl-2-oxazolyl)-5-(t-butyldiphenylsilyl)-methyl-3-methylisoxazole

Figure 5 shows the thermal ellipsoids along with the atom numbering scheme. Hydrogen atoms are omitted for clarity. Atomic coordinates, bond lengths, and bond angles are shown in Tables 3 to 5, respectively. All isoxazole distances are as expected. The maximum deviation from planarity is 0.3 Å. The plane of the oxazoline ring as defined by O(2), C(5) and N(2) is out of plane with the isoxazole ring by 7°. The rest of the oxazoline ring is tilted toward the planar part of the oxazoline by 14.7°. The two phenyl groups bound to the silicon are tilted toward each other by 50.1°. The bulky silyl group makes the *s-trans* form the preferred conformation (structure V in Fig. 6). In the isoxazoleoxazoline reported earlier in which the silyl group was replaced with an α-hydroxytolyl group (structure VI, Fig. 6) the preferred conformation was the *s-cis* isomer. In V, the oxazoline nitrogen N(2) is on the same side of the isoxazole as the C(3) methyl group. If indeed this

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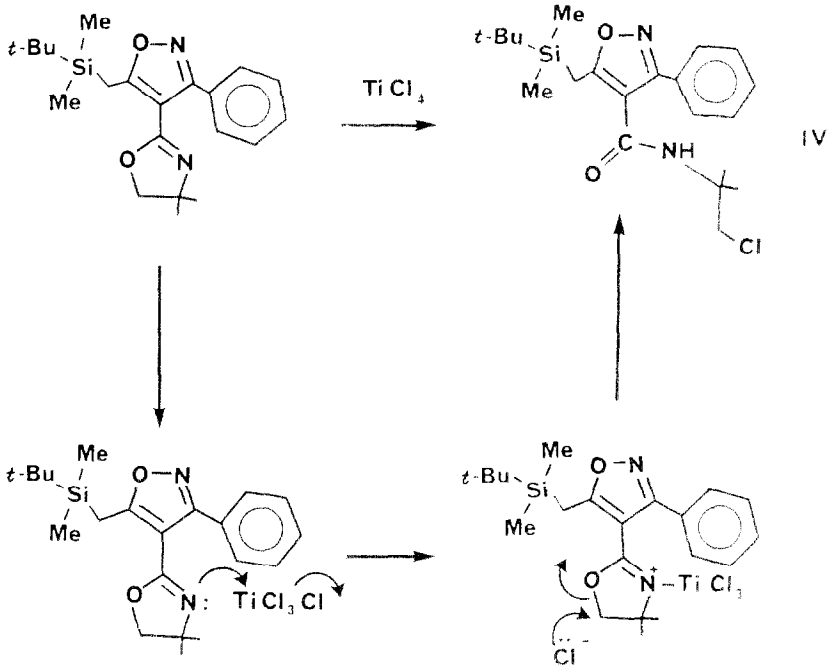

Fig. 4. Oxazoline ring cleavage.

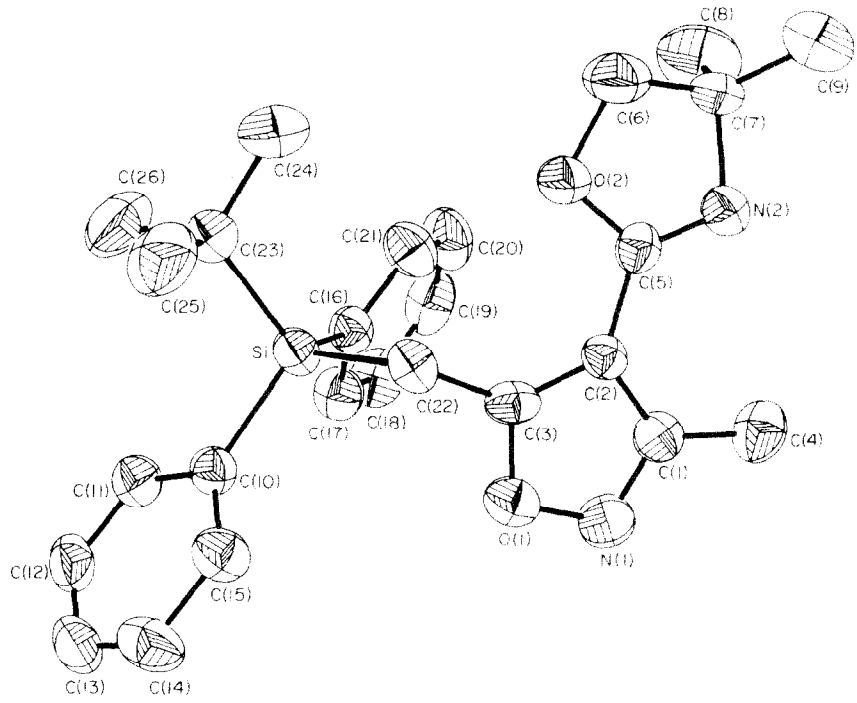

Fig. 5. Structure of 4-(4,5-dihydro-4,4-dimethyl-2-oxazolyl)-5-(t-butyldiphenylsilyl)methyl-3-methylisoxazole.

Table 3

Atomic coordinates ($\times 10^4$) and isotropic thermal parameters (2×10^3)

	x	y	z	U^a
Si	4580(1)	1535(1)	2439(1)	40(1)
C(1)	5902(3)	6152(3)	3639(2)	45(1)
C(2)	4676(3)	4976(3)	3513(2)	37(1)
C(3)	5346(3)	4110(3)	3710(2)	40(1)
C(4)	5857(4)	7428(3)	3535(3)	64(2)
C(5)	3057(3)	4763(3)	3215(2)	40(1)
C(6)	618(4)	3563(3)	2857(4)	76(2)
C(7)	756(3)	4865(3)	2660(3)	50(1)
C(8)	12(4)	4783(5)	1348(4)	101(3)
C(9)	111(4)	5537(4)	3290(4)	98(3)
C(10)	6388(3)	1206(3)	2855(2)	42(1)
C(11)	6609(3)	467(3)	2032(3)	52(2)
C(12)	7886(4)	148(3)	2351(4)	62(2)
C(13)	8994(4)	560(3)	3511(4)	66(2)
C(14)	8832(4)	1287(3)	4338(3)	65(2)
C(15)	7550(3)	1612(3)	4024(3)	53(2)
C(16)	4243(3)	2253(3)	1148(2)	43(1)
C(17)	5293(4)	2578(3)	666(3)	54(2)
C(18)	5048(4)	3146(3)	−254(3)	67(2)
C(19)	3743(4)	3420(3)	−724(3)	69(2)
C(20)	2708(4)	3127(3)	−255(3)	69(2)
C(21)	2955(4)	2564(3)	669(3)	59(2)
C(22)	4800(3)	2741(3)	3721(2)	46(1)
C(23)	2880(3)	−43(3)	2142(3)	51(2)
C(24)	1340(4)	122(4)	1823(4)	83(2)
C(25)	3273(4)	−502(4)	3265(3)	82(2)
C(26)	2628(4)	−1097(3)	1139(4)	89(2)
N(1)	7201(3)	5999(3)	3882(2)	60(1)
O(2)	2082(2)	3515(2)	3003(2)	65(1)
O(1)	6860(2)	4693(2)	3926(2)	55(1)
N(2)	2486(3)	5599(2)	3117(2)	54(1)

[a] Equivalent isotropic U defined as one-third of the trace of the orthogonalised U_{ij} tensor.

Table 4

Bond lengths (Å)

Si–C(10)	1.874(3)	Si–C(16)	1.877(3)
Si–C(22)	1.903(3)	Si–C(23)	1.903(3)
C(1)–C(2)	1.432(4)	C(1)–C(4)	1.480(5)
C(1)–N(1)	1.305(5)	C(2)–C(3)	1.359(5)
C(2)–C(5)	1.459(4)	C(3)–C(22)	1.469(4)
C(3)–O(1)	1.352(3)	C(5)–O(2)	1.356(3)
C(5)–N(2)	1.256(4)	C(6)–C(7)	1.493(5)
C(6)–O(2)	1.442(5)	C(7)–C(8)	1.524(5)
C(7)–C(9)	1.500(7)	C(7)–N(2)	1.499(3)
C(10)–C(11)	1.402(5)	C(10)–C(15)	1.400(4)
C(11)–C(12)	1.379(6)	C(12)–C(13)	1.375(5)
C(13)–C(14)	1.360(6)	C(14)–C(15)	1.388(5)
C(16)–C(17)	1.391(5)	C(16)–C(21)	1.391(5)
C(17)–C(18)	1.377(5)	C(18)–C(19)	1.379(6)
C(19)–C(20)	1.363(7)	C(20)–C(21)	1.378(5)
C(23)–C(24)	1.533(5)	C(23)–C(25)	1.529(6)
C(23)–C(26)	1.530(6)	N(1)–O(1)	1.418(4)

Table 5

Bond angles (°)

C(10)–Si–C(16)	110.3(2)	C(10)–Si–C(22)	110.4(1)
C(16)–Si–C(22)	108.0(1)	C(10)–Si–C(23)	108.1(1)
C(16)–Si–C(23)	113.2(1)	C(22)–Si–C(23)	106.8(2)
C(2)–C(1)–C(4)	129.1(3)	C(2)–C(1)–N(1)	111.1(3)
C(4)–C(1)–N(1)	119.8(3)	C(1)–C(2)–C(3)	104.9(3)
C(1)–C(2)–C(5)	127.0(3)	C(3)–C(2)–C(5)	128.1(2)
C(2)–C(3)–C(22)	135.0(2)	C(2)–C(3)–O(1)	109.1(2)
C(22)–C(3)–O(1)	115.9(3)	C(2)–C(5)–O(2)	115.1(3)
C(2)–C(5)–N(2)	127.0(2)	O(2)–C(5)–N(2)	117.9(3)
C(7)–C(6)–O(2)	104.4(3)	C(6)–C(7)–C(8)	111.4(3)
C(6)–C(7)–C(9)	113.7(4)	C(8)–C(7)–C(9)	110.3(3)
C(6)–C(7)–N(2)	103.0(3)	C(8)–C(7)–N(2)	106.8(3)
C(9)–C(7)–N(2)	111.3(2)	Si–C(10)–C(11)	122.1(2)
Si–C(10)–C(15)	121.8(3)	C(11)–C(10)–C(15)	116.0(3)
C(10)–C(11)–C(12)	122.2(3)	C(11)–C(12)–C(13)	119.8(6)
C(12)–C(13)–C(14)	119.9(4)	C(13)–C(14)–C(15)	120.6(3)
C(10)–C(15)–C(14)	121.5(3)	Si–C(16)–C(17)	122.8(2)
Si–C(16)–C(21)	120.8(3)	C(17)–C(16)–C(21)	116.3(3)
C(16)–C(17)–C(18)	121.7(3)	C(17)–C(18)–C(19)	120.5(4)
C(18)–C(19)–C(20)	118.8(4)	C(19)–C(20)–C(21)	120.8(4)
C(16)–C(21)–C(20)	121.8(4)	Si–C(22)–C(3)	116.3(2)
Si–C(23)–C(24)	112.6(2)	Si–C(23)–C(25)	108.1(2)
C(24)–C(23)–C(25)	107.9(4)	Si–C(23)–C(26)	111.2(3)
C(24)–C(23)–C(26)	108.3(3)	C(25)–C(23)–C(26)	108.6(3)
C(1)–N(1)–O(1)	105.8(2)	C(5)–O(2)–C(6)	105.1(3)
C(3)–O(1)–N(1)	109.0(2)	C(5)–N(2)–C(7)	106.0(2)

nitrogen assists in the metalation reaction, one would expect that this silyl derivative should react at the C(3) position in subsequent metalations. However, experiments in this direction have not yet been successful in that no C(3) metalation has been observed. The subsequent metalation of the silyl derivative at the C(5) position suggests that either the isoxazole or the oxazoline oxygen may assist in the metalation since it is on the same side as the isoxazole C(5) methylene group. Indeed, if one looks at the non-bonded distance between the isoxazole oxygen and one of the C(5) methylene hydrogens one finds a distance of 2.35 Å which is clearly short enough to coordinate to the base that deprotonates the methylene group. This

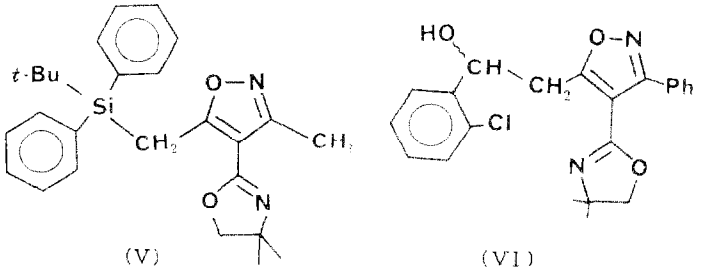

Fig. 6. *s-trans*- (V) and *s-cis*-isoxazolyloxazolines (VI).

is in contrast to the structure of the benzaldehyde adduct of the 3-phenyl-5-methyl-4-oxazolylisoxazole (VI) in which the C(5) methyl of the isoxazole and the oxazoline oxygen are on opposite sides of the isoxazole ring. A definitive conclusion as to whether the oxazoline oxygen assists in the metalation cannot be reached until more derivatives have been synthesized and characterized. The application of this methodology to the synthesis of target molecules of biological significance is currently under active investigation in our laboratories, and our progress will be reported in due course.

Experimental

Mass spectra were measured on a VG 7070 GC/MS with model 11/250 data system. The following abbreviations are used: Electron Impact, EI; Chemical Ionization, CI; Fast Atom Bombardment, FAB. ^{1}H NMR were obtained on a Varian Em-360 or JEOL FX-90Q spectrometers and are reported in ppm downfield from tetramethylsilane as internal standard. When peak multiplicities are reported, the following abbreviations are used: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broadened. ^{2}H and ^{13}C NMR were obtained on the JEOL. IR spectra were obtained on a Digilab FTS-80 or Qualimatic Spectrometer as neat liquids or melts on NaCl plates unless noted otherwise. Combustion analyses were performed either by Mic Anal Organic Analysis or a LECCO CHN-600 carbon, hydrogen and nitrogen analyzer. Preparative thin layer chromatography (PTLC) was performed on a Harrison Associates Chromatotron, using silica gel unless specified otherwise. For reactions under inert atmosphere, the inert gas (Ar or N_2) was passed over activated catalyst R3-11 followed by indicator Drierite. Tetrahydrofuran (THF) was distilled from sodium and benzophenone. All chromatography solvents (hexane, CH_2Cl_2, $CHCl_3$, EtOAc, MeOH) were distilled. Organolithium reagents were titrated using the procedure of Ronald [13].

Crystals of V were obtained by recrystallization from boiling hexane. Cell constants were determined by a least-squares fitting of setting angles for 25 reflections between 28° and 30°. Formula $C_{26}H_{32}N_2O_2Si$, m.w. = 432.644. Triclinic space group $P\bar{1}$, a 10.120(1), b 11.329(1), c 12.741(2) Å, α 96.23(1), β 112.62(1), γ 109.25(1)°, μ 1.2 cm^{-1}, $d_{calc.}$ 1.18 g/cm^{-3}, $F(000) = 464$, $Z = 2$.

Data were collected on a Nicolet R3/m diffractometer by the ω scan technique [14] using graphite monochromatized Mo-K_α radiation (λ 0.71069 Å). The measured intensities were corrected for Lorentz and polarization effects but not for absorption. The structure was solved using the SHELXTL program [15]. All non-hydrogen atoms were refined anisotropically; all hydrogen atoms were restricted N–H and C–H distances of 0.96 Å and their thermal parameters were set at 0.2. 3378 reflections were collected with 2632 unique reflections ($I(F) > 3\sigma(F)$). The final R value was 0.049 with $R_w = 0.052$. The largest peak on final Fourier difference may was 0.31e$^-$/Å^3 near C.

A list of anisotropic thermal parameters, H atom coordinates, isotropic thermal parameters, and observed and calculated structure factors have been provided to the editor (19 pages).

4-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-5-(t-butyldimethylsilyl)methylisoxazole, R = Ph (II, Table 1, entry 1). An oven dried round bottom flask was charged with 4,4-dimethyl-2-(3-phenyl-5-methyl-isoxazol-4-yl)-Δ^2-oxazoline, (I), (9.5 g, 37.2 mmol)

and freshly distilled THF (25 ml). To this solution, cooled to −78°C under nitrogen atmosphere, butyllithium (21 ml, 37.2 mmol) was added dropwise and allowed to metalate for 2 h at −78°C. The anion was quenched by the dropwise addition of t-butyldimethylsilyl chloride (5.6 g, 37.2 mmol) in THF (10 ml), followed by warming to room temperature overnight. The THF solution was then concentrated and the residue extracted with three 25 ml portions of CH_2Cl_2; the extract was dried over anhydrous Na_2SO_4, concentrated and the residue chromatographed on silica gel (CH_2Cl_2). The product IIa was obtained as an oil which crystallized on standing. (10.8 g, 78.3%): m.p. 50–53°C. ^{1}H NMR: δ 7.0–8.0 (m, 5H); 3.91 (s, 2H); 2.61 (s, 2H); 1.32 (s, 6H); 0.95 (s, 9H); 0.00 (s, 6H) ppm. ^{13}C NMR: δ 176.30, 161.10, 156.16, 129.28, 128.74, 127.79, 102.52, 87.63, 78.27, 67.19, 28.04, 25.95, 16.59, 14.51, −6.05 ppm. IR: 3065, 2958, 2929, 1667, 1652, 1464, 1020, 813, 695 cm^{-1}. Mass spectrum: FAB: *m/z* 371 (18.0% rel. intensity), 313 (25.1), 73 (100). EI: 370 (0.4), 355 (3.7), 313 (100), 258 (2.2), 241 (8.7), 239 (7.9), 199 (10.5), 77 (15.0), 75 (17.2), 73 (56.7), 59 (8.1), 56 (12.0). CI: 373 (2.2), 372 (7.5), 371 (25.7), 314 (25.9), 313 (100), 73 (30.5). Anal. Found: C, 68.00; H, 8.10; N, 7.82. $C_{21}H_{30}N_2O_2Si$ calcd.: C, 68.05; H, 8.18; N, 7.56%.

4-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-5-(t-butyldiphenylsilyl)methyl-3-phenylisoxazole, R = Me) (II, Table 1, entry 4). M.p. 84–85°C. b.p. 185–195°C (0.15 mmHg). Mass spectrum: *m/z* 432 (M^+, 1.1% rel. intensity), 417 (0.8), 375 (100), 303 (12.3), 261 (23), 199 (16), 197 (19), 135 (56). IR: 1425, 1105 (Ph–Si stretch) cm^{-1}. ^{1}H NMR: 7.1–7.7 (m, 10H); 3.7 (s, 2H); 3.3 (s, 2H); 2.3 (s, 3H); 1.3 (s, 6H); 1.2 (s, 9H) ppm. ^{13}C NMR: 173.42, 158.22, 155.18, 135.22, 132.36, 128.61, 126.64, 103.87, 74.97, 66.21, 27.59, 26.76, 17.76, 12.40, 10.97 ppm. Anal. Found: C, 72.22; H, 7.5; N, 6.59. $C_{26}H_{32}N_2O_2Si$ calcd.: C, 72.18; H, 7.46; N, 6.47%.

4-N,N-Dibenzyl-5-(t-butyldimethylsilyl)methyl-3-phenylisoxazole carboxamide, R = Ph) (II, Table 1, entry 2). M.p. 89–91°C. ^{1}H NMR: δ 7.50–6.00 (m, 15H); 4.27 (s, 2H); 3.76 (s, 2H); 1.97 (s, 2H); 0.80 (s, 9H); 0.00 (s, 6H) ppm. ^{13}C NMR: δ 172.37, 164.50, 159.67, 136.25, 129.76, 128.98, 128.57, 127.61, 127.08, 110.10, 51.04, 26.01, 16.59, 13.08, −5.81 ppm. Mass spectrum, CI: *m/z* 497 (4.4% rel. intensity), 440 (32.0), 439 (92.7), 349 (17.3), 92 (10.9), 91 (100), 77 (9.1), 75 (13.6), 73 (45.7). IR: 3032, 2956, 2897, 1620, 1590, 1570, 1461, 1454, 1245, 1194, 1070, 827, 705 cm^{-1}. Anal. Found: C, 75.15; H, 7.46; N, 5.46. $C_{31}H_{36}N_2O_2Si$ calcd.: C, 74.94; H, 7.32; N, 5.64%.

5-(t-Butyldimethylsilyl)methyl-3-phenyl-4-diisopropylisoxazole carboxamide, R = Ph) (II, Table 1, entry 3). M.p. 96–99°C, b.p. 145°C/0.06 mmHg. ^{1}H NMR: 7.00–8.00 (m, 5H);; 3.00–4.00 (m, 2H); 2.11 (s, 2H); 1.47 (s, 6H); 1.33 (s, 6H); 0.82 (s, 9H); 0.70 (s, 6H); 0.53 (s, 6H); 0.00 (s, 6H) ppm. ^{13}C NMR: 171.1, 163.1, 159.4, 129.8, 128.9, 128.6, 127.7, 111.8, 51.0, 45.5, 26.1, 20.2, 20.1, 16.7, 12.9, −5.8 ppm. IR: 3059, 2960, 1622, 1463, 1030, 838, 779, 723 cm^{-1}. Mass spectrum, CI: *m/z* 401 (7.4% rel. intensity), 344 (26.8), 343 (100), 301 (19), 226 (12.0), 141 (13.4), 118 (21.7), 77 (11.6), 75 (24.6), 74 (10.2), 73 (67.8), 57 (11.2). EI: 385 (2.2), 345 (5.5), 344 (23.4), 343 (87.0), 301 (20.5), 226 (11.6), 144 (13.7), 143 (10.8), 141 (20.3), 118 (21.9), 77 (19.9), 75 (28.8), 74 (14.4), 73 (100, 59 (14.5), 57 (14.4). Anal. Found: C, 68.96; H, 9.41; N, 6.79. $C_{23}N_{36}H_2N_2O_2Si$ calcd.: C, 68.94; H, 9.07; N, 6.99%.

II desilylates with ease in the presence of *N,N,N*-trimethyl-*N*-benzylammonium fluoride [12], THF, −78°C, to produce I in good yields (84% yield).

(3-Chloro-2-methyl-5-(t-butyldimethylsilyl)methyl-3-phenyl-4-isoxazole-propylcar-

boxamide, R = Ph) (IV). ^{1}H NMR: δ 7.0–8.0 (m, 5H), 3.74 (s, 2H), 2.71 (s, 2H), 1.15 (s, 6H), 0.92 (s, 9H), 0.00 (s, 6H) ppm. ^{13}C NMR: 177.9, 161.3, 159.9, 130.2, 129.2, 128.9, 128.4, 127.6, 63.7, 54.2, 50.8, 26.1, 24.9, 14.7, 0.9, −5.9 ppm. Mass spectrum EI: *m/z* 407 (2.1% rel. intensity), 355 (3.5), 349 (4.4), 314 (25.2), 313 (100), 241 (10.3), 239 (9.2), 199 (12.2), 77 (16.7), 75 (24.8), 73 (70.8). Isotope cluster abundance calculations for $C_{21}H_{32}N_2O_2SiCl$ (*M* + H): *m/z* 407 (100% rel. intensity), 408 (20.09), 409 (40.01), 410 (10.96). Found: 407 (100), 408 (33), 409 (42.8), 410 (9.5).

5-(t-Butyl-dimethylsilyl)methyl-(S)-2-methoxymethy-4-isoxazole-pyrrolidinylcarboxamide, R = Me (II, Table 1, entry 5). B.p. 160–170 °C, 0.06 mmHg. Mass spectrum, *m/z*, 353 (*M* + 1, 5.2), 337 (5.3), 296 (13.4), 295 (63.2), 239 (13.9), 238 (65.3), 149 (25.5), 141 (12.9), 115 (3.8), 75 (34.1), 73 (100), 71 (15), 70 (14.7), 59 (15.7), 57 (36.7), 55 (11.6). ^{13}C NMR: 163.7, 158.7, 113.0, 73.6, 59.9, 57.4, 228.6, 27.0, 17.5, 14.7, 11.5, −4.9 ppm. ^{1}H NMR: 3.40 (s, br, 5H), 3.33 (s, 3H), 2.20 (s, 3H), 1.89 (s, br, 6H), 0.90 (s, 9H), 0.00 (s, 6H) ppm. IR: 2940, 1618, 1590, 1451, 1439, 1280, 1247, 1189, 1073, 1000, 820, 690 cm^{-1}.

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