A study on the influence of a silicon group on the Curtius reaction

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The effect of a dimethyl(phenyl)silyl group at different positions with respect to an acyl azide moiety on the Curtius reaction has been investigated. A silyl group at the β-position enhanced the reaction rate by about three times compared to a non-silylated analog. However, a silyl group at the γ-position had only a minor influence on the reaction. A diacyl azide having a silyl group at the β-position with respect to one acyl azide group and at the γ-position with respect to the other acyl azide group has been prepared and subjected to the Curtius reaction in order to evaluate the possible synthetic potential which originates from the control exerted by the silicon group in such systems.

Introduction

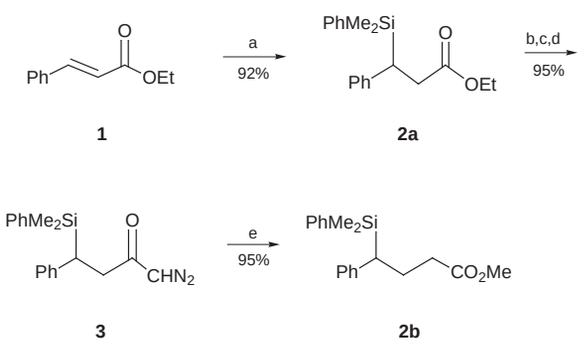
The stabilization of an electron deficient centre such as a carbocation or a carboradical at the β-position (β-effect)[1] with respect to a silicon group is the central theme of organosilicon chemistry applied to organic synthesis. This is clearly demonstrated by the enhanced rates of unimolecular solvolysis[2] of β-(trimethylsilyl) esters compared to the corresponding silicon-free analogues. The regio- and stereo-selectivity of electrophilic substitution reactions of allyl-, vinyl-[3] and aryl-silanes[4] have been shown to be controlled by the β-effect. This stabilizing effect also plays an important role in directing the regioselectivity in various organic reactions. Some recent examples include Baeyer–Villiger oxidation,[5] Bamford–Stevens reaction,[6] Beckmann fragmentation,[7] Norrish type I and II cleavages,[8] palladium-catalysed nucleophilic substitution,[9] Nazarov cyclizations,[10,11] decarboxylation reactions[12] and stereospecific 1,2-silyl shifts.[13] The stabilization of an electron deficient centre at the γ-position with respect to a silicon group (γ-effect) does not appear to be as prevalent as the β-effect. Nevertheless, the existence of the γ-effect[14] has been exemplified by the solvolysis of γ-silyl-substituted compounds.[15] There are also a few examples where the γ-effect has been successfully used in organic synthesis such as reactions of homoallylsilanes,[16] the Nef reaction[17] and the oxidative fragmentation of γ-hydroxysilanes.[18] The effect of a silicon group beyond the γ-position is rarely observed. This is evidently due to the fact that the 'functional groups are too far away to have an effect on one another'.[19]

The Curtius reaction[20] involves a unimolecular rearrangement[21] of acyl azides ($RCON_3$) to isocyanates (RNCO) with retention of configuration[22] at the migrating group. This reaction has been successfully applied in many useful synthetic transformations for the generation of a primary amine functionality from a carboxylic acid with one fewer carbon atom, and it has also been used in the synthesis of many complex frameworks for natural product syntheses.[23,24] As a part of our ongoing programme on the use of silicon directed reactions in organic synthesis,[24] we were interested in studying the effect of a silicon group at different positions with respect to the acyl azide group on this rearrangement reaction. To the best of our knowledge, the effect of a silicon group on the Curtius reaction is not well known. The work describes a systematic study of the effect of a silicon group at various positions.

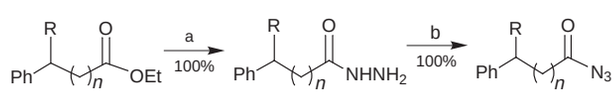
The required silyl-substituted acyl azides were prepared and the kinetic studies were performed to quantify the rate of the reaction. Similarly, a 1,4-diacyl azide was prepared in which the silicon group was at the β-position with respect to one acyl azide group and at the γ-position with respect to the other. The influence of their relative positions *vis-a-vis* the silicon group was also investigated.

Results and discussion

The acyl azides **5a**,**b** having a dimethyl(phenyl)silyl group ($PhMe_2Si$) at the β- and γ-positions respectively were prepared from the corresponding acid hydrazides **4a**,**b**. The latter were obtained from the corresponding silyl esters **2a**,**b** by hydrazinolysis in methanol. Silyl cupration[25] of ethyl cinnamate (**1**) provided the β-silyl ester **2a** whereas the γ-silyl ester **2b** was obtained from it by one carbon homologation *via* the α-diazomethyl ketone **3** (Schemes 1 and 2). The corresponding



Scheme 1 *Reagents and conditions*: a, $(PhMe_2Si)_2CuCNLi_2$; b, NaOH, EtOH; c, $(COCl)_2$, DMF; d, CH_2N_2; e, light

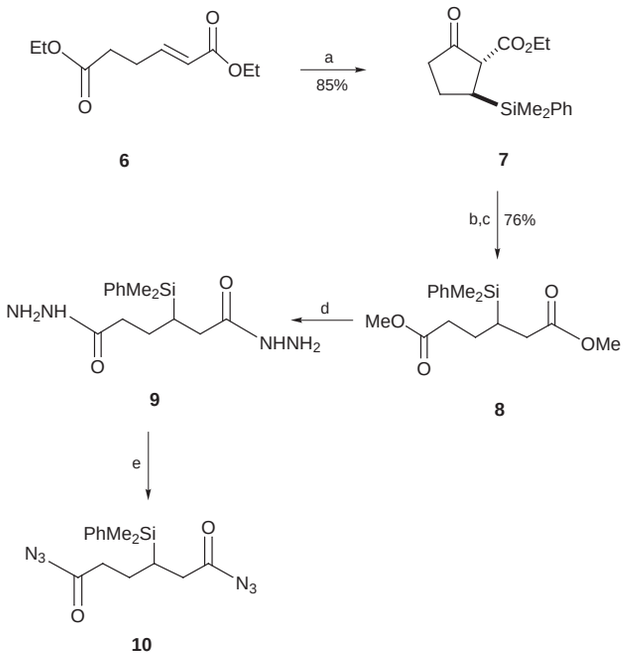


2a *n* = 1; R = $SiMe_2Ph$ **4a** *n* = 1; R = $SiMe_2Ph$ **5a** *n* = 1; R = $SiMe_2Ph$
2b *n* = 2; R = $SiMe_2Ph$ **4b** *n* = 2; R = $SiMe_2Ph$ **5b** *n* = 2; R = $SiMe_2Ph$
2c *n* = 1; R = H **4c** *n* = 1; R = H **5c** *n* = 1; R = H
2d *n* = 2; R = H **4d** *n* = 2; R = H **5d** *n* = 2; R = H

Scheme 2 *Reagents and conditions*: a, NH_2NH_2; b, $NaNO_2$, HCl

esters **2c**,**d** without a dimethyl(phenyl)silyl group were readily available and were converted to the corresponding acyl azides **5c**,**d** *via* the acid hydrazides **4c**,**d** respectively. The preparation of diacyl azide **10** having a $PhMe_2Si$ group positioned β with respect to one acyl azide group and γ to the other, began with silyl cupration[25] on the diester **6**. The cyclised β-keto ester **7** was obtained and was easily converted into the required diester **8**. The diesters were transformed into the dihydrazide **9** followed by the formation of the required diacyl azide **10** (Scheme 3).

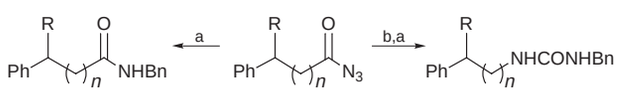
The acyl azides and the products of the Curtius reaction, *viz* the corresponding isocyanates, are known to be quite reactive. Moreover, their proportion may vary with respect to time and temperature giving rise to inherent difficulties in studying the kinetics. Therefore, both substrates and the products were not



Scheme 3 *Reagents and conditions*: a, $(PhMe_2Si)_2CuCNLi_2$; b, KOH, MeOH; aq. HCl; c, CH_2N_2; d, NH_2NH_2; e, $NaNO_2$, aq. HCl

isolated as such, but rather 'frozen' by means of reacting them with benzylamine. Consequently, acyl azides and isocyanates yielded benzyl amide and urea derivatives respectively.

Thus, Curtius reaction of acyl azides (**5a**–**d**) provided the corresponding isocyanates which were reacted *in situ* with benzylamine in the presence of triethylamine and a catalytic amount of 4-dimethylaminopyridine (DMAP) to provide the urea derivatives **12a**–**d** (Scheme 4). Acyl azides under identical



11a n = 1; R = $SiMe_2Ph$	**5a** n = 1; R = $SiMe_2Ph$	**12a** n = 1; R = $SiMe_2Ph$
11b n = 2; R = $SiMe_2Ph$	**5b** n = 2; R = $SiMe_2Ph$	**12b** n = 2; R = $SiMe_2Ph$
11c n = 1; R = H	**5c** n = 1; R = H	**12c** n = 1; R = H
11d n = 2; R = H	**5d** n = 2; R = H	**12d** n = 2; R = H

Scheme 4 *Reagents and conditions*: a, $BnNH_2$, DMAP, Et_3N; b, room temp., 36 h

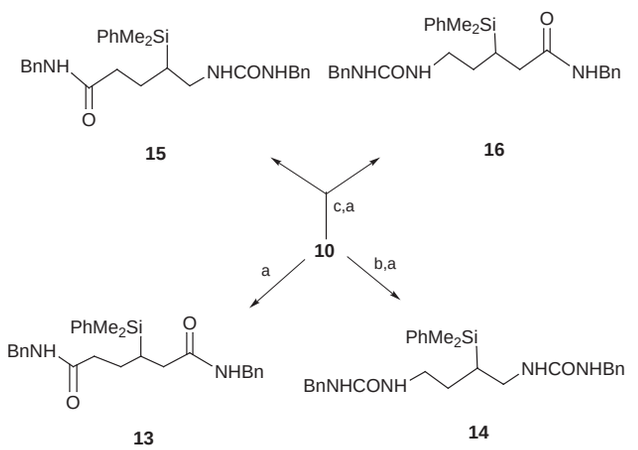
conditions gave the corresponding benzylamides **11a**–**d**. Similarly, the diacyl azide **10** and the corresponding diisocyanate provided dibenzyl amide **13** and diurea **14** respectively. An incomplete Curtius reaction of diacyl azide **10** provided, along with dibenzylamide **13** and the diurea derivative **14**, a mixture of mono-benzylamides **15** and **16** formed from the corresponding mono-isocyanate intermediates (Scheme 5).

The acyl azides were prepared at 0 °C and then brought to 26 °C for kinetic experiments. Aliquots were taken at different intervals and quenched with excess of benzylamine at 0 °C. Each aliquot was then analysed by HPLC. The amount of amides **11a**–**d** and urea derivatives **12a**–**d** formed at different time intervals were assayed. The first order rate constants were then calculated from the slope of the plots: ln $C(t_0)/C(t)$ *vs.* $(t - t_0)$ where $C(t)$ is the concentration of the amides **11a**–**d** at time t and $C(t_0)$ is the initial concentration. The rate constant values as shown in Table 1 clearly indicate that a β-silyl-substitution enhances the rate of the Curtius reaction by a factor of 3 whilst the enhancement for a γ-silyl-substitution is marginal.

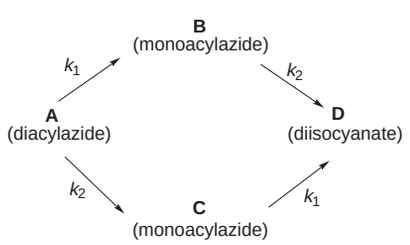
The kinetic experiment for diacyl azide **10** was also carried out at 26 °C. The effect of the silyl group on the rate constants

Table 1 Rate constants of the Curtius reaction of acyl azides **5a**–**d** at 26 °C

Acyl azide	$k/10^3$ min^{-1}	$t_{1/2}$/min
5a	5.32	130
5b	2.02	343
5c	1.79	387
5d	1.76	393



Scheme 5 *Reagents and conditions*: a, $BnNH_2$, DMAP, Et_3N; b, room temp., 36 h; room temp., 3 h



Scheme 6

for the Curtius reaction of the β-acyl azide group and the γ-acyl azide group were obtained from the model shown in Scheme 6 where **A** represents the diacyl azide, **B** and **C** are monoisocyanates and **D** represents the diisocyanate derivative. The rate constants k_1 and k_2 were calculated assuming that the acyl azide group (CON_3) and the isocyanate group (NCO) at either the β- or γ-positions with respect to the silyl group have the same effect on the Curtius reaction of the other acyl azide group. In other words, the rate constants k_1 for transformation from **A** to **B** and **C** to **D** are equal. Similarly, the rate constants k_2 for the transformation from **A** to **C** and **B** to **D** are equal. The rate constants k_1 and k_2 were then found from the slopes of the plots: ln $\{[A(t_0) + B(t_0)]/[A(t) + B(t)]\}$ and ln $\{[A(t_0) + C(t_0)]/[A(t) + C(t)]\}$ *vs.* $(t - t_0)$ (for details of the derivation, see the appendix). The rate constant for the acyl azide group β to the dimethyl(phenyl)silyl group (k_1) was found to be 4.54×10^{-3} min^{-1} ($t_{1/2}$ 153 min) whilst for the acyl azide group γ to the dimethyl(phenyl)silyl group (k_2) was found to be 2.02×10^{-3} min^{-1} ($t_{1/2}$ 344 min).

Conclusions

The present investigation brought to light the fact that a silicon group situated at the β-position with respect to an acyl azide group enhances the rate of the Curtius reaction by about 3 times whilst a γ-silyl substitution has a marginal influence (rate enhancement by about 1.2 times). This lends support to the proposition that during the concerted intramolecular rearrangement of an acyl azide to an isocyanate, an electron deficient centre at the migration origin is created. The β-silicon

substitution could be useful for the regioselective preparation of isocyanates from diacyl azides. This fact, along with the power of stereochemical control[26] by a silicon group, has potential in organic synthesis.

Experimental

All mps were recorded with a Fisher–Johns apparatus. The ^{1}H NMR spectra were recorded on a Varian (model EM360) 60 MHz, a Bruker (model AC200) 200 MHz or a Varian (model VXR300) 300 MHz instrument. ^{1}H NMR chemical shifts (δ) are given in ppm downfield from internal tetramethylsilane ($\delta = 0.00$) or from residual chloroform ($\delta = 7.26$) and J (coupling constant) values in Hz. The IR spectra were recorded on a Perkin-Elmer 783 spectrophotometer. Mass spectra were recorded on a Shimadzu GCMS-QP 1000A instrument. HPLC analysis was performed on a Bruker instrument equipped with a RP-18 column and a UV monitor. Air sensitive reactions were carried out under an Ar/N_2 atmosphere. Solvents were freshly dried and distilled prior to use. Ether refers to diethyl ether.

Kinetic experiments were performed at 26 ± 0.2 °C. The acyl azides in chloroform solution were prepared at 0 °C and then transferred to the 26 °C thermostat. Aliquots were taken at different intervals over 2–3 half lives, quenched with an excess of benzylamine in the presence of triethylamine and a catalytic amount of DMAP at 0 °C, and then left under those conditions overnight. Each aliquot was diluted with ethyl acetate and washed with dilute hydrochloric acid followed by brine. Samples were then analysed by an HPLC fitted with a UV monitor fixed at λ_{max} 254 nm and a LiChrospher® 100 RP-18 (5 μm) column using acetonitrile–water or acetonitrile–water–THF as mobile phase. The amount of amides and ureas were quantified from the respective peak areas. The mixture of mono-benzyl amides **15** and **16** was not separable by normal column chromatography. We have assumed that the extinction coefficients (ε values) for both are the same.

Diethyl hex-2-enedioate 6

Diethyl ethoxycarbonylmethylphosphonate (7 cm^3, 35 mmol) was added dropwise to a stirred oil-free suspension of sodium hydride (50% in oil) (1.75 g, 35 mmol) in dry THF (90 cm^3) under nitrogen at room temperature. The mixture was stirred at room temperature for 2 h, cooled on an ice–water bath and a solution of ethyl 3-oxopropanoate (3.9 g, 30 mmol) in THF (35 cm^3) was added. After 3 h at room temperature, the reaction mixture was poured into water and extracted with ether (400 cm^3). The organic extract was washed with water and brine, dried (Na_2SO_4) and evaporated under reduced pressure. The residue was chromatographed (SiO_2) to give **6** (5.9 g, 98%); R_f (SiO_2, hexane–ethyl acetate 90:10) 0.5; ν_{max}(film)/cm^{-1} 1720, 1640, 1250, 1080; δ_H(200 MHz, $CDCl_3$) 1.25 (3 H, t, J 7), 1.28 (3 H, t, J 7), 2.30–2.60 (4 H, m), 4.14 (2 H, q, J 7), 4.17 (2 H, q, J 7), 5.84 (1 H, dt, J 15.6, 1.6), 6.94 (1 H, dt, J 15.6, 6.4).

(2*RS*,3*SR*) 3-[Dimethyl(phenyl)silyl]-2-ethoxycarbonylcyclopentanone 7

Dimethyl(phenyl)silyllithium[27] (150 cm^3 of a 0.6 M solution in THF; 90 mmol) was added to a stirred suspension of copper(I) cyanide (4 g, 45 mmol) in THF (75 cm^3) under argon at 0 °C. After 0.5 h, the solution was cooled to −78 °C and the diester **6** (8 g, 40 mmol) was added. The mixture was stirred under these conditions for 3 h, quenched with saturated aqueous ammonium chloride and extracted with hexane (3 × 200 cm^3). The combined extract was washed with water and brine, dried over Na_2SO_4 and evaporated under reduced pressure. The residue was chromatographed (SiO_2, hexane–ethyl acetate 97:3) to give the cyclised β-keto ester **7** (9.8 g, 85%); R_f (SiO_2, hexane–ethyl acetate 90:10) 0.56; mp 38–42 °C; ν_{max}(film)/cm^{-1} 1760, 1740, 1260, 1110; δ_H(60 MHz, $CDCl_3$) 0.50 (6 H, s), 1.50 (3 H, t, J 8), 2.00–3.10 (6 H, m), 4.30 (2 H, q, J 8), 7.30–7.90 (5 H, m) (Found: C, 66.0; H, 7.9%. $C_{16}H_{22}O_3Si$ requires C, 66.2; H, 7.6%).

Dimethyl 3-[dimethyl(phenyl)silyl]hexanedioate 8

The β-keto ester **7** (4.64 g, 16 mmol) was dissolved in 20% ethanolic KOH solution (60 cm^3) and the mixture was refluxed for 3.5 h. The mixture was concentrated under reduced pressure, acidified with dilute hydrochloric acid and extracted with ethyl acetate (3 × 100 cm^3). The combined organic extract was washed with water and brine, dried over Na_2SO_4 and evaporated under reduced pressure. The residue was esterified with ethereal diazomethane solution to give the diester **8** (3.74 g, 76%); R_f (SiO_2, hexane–ethyl acetate 90:10) 0.56; ν_{max}(film)/cm^{-1} 1730, 1250, 1110; δ_H(200 MHz, $CDCl_3$) 0.31 (6 H, s), 1.35–1.50 (1 H, m), 1.50–1.65 (1 H, m), 1.80–2.00 (1 H, m), 2.14–2.43 (4 H, m), 3.58 (3 H, s), 3.64 (3 H, s), 7.34–7.52 (5 H, m); *m*/*z* (EI) 308 (M$^+$, 1.5%), 293 (3), 277 (4.6), 135 (100) (Found: C, 62.0; H, 8.1%. $C_{16}H_{24}O_4Si$ requires C, 62.3; H, 7.8%).

Ethyl 3-[dimethyl(phenyl)silyl]-3-phenylpropionate 2a[25b]

Procedure as described for **7**, yield: 92%; R_f (hexane–ethyl acetate 95:5) 0.5; ν_{max}(film)/cm^{-1} 1735, 1250, 1110; δ_H(200 MHz, $CDCl_3$) 0.21 (3 H, s), 0.24 (3 H, s), 1.03 (3 H, t, J 7), 2.55–2.88 (3 H, m), 3.90 (2 H, q, J 7), 6.90–7.80 (10 H, m) (Found: C, 72.9; H, 8.0%. $C_{19}H_{24}O_2Si$ requires C, 73.0; H, 7.7%).

Methyl 4-[dimethyl(phenyl)silyl]-4-phenylbutanoate 2b

Sodium hydroxide (1 g, 25 mmol) was added to a stirred solution of **2a** (936 mg, 3 mmol) in ethanol (10 cm^3) at room temperature. After 10 h, the solvent was evaporated, the residue was acidified with cold dilute hydrochloric acid and extracted with ethyl acetate (50 cm^3). The organic extract was washed with water and brine, dried over Na_2SO_4 and evaporated. The residue was dissolved in dry dichloromethane (5 cm^3) and DMF (0.03 cm^3) was added followed by the addition of oxalyl chloride (0.55 cm^3, 6 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 2 h and the solvent was evaporated under vacuum. The residue was dissolved in dry THF and an excess of an ethereal solution of diazomethane was added to it at 0 °C. The reaction mixture was left inside the refrigerator overnight and the solvent was evaporated. The residue was chromatographed (SiO_2, hexane–ethyl acetate 90:10) to give the diazomethyl ketone **3** (710 mg, 76%); R_f (hexane–ethyl acetate 9:1) 0.33; ν_{max}(film)/cm^{-1} 2103, 1641, 1599, 1249, 1113; δ_H(200 MHz, $CDCl_3$) 0.22 (3 H, s), 0.24 (3 H, s), 2.6 (1 H, dd, J 2.4, 13.4), 2.74 (1 H, dd, J 11.1, 13.4), 2.87 (1 H, d, J 2.4, 11.1), 5.01 (1 H, s), 6.92–7.42 (10 H, m). A solution of **3** (500 mg, 1.62 mmol) in dry methanol (20 cm^3) was photolysed (medium pressure, Pyrex filter) in a reactor for 2 h. The solvent was evaporated to give ester **2b** (455 mg, 90%); R_f (hexane–ethyl acetate 95:5) 0.57; ν_{max}(film)/cm^{-1} 1730, 1240, 1100; δ_H(200 MHz, $CDCl_3$) 0.18 (3 H, s), 0.26 (3 H, s), 1.87–2.34 (5 H, m), 3.56 (3 H, s), 6.80–7.40 (10 H, m); *m*/*z* (EI) 312 (M$^+$, 2.7%), 297 (19.6), 281 (1.2), 135 (100) (Found: C, 72.9; H, 8.0%. $C_{19}H_{24}O_2Si$ requires C, 73.0; H, 7.7%).

Preparation of acid hydrazides: a general procedure

3-[Dimethyl(phenyl)silyl]-3-phenylpropionohydrazide 4a. The ester **2a** (925 mg, 3 mmol) was dissolved in methanol (10 cm^3) and hydrazine hydrate (2 cm^3) was added. The solution was left at room temperature for 3 days or refluxed for 12 h under nitrogen. The solvent and excess hydrazine were evaporated under vacuum to give the acid hydrazide **4a** (925 mg, 100%) which was used directly for the next reaction. Similarly, mono hydrazides **4b–d** and dihydrazide **9** were prepared from the corresponding esters **2b–d** and **8** respectively, following the above protocol with quantitative yields. For **4a**: mp 57–62 °C; ν_{max}(KBr)/cm^{-1} 3450, 3250, 1650, 1620, 1510, 1490, 1450, 1440, 1250, 1110.

4-[Dimethyl(phenyl)silyl]-4-phenylbutanohydrazide 4b. ν_{max}(KBr)/cm^{-1} 3300 (br), 1650, 1500, 1460, 1430, 1250, 1120.

3-Phenylpropionohydrazide 4c. Mp 95–97 °C; ν_{max}(KBr)/cm^{-1} 3320, 3280, 3160, 1630, 1530, 1450.

4-Phenylbutanohydrazide 4d. Mp 77–78 °C; ν_{max}(KBr)/cm^{-1} 3290, 3180, 1650, 1635, 1525.

3-[Dimethyl(phenyl)silyl]hexanediodihydrazide 9. Mp 168–170 °C; ν_{max}(KBr)/cm^{-1} 3280, 1650, 1620, 1530, 1250, 1110.

Preparation of acid azides: a general procedure

3-[Dimethyl(phenyl)silyl]-3-phenylpropionyl azide 5a. The acid hydrazide **4a** (298 mg, 0.926 mmol) was dissolved in DMF (5 cm^3) containing aqueous hydrochloric acid (4 M, 0.5 cm^3, 2 mmol), cooled to −5 °C and treated with a saturated solution of sodium nitrite (70 mg, 1 mmol) in water. Stirring was continued at −5 °C to 0 °C for 10 min, diluted with ice water (50 cm^3) and was extracted with cold (0 °C) ethanol-free chloroform (2 × 10 cm^3). The organic extract was washed with ice cold water and dried over anhydrous $MgSO_4$ at 0 °C.

Similarly, monoacyl azides **5b–d** were prepared from the corresponding mono hydrazides **4b–d** following the above protocol. For the preparation of the diacyl azide **10** aq. hydrochloric acid (4 equiv.) and sodium nitrite (2 equiv.) were used.

Preparation of benzylamides: a general procedure

***N*-Phenylmethyl-3-[dimethyl(phenyl)silyl]-3-phenylpropionamide 11a.** A solution of acyl azide **5a** in chloroform (20 cm^3) [prepared from 298 mg (1 mmol) of acid hydrazide **4a**] was treated with benzylamine (0.33 cm^3, 3 mmol), triethylamine (0.28 cm^3, 2 mmol) and DMAP (25 mg, 0.2 mmol) at 0 °C. After 12 h, the mixture was allowed to attain room temperature. The reaction mixture was washed with dilute hydrochloric acid and brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was chromatographed (SiO_2, $CHCl_3$–MeOH, 99:1) to give **11a** (345 mg, 90%). Similarly other benzylamides **11b–d** were prepared. For diacyl azide **10**, benzylamine (6 molar equiv.), triethylamine (4 molar equiv.) and DMAP (0.4 molar equiv.) were used instead. For **11a**: R_f (hexane–ethyl acetate 80:20) 0.44; mp 125–128 °C; ν_{max}(KBr)/cm^{-1} 3220, 1620, 1540, 1250, 1110; δ_H(60 MHz, $CDCl_3$) 0.20 (6 H, s), 2.40–3.10 (3 H, m), 4.2 (2 H, d, *J* 6), 5.50 (1 H, br s), 6.80–7.40 (15 H, m); *m*/*z* (EI) 373 (M$^+$, 19.5%), 358 (2), 135 (100), 91 (34.8) (Found: C, 77.0; H, 7.4; N, 3.6%. $C_{24}H_{27}NOSi$ requires C, 77.2; H, 7.3; N, 3.8%).

***N*-Phenylmethyl-4-[dimethyl(phenyl)silyl]-4-phenylbutanamide 11b.** Yield 87%; R_f (hexane–ethyl acetate 85:15) 0.37; ν_{max}(film)/cm^{-1} 3260, 1700, 1640, 1530, 1250, 1110; δ_H(60 MHz, $CDCl_3$) 0.18 (3 H, s), 0.20 (3 H, s), 1.70–2.30 (5 H, m), 4.30 (2 H, d, *J* 6), 5.40 (1 H, br s), 6.70–7.50 (15 H, m); *m*/*z* (EI) 387 (M$^+$, 1%), 372 (2.2), 310 (2), 283 (47.8), 192 (97.8), 135 (100), 91 (69.5) (Found: C, 77.2; H, 7.6; N, 3.4%. $C_{25}H_{29}NOSi$ requires C, 77.5; H, 7.5; N, 3.6%).

***N*-Phenylmethyl-3-phenylpropionamide 11c.** Yield 88%; R_f (hexane–ethyl acetate 80:20) 0.36; mp 84 °C; ν_{max}(KBr)/cm^{-1} 3300, 1640, 1550; δ_H(60 MHz, $CDCl_3$) 2.45 (2 H, t, *J* 8), 3.00 (2 H, t, *J* 8), 4.35 (2 H, d, *J* 6), 6.20 (1 H, br s), 7.00–7.50 (10 H, m).

***N*-Phenylmethyl-4-phenylbutanamide 11d.** Yield 89%; R_f (hexane–ethyl acetate 85:15) 0.25; mp 80–81 °C; ν_{max}(KBr)/cm^{-1} 3260, 1650, 1550; δ_H(60 MHz, $CDCl_3$) 1.80–2.40 (4 H, m), 2.6 (2 H, t, *J* 8), 4.35 (2 H, d, *J* 6), 5.95 (1 H, br s), 7.00–7.50 (10 H, m).

***N*,*N*′-Bis(phenylmethyl)-3-[dimethyl(phenyl)silyl]hexanediamide 13.** Yield 84%; R_f (hexane–ethyl acetate 70:30) 0.18; mp 90–93 °C; ν_{max}($CHCl_3$ film)/cm^{-1} 3282, 1640, 1552, 1256, 1107; δ_H(200 MHz, $CDCl_3$) 0.28 (6 H, s), 1.38–1.44 (1 H, m), 1.51–1.62 (1 H, m), 1.84–2.35 (5 H, m), 4.25–4.39 (4 H, m), 6.23 (1 H, t, *J* 5.2), 6.57 (1 H, t, *J* 5.6), 7.10–7.45 (15 H, m); *m*/*z* (EI) 458 (M$^+$, 3.5%), 443 (12.3), 381 (12), 310 (24.6), 232 (30.7), 217 (3.3), 135 (45.8), 91 (100) (Found: C, 73.0; H, 7.5; N, 6.0%. $C_{28}H_{34}N_2O_2Si$ requires C, 73.3; H, 7.5; N, 6.1%).

Preparation of benzylurea derivatives: a general procedure

***N*-{2-[Dimethyl(phenyl)silyl]-2-phenylethyl}-*N*′-phenylmethylurea 12a.** A solution of acyl azide **5a** in chloroform (20 cm^3) [prepared from 298 mg (1 mmol) of acid hydrazide **4a**] was left at room temperature (about 30 °C) for about 36 h, concentrated and treated with benzylamine (0.33 cm^3, 3 mmol), triethylamine (0.28 cm^3, 2 mmol) and DMAP (25 mg, 0.2 mmol) at 0 °C. After 12 h, the mixture was allowed to attain room temperature. The reaction mixture was washed with dilute hydrochloric acid and brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was chromatographed (SiO_2, $CHCl_3$–MeOH, 97:3) to give pure urea derivative **12a** (338 mg, 87%); for diacyl azide **10**, benzylamine (6 molar equiv.), triethylamine (4 molar equiv.) and DMAP (0.4 molar equiv.) were used instead. **12a**: R_f (hexane–ethyl acetate 70:30) 0.56; mp 108 °C; ν_{max}(KBr)/cm^{-1} 3340, 1640, 1590, 1250, 1110; δ_H(60 MHz, $CDCl_3$) 0.25 (6 H, s), 2.50 (1 H, dd, *J* 5, 12), 3.40–3.80 (2 H, m), 4.15 (2 H, d, *J* 6), 4.40 (1 H, br s), 4.50 (1 H, br s), 6.80–7.50 (15 H, m); *m*/*z* (EI) 389 ([M + 1]$^+$, 5.0%), 373 (2.4), 135 (100), 91 (58.7) (Found: C, 73.9; H, 7.5; N, 7.0%. $C_{24}H_{28}N_2OSi$ requires C, 74.2; H, 7.3; N, 7.2%).

***N*-{2-[Dimethyl(phenyl)silyl]-2-phenylpropyl}-*N*′-phenylmethylurea 12b.** Yield 90%; R_f ($CHCl_3$–MeOH 98:2) 0.2; mp 78 °C; ν_{max}($CHCl_3$ film)/cm^{-1} 3320, 3080, 1640, 1580, 1250, 1110; δ_H(60 MHz, $CDCl_3$) 0.17 (3 H, s), 0.20 (3 H, s), 1.70– 2.30 (3 H, m), 2.90–3.20 (2 H, m), 4.20 (2 H, d, *J* 6), 4.50 (2 H, br s), 6.90–7.40 (15 H, m); *m*/*z* (EI) 402 (M$^+$, 6.2%), 387 (2.0), 312 (10), 135 (100), 91 (32.6) (Found: C, 74.3; H, 7.7; N, 6.8%. $C_{25}H_{30}N_2OSi$ requires C, 74.6; H, 7.5; N, 7.0%).

***N*-2-Phenylethyl-*N*′-phenylmethylurea 12c.** Yield 84%; R_f (hexane–ethyl acetate 70:30) 0.32; mp 95–97 °C; ν_{max}(KBr)/cm^{-1} 3350, 3320, 1630, 1570, 1490, 1450; δ_H(60 MHz, $CDCl_3$) 2.60 (2 H, t, *J* 6), 3.16 (2 H, t, *J* 6), 4.10 (2 H, d, *J* 6), 5.50 (1 H, br s), 5.90 (1 H, br s), 6.90–7.40 (10 H, m); *m*/*z* (EI) 254 (M$^+$, 41.3%), 163 (14.1), 106 (28.6), 91 (100).

***N*-2-Phenylpropyl-*N*′-phenylmethylurea 12d.** Yield 81%; R_f ($CHCl_3$–MeOH 98:2) 0.14; mp 98 °C; ν_{max}(KBr)/cm^{-1} 3310, 3290, 1625, 1580, 1450; δ_H(60 MHz, $CDCl_3$) 1.7 (2 H, quintet, *J* 8), 2.60 (2 H, t, *J* 8), 3.20 (2 H, q, *J* 8), 4.25 (2 H, d, *J* 6), 5.30 (1 H, t, *J* 5), 5.60 (1 H, t, *J* 5), 7.00–7.50 (10 H, m); *m*/*z* (EI) 268 (M$^+$, 64%), 177 (4), 149 (34.7), 119 (19.5), 106 (69.5), 91 (100), 77 (15.2).

***N*,*N*′-Bis(phenylmethylaminocarbonyl)-2-[dimethyl(phenyl)silyl]butane-1,4-diamine 14.** Yield 82%; R_f ($CHCl_3$–MeOH 95:5) 0.53; mp 104–106 °C; ν_{max}(KBr)/cm^{-1} 3338, 3065, 1628, 1569, 1250, 1107; δ_H(200 MHz, $CDCl_3$) 0.24 (6 H, s), 0.97–1.01 (1 H, m), 1.27–1.37 (1 H, m), 1.50–1.65 (1 H, m), 3.04–3.15 (3 H, m), 3.24–3.32 (1 H, m), 4.14 (2 H, d, *J* 6.7), 4.18 (2 H, d, *J* 6.7), 5.43 (1 H, t, *J* 5.6), 5.65 (1 H, unresolved triplet), 5.74 (1 H, t, *J* 5.8), 5.81 (1 H, unresolved triplet), 7.17–7.45 (15 H, m); *m*/*z* (EI) 490 (M$^+$, 2.1%), 475 (0.5), 341 (3.7), 327 (7.7), 135 (75), 106 (82), 91 (100) (Found: C, 68.8; H, 7.6; N, 11.3. $C_{28}H_{36}N_4O_2Si$ requires C, 68.8; H, 7.4; N, 11.5%).

Preparation of mono-benzylamide: a general procedure

***N*-Phenylmethyl-4-[dimethyl(phenyl)silyl]-5-(phenylmethylaminocarbonylamino)pentanamide 15 and *N*-phenylmethyl-3-[dimethyl(phenyl)silyl]-5-(phenylmethylaminocarbonylamino)-pentanamide 16.** A solution of the diacyl azide **10** in chloroform [prepared from diacid dihydrazide **9** (155 mg, 0.5 mmol) following the general method] was left at room temperature (~30 °C) for about 3 h, concentrated and treated with benzylamine (0.33 cm^3, 3 mmol), triethylamine (0.28 cm^3, 2 mmol) and DMAP (25 mg, 0.2 mmol) at 0 °C. After 12 h, the mixture was allowed to attain room temperature. The reaction mixture was washed with dilute hydrochloric acid and brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was chromato-

graphed (SiO_2, $CHCl_3$–MeOH, 96:4) to give a mixture of monoamides **15** and **16** (about 4:1 ratio) (116 mg, 50%) and diamide **13** (45 mg, 20%) and diurea derivative **14** (50 mg, 20%). For **15** and **16** mixture: R_f (hexane–ethyl acetate 1:1) 0.33; mp 95–97 °C; ν_{max}(KBr)/cm^{-1} 3308, 3073, 1634, 1564, 1450, 1431, 1251, 1111; δ_H(200 MHz, $CDCl_3$) 0.27 (6 H, s, from **15**), 0.29 (6 H, s, from **16**), 0.85–1.05 (1 H, m), 1.55–1.65 (1 H, m), 1.70–1.95 (1 H, m), 2.15–2.40 (2 H, m), 3.10–3.35 (2 H, m), 4.08 (2 H, d, *J* 5.8), 4.21 (1 H, dd, *J* 5.6, 15), 4.30 (2 H, dd, *J* 5.2, 15), 5.01 (1 H, t, *J* 5.8, from **15**), 5.11 (1 H, t, *J* 5.3, from **15**), 5.18 (1 H, t, *J* 5.8, from **16**), 5.54 (1 H, t, *J* 5.6, from **16**), 6.38 (1 H, t, *J* 5.6, from **16**), 6.72 (1 H, t, *J* 5.6, from **15**) 7.13–7.47 (15 H, m); *m*/*z* (EI) 475 (M^+, 3.5%), 3.40 (5.6), 326 (19.2), 135 (64), 91 (100) (Found: C, 69.8; H, 7.7; N, 8.5%. $C_{28}H_{35}N_3O_2Si$ requires C, 71.0; H, 7.5; N, 8.9%).

Appendix

Considering the sequence of reactions as depicted in Scheme 6, the rate equations can be expressed as eqns. (1)–(4), where $A(t)$,

$$-\mathrm{d}A(t)/\mathrm{d}t = (k_1 + k_2)A(t) \quad (1)$$

$$\mathrm{d}B(t)/\mathrm{d}t = k_1A(t) - k_2B(t) \quad (2)$$

$$\mathrm{d}C(t)/\mathrm{d}t = k_2A(t) - k_1C(t) \quad (3)$$

$$\mathrm{d}D(t)/\mathrm{d}t = k_2B(t) + k_1C(t) \quad (4)$$

$B(t)$, $C(t)$ and $D(t)$ are the concentrations of A, B, C and D at time t respectively.

The solution of eqn. (1) is eqn (5), where $A(t_0)$ represents the initial concentration at time t_0 where $t_0 \neq 0$.

$$A(t) = A(t_0)\exp[-(k_1 + k_2)(t - t_0)] \quad (5)$$

Consider eqn. (6). Manipulation of eqn. (2) and eqn. (6) leads to eqn. (7), where $A'(t_0) = A(t_0)\exp[(k_1 + k_2)t_0]$.

$$B(t) = \exp(-k_2t)fB(t) \quad (6)$$

$$\mathrm{d}fB(t)/\mathrm{d}t = k_1A'(t_0)\exp(-k_1t) \quad (7)$$

On integration of eqn. (7), eqn. (8) is obtained. Combination

$$fB(t) - fB(t_0) = A'(t_0)[\exp(-k_1t_0) - \exp(-k_1t)] \quad (8)$$

followed by rearrangement of eqns. (8) and (6) gives eqn. (9). Similarly, one can obtain eqn. (10).

$$B(t) = B(t_0)\exp[-k_2(t - t_0)] + A(t_0)\{\exp-[k_2(t - t_0)] - \exp-[(k_1 + k_2)(t - t_0)]\}$$
$$\text{or } \ln[A(t_0) + B(t_0)]/[A(t) + B(t)] = k_2(t - t_0) \quad (9)$$

$$\ln[A(t_0) + C(t_0)]/[A(t) + C(t)] = k_1(t - t_0) \quad (10)$$

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