Fluoride Ion Mediated Peterson Alkenation of Bis(trimethylsilyl)methylimines: a Novel Synthesis of 2-Aza-1,3-dienes and *N*-Vinyl-β-lactams

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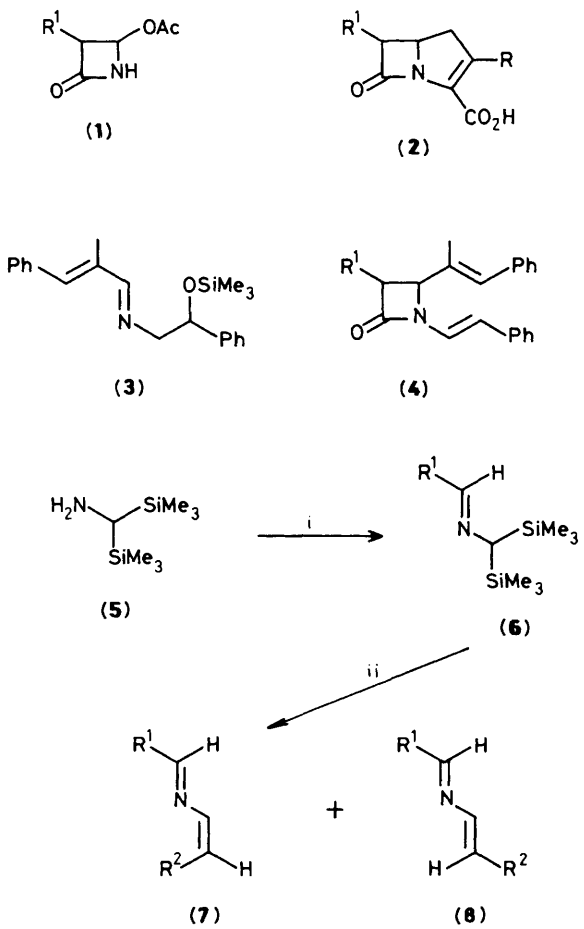
The formation of bis(trimethylsilyl)methylimines and their transformation into aza-1,3-dienes by means of a fluoride-induced catalytic Peterson alkenation is reported; when the procedure was applied to *N*-[bis(trimethylsilyl)methyl]-azetidin-2-ones, a wide range of *N*-vinyl derivatives were obtained in high yields.

During our studies towards the synthesis of β-lactam antibiotics, we have described[1a,b] the preparation of 4-acetoxyazetidin-2-ones (**1**), useful precursors of bicyclic β-lactam compounds (**2**).[1c] The method involved the preparation of compounds of type (**4**), starting from 1-aza-1,3-dienes (**3**). In recent years, azadienes have found much interest in organic synthesis, especially for their use in Diels–Alder cycloadditions,[2] including those carried out using unactivated azadienes.[3] The recent account of Georg *et al.*[4] regarding the preparation of compounds of type (**4**) by means of cycloaddition reaction between acid chlorides and 2-aza-1,3-dienes, has prompted us to report our results.

Several methods have been developed for preparation of 2-aza-1,3-dienes, but most of them are limited in scope.[3,5] Therefore, we thought that imines of type (**6**) (Scheme 1) would lead to a wider range of 2-aza-1,3-dienes in a straightforward manner *via* Peterson alkenation.[6]

Our finding is that Schiff's bases (**6**) derived from bis(trimethylsilyl)methylamine (**5**),† upon treatment with carbonyl compounds in the presence of anhydrous tetrabutylammonium fluoride (TBAF) as a catalyst, gave 2-aza-1,3-dienes in good to excellent yields. To illustrate this catalytic Peterson reaction some representative examples are summarized in Table 1. It is interesting to note the wide scope of this method, since very different 2-azabuta-1,3-dienes can be obtained starting from the appropriate carbonyl compounds, which are used in the preparation of Schiff's bases‡ as well as in the alkenation step. Although the *syn-anti* absolute stereochemistry of the carbon–nitrogen double bond was not determined, the ^{1}H n.m.r. spectra (300 MHz, $CDCl_3$) of the crude reaction mixtures showed only one singlet for CH=N protons



a; $R^1 = R^2 = Bu^t$
b; $R^1 = Bu^t$; $R^2 = 4\text{-}MeC_6H_4$
c; $R^1 = Bu^t$; $R^2 = 4\text{-}ClC_6H_4$
d; $R^1 = Bu^t$; $R^2 = Ph$
e; $R^1 = Bu^t$; $R^2 = PhCH{=}CH$
f; $R^1 = Ph$; $R^2 = 4\text{-}MeC_6H_4$
g; $R^1 = R^2 = 4\text{-}MeC_6H_4$

Scheme 1. *Reagents and conditions:* i, R^1CHO, Ph, $-H_2O$; ii, Bu_4NF (TBAF), R^2R^3CO, room temp.

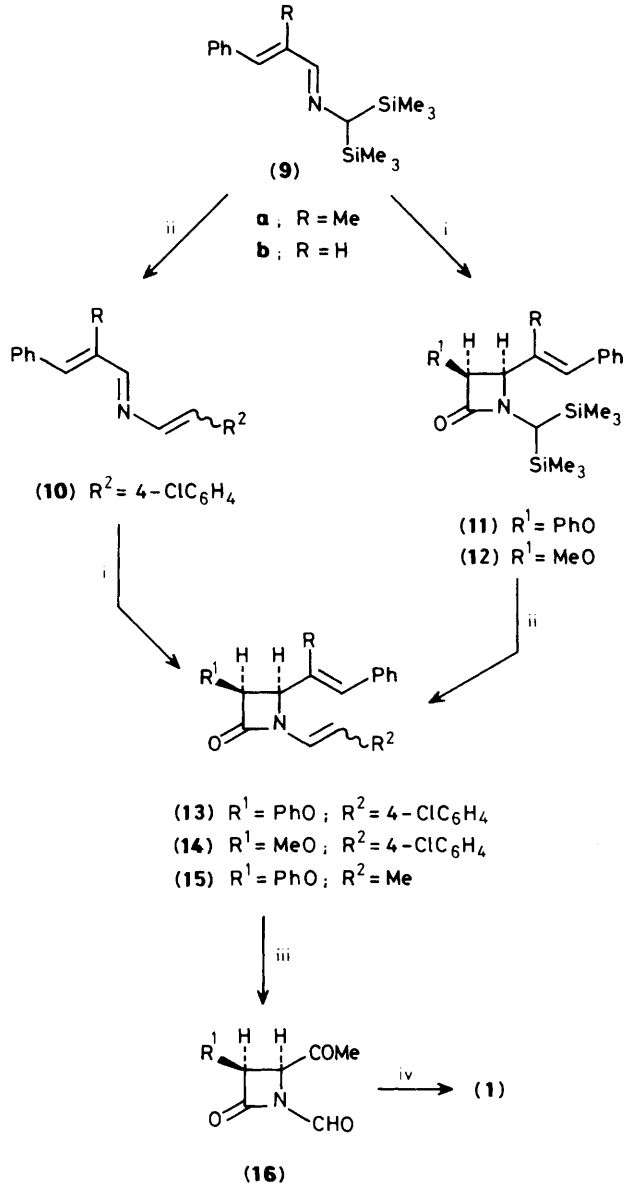
Table 1. 2-Azabuta-1,3-dienes from Schiff's bases (**6**).

Compound[a]	Yield (%)[b]	Molar ratio (**7**)/(**8**)	B.p./°C (*p*/Torr)[h]
(**a**)	70[c,d]	52/48	90(22)
(**b**)	78	45/55	95(0.05)
(**c**)	65	36/64	105(0.07)
(**d**)	70	31/67	110(0.02)
(**e**)	77	50/50	110(0.02)
(**f**)	66[e]	52/48	95—98[g]
(**g**)	65[e,d]	50/50	108—110[g]

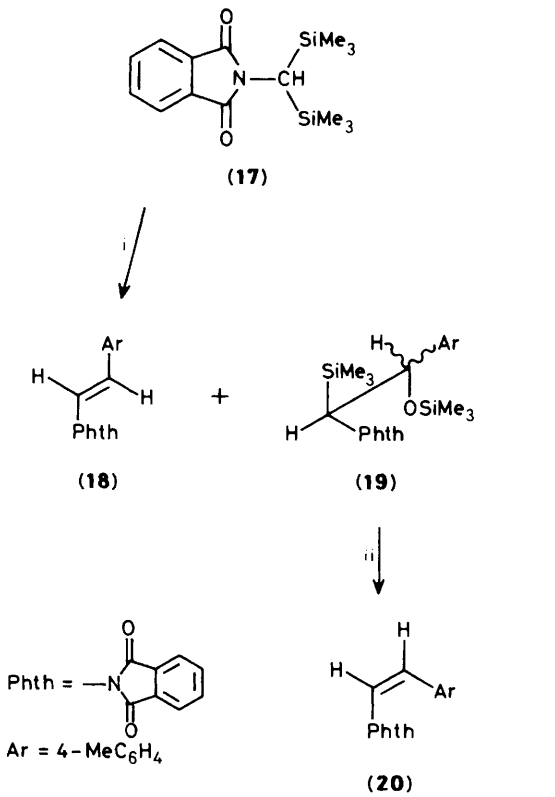
[a] All compounds were prepared at room temperature using equimolar amounts of imine and carbonyl compounds, catalysed by 5% TBAF. [b] Yield of pure isolated products. [c] 1,2-Dimethoxyethane as solvent. [d] 5% Molar $LiN(SiMe_3)_2$ was added together with TBAF catalyst, in order to ensure complete dryness in the reaction solution. [e] Reaction carried out at −78 °C. [f] Determined by ^{1}H n.m.r. (300 MHz) spectroscopy. [g] M.p.; *E* isomer isolated by crystallization (hexane–chloroform. [h] 1 Torr = 133.322 Pa.

† This compound was prepared by reductive silylation of cyanotrimethylsilane, following the procedure described by J. P. Picard, A. Aziz-Elyusufi, R. Calas, J. Dunoguès, and N. Duffaut, *Organometallics*, 1984, **3**, 1660. See also: J. M. Aizpurua and J. P. Picard, '8th International Symposium on Organosilicon Chemistry,' St. Louis, U.S.A., 1987.

‡ These Schiff's bases can be prepared by conventional procedures.



Scheme 2. *Reagents and conditions:* i, $R^1CH_2CO_2H$, NEt_3, $PhOPOCl_2$, CH_2Cl_2, 6 h, room temp.; ii, TBAF, R^2CHO, THF, molecular sieves; iii, O_3, −78 °C, CH_2Cl_2, then Me_2S; iv, ref. 1.



Scheme 3. *Reagents and conditions:* i, ArCHO, TBAF, THF, room temp., 24 h; ii, $CF_3SO_2OSiMe_3$, $CHCl_3$.

in compounds (**7**) and (**8**).§ On the other hand, a marked difference of stability was observed between *E* and *Z* isomers; while *E* isomers were unstable at room temperature, *Z* isomers were stable under these conditions. These results seem to be in agreement with the observations of Mariano and co-workers,[7] who found that only (*E*)-azadienes are reactive in cycloadditions.

We then examined the preparation of *N*-vinyl-β-lactams of type (**4**) by using the methodology outlined in Scheme 2, which involves the [2 + 2] cycloaddition between azadienes and acid chlorides or equivalents.[8] First, the reaction was tested with (**10a**) and phenoxyacetic acid in the presence of triethylamine and induced by phenyl dichlorophosphate.[9] Under these conditions, β-lactam (**13a**) was obtained in poor yield as a mixture of *E* and *Z* isomers about the enamide double bond. However, we found that better yields were obtained when the reaction was carried out starting from 1-aza-1,3-dienes (**9**) followed by Peterson type reaction of the resulting *cis*-*N*-(bis-trimethylsilylmethyl)-β-lactams.¶ Under these conditions, the *N*-vinyl-β-lactams (**13a**) and (**14b**) were obtained in 62 and 48% overall yield, respectively, from (**9**) and 4-chlorobenzaldehyde. From a practical point of view (**11a**) was treated with excess of acetaldehyde (1 : 10) with TBAF catalysis and the resulting crude β-lactam (**15a**) was converted into (**16**) (m.p. 110—112 °C) in 80% yield. Since compounds of type (**16**) can be transformed into the corresponding 4-acetoxyazetidin-2-ones,[1] our procedure constitutes a new approach to β-lactam building blocks.††

Finally, to test the scope of this catalytic Petersen reaction, preparation of other *N*-vinyl heterocyclic compounds was examined. For example, compound (**17**) (Scheme 3) easily prepared from phthalic anhydride and the amine (**5**), upon treatment with 4-methylbenzaldehyde under TBAF catalysis, afforded a mixture of the *trans*-alkene (**18**) [^{1}H n.m.r.

§ *E.g.*, for 1,4-di-t-butyl-2-azabuta-1,3-diene, CH=N, *E* isomer δ 7.69; CH=N, *Z* isomer: δ 7.52.

¶ *Relevant data:* ^{1}H n.m.r. (300 MHz, $CDCl_3$) δ: (**11a**) 5.28 (d, 1H, *J* 5.1 Hz, CH), 4.41 (d, 1H, *J* 5.1 Hz, CH), 0.20 (s, 9H, $SiMe_3$), 0.16 (s, 9H, $SiMe_3$). (**12b**) 4.56 (d, 1H, *J* 4.2 Hz, CH), 4.14 (d,d, 1H, *J* 9.5, 4.2 Hz, C*H*CH=), 2.25 (s, 1H, CHSi), 0.15 (s, 9H, $SiMe_3$). (**15a**) *E* isomer: 6.60 (d,d, 1H, *J* 1.6, 14.6 Hz), 5.96 (d, 1H, *J* 5.2 Hz), 5.22 (q,d, 1H, *J* 6.7, 14.6 Hz), 4.85 (d, 1H, *J* 5.2 Hz). (**15a**) *Z* isomer: 6.27 (d,d, 1H, *J* 1.8, 9.6 Hz), 5.38 (d, 1H, *J* 5.2 Hz), 4.94 (q,d, 1H, *J* 7.3, *J* 9.6 Hz), 4.63 (d, 1H, *J* 5.1 Hz), 1.75 (d,d, 3H, *J* 7.3, *J* 1.8 Hz).

†† Following the submission of this manuscript, a paper reporting similar methodology was published (see G. I. Georg, J. Kant, P. He, A. Ly, and L. Lampe, *Tetrahedron Lett.*, 1988, **29**, 2409).

($CDCl_3$), δ: 6.70 (d, 1H, *J* 17.5 Hz, CH), 6.64 (d, 1H, *J* 17.5 Hz, CH)], together with the *erythro* and *threo* diastereoisomers of 1-trimethylsilyl-2-(4-methylphenyl)phthalimidoethanols (**19**)‡‡ [^{1}H n.m.r. ($CDCl_3$), δ: 5.18 (d, C*H*-$OSiMe_3$), 5.15 (d, C*H*-$OSiMe_3$), 3.85 (d, C*H*-$SiMe_3$), 3.81 (d, C*H*-$SiMe_3$)], and the starting material (**17**). The *cis*-alkene (**20**) [^{1}H n.m.r. ($CDCl_3$), δ: 7.01 (d, *J* 8.1 Hz, CH), 6.69 (d, *J* 8.1 Hz, CH)] could be characterized when the diastereoisomeric mixture of (**19**) was treated with trimethylsilyl trifluoromethanesulphonate.[10]

In conclusion, the results reported here demonstrate the synthetic potential of bis(trimethylsilyl)methylamine (**5**), which may be readily extended to further applications, especially in heterocyclic chemistry.[2,11]

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‡‡ Although we have not assigned the proton shifts to each diastereoisomer, the C*H*-$OSiMe_3$ protons appear at higher fields in the *erythro* isomer than in the *threo* isomer. See ref. 6c.