COMMUNICATION

Synthesis of new trialkylsilylmethyloxazinones *via* intramolecular trapping of β-silyl carbocations by an *N*-Boc group

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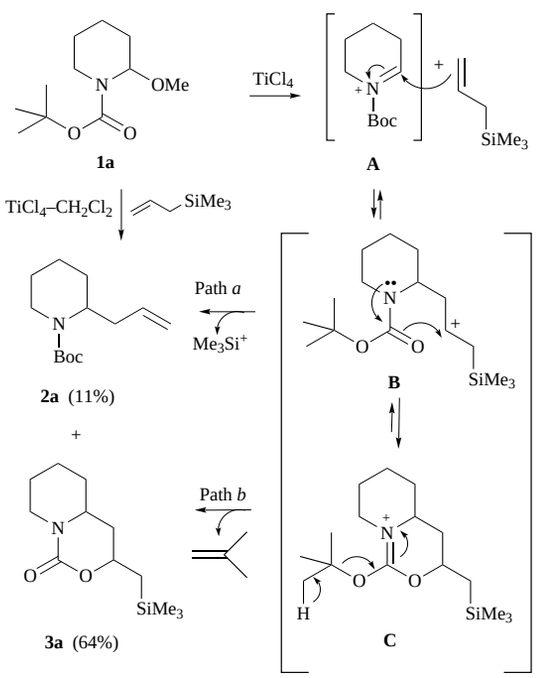
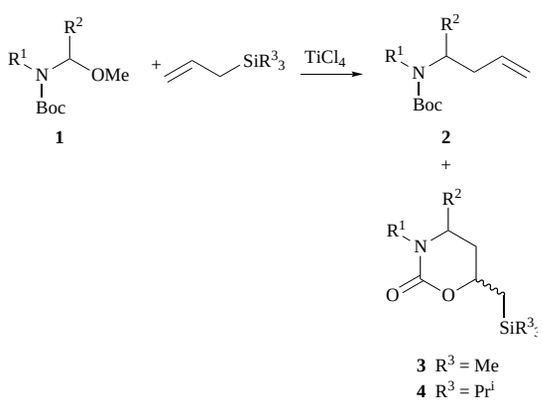
***N*-Boc amino ethers 1a–e when treated with allyltrialkylsilanes in the presence of $TiCl_4$ afford the expected allylation compounds 2a–e and/or the unprecedented silylated oxazinones 3a–e or 4a–e.**

In connection with our interest in the chemistry of piperidines, we required a sample of 2-propylpiperidine. A trivial retrosynthetic analysis suggested that this compound could be prepared by allylation of an *N*-acyliminium salt, a well established reaction to elaborate homoallylic amines.[1] Therefore, we chose 2-methoxy-1-*tert*-butoxycarbonylpiperidine **1a** as the precursor of the required iminium salt. Upon treatment of this compound with allyltrimethylsilane in the presence of titanium tetrachloride, two compounds were formed. Besides the expected allylated compound **2a**, we surprisingly isolated the new silylated oxazinone **3a** as the major product of the reaction (Scheme 1).



Scheme 1

To the best of our knowledge, the formation of such an oxazinone starting from α-methoxycarbamates has never been reported. A simple mechanistic analysis (see Scheme 1) suggested that this compound was formed *via* cyclic iminium ion **C**,† which, in turn, resulted from the intramolecular trapping of the β-silyl carbocation **B** by the *N*-Boc group, followed by the loss of 2-methylpropene (Path *b*). Concurrently, either intermediates **B** or **C** underwent the classical C–Si bond cleavage to afford the expected *N*-Boc homoallylic amine **2a** (Path *a*). Trapping of β-silyl stabilised carbocations, with 1,2-silyl shift or not, is now well documented.[3] However, no example of this process involving the oxygen of a carbamate group as the trapping agent has been described so far. We report hereafter the results of a study aimed at assessing the generality of this reaction. In particular, we have examined the influence of the structure of both reactants on the chemoselectivity of this reaction using various amino ethers **1** and allylsilanes (Scheme 2).



Scheme 2

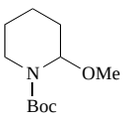
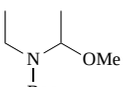
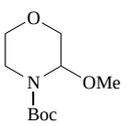
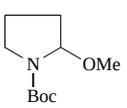
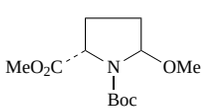
The required *N*-Boc amino ethers **1a–e** were readily prepared in good yields (67–96%) by α-electromethoxylation of the corresponding N-protected amines following a modified version of Shono's[4] method.‡ Compounds **1a–e** were then subjected to the following procedure. To a cooled (−78 °C) solution of substrate **1** (1 mmol) and allylsilane (4 mmol) in CH_2Cl_2 was added dropwise $TiCl_4$ (1.5 mmol). After stirring at −78 °C overnight, the reaction mixture was quenched at this temperature with saturated aqueous sodium acetate (1 ml), and then submitted to a standard aqueous work-up.§ Our results with two different allyltrialkylsilanes (R = Me or Pr^i, Scheme 2) are summarised in Table 1.

† Concerted [$4\pi^+ + 2$] cycloaddition of iminium **A** and allyltrimethylsilane leading to intermediate **C** cannot be excluded at this stage.[2]

‡ Electromethoxylation of *N*-Boc protected amines was conducted in an undivided cell fitted with two graphite electrodes in MeOH (0.5 M) using tetraethylammonium toluene-*p*-sulfonate (0.06 M) as a supporting electrolyte. In order to avoid over oxidation, the use of low current density (10 mA cm^{-2}) and temperature (−10 °C) were necessary.

§ These temperature and quenching conditions are crucial for the isolation of compounds **2** and **3** or **4**. Other experimental conditions ($Na_2CO_3 \cdot 10H_2O$ or aqueous $NaHCO_3$ or Na_2CO_3) resulted in the partial or complete cleavage of the carbamate groups leading to the corresponding deprotected homoallylic amines.

Table 1 Reaction of allylsilanes with 2-methoxy-*N*-Boc amines

Entry	R^3	Substrate **1**	Ratio[a] **2**:**3** or **4**	Diastereomeric ratio[b] of **3** or **4**	Yield[c] (%) **2**	Yield[c] (%) **3** or **4**
1	CH_3		12:88	30:70	11	64
2	Pr^i		0:100	37:63	—	76
		1a				
3	CH_3		10:90	37:63	9	73
4	Pr^i		0:100	33:67	—	80
		1b				
5	CH_3		28:72	25:75	21	33
6	Pr^i		0:100	33:67	—	46
		1c				
7	CH_3		31:69	32:68	21	42
8	Pr^i		0:100	43:57	—	73
		1d				
9	CH_3		55[d]:45	10:11:22:57	31	23
10	Pr^i		0:100	1:8:33:58	—	35
		1e				

[a] Determined by ^{1}H NMR spectroscopy on crude mixture. [b] Determined by capillary GC. [c] Isolated yields. All compounds gave satisfactory spectroscopic data. [d] Diastereomeric ratio: 20:80.

With allyltrimethylsilane as the reactant, compounds **1a**–**d** afforded predominantly oxazinones **3a**–**d** as a mixture of two diastereomers, along with allylation products **2a**–**d**. The observed ratios of **2** and **3** were dependent on the nature of the substrate. Whereas acyclic and piperidine derivatives displayed a good selectivity in favour of **3** (entries 1, 3), the morpholine and pyrrolidine derivatives **1c** and **1d** led to a decreased chemoselectivity (entries 5, 7). The flatness of the five-membered ring of intermediate **B** stemming from **1d** was probably responsible for this result. Additional steric interaction in the case of the (*S*)-proline derivative **1e** (entry 9) might explain the observed lack of chemoselectivity.¶

At this point, we reasoned that increasing the stability of the intermediate cation **B** by employing allyltriisopropylsilane instead of allyltrimethylsilane would improve the selectivity in favour of Path *b*, as it is now well established that the triisopropylsilyl (TIPS) hindered silicon group is less electrofugal and exhibits a larger silicon β-effect than its trimethyl analogue.[6] As expected, upon reaction of allyltriisopropylsilane with **1a**–**e**, the Si–C bond cleavage leading to allylation compounds **2** was totally precluded (see Table 1). In all cases, even that with substituted substrate **1e**, only TIPS-containing oxazinones **4** were detected in the reaction mixture and subsequently isolated (entries 2, 4, 6, 8, 10).‖

Our recent finding[7] of the facile intramolecular opening of epoxides by benzyl and to a lesser extent by methyl carbamates prompted us to examine the influence of the nature of the carbamate on the reaction course. Under the conditions described above, the *N*-benzyloxycarbonyl amino ether analogue of **1a** did not behave as the *N*-Boc derivative, but rather as the *N*-methoxycarbonyl analogue which has been found to give exclusively allylation compounds.[8] On the other hand, when submitted to similar conditions, 2-methoxy-1-isopropoxycarbonylpiperidine afforded a 75:25 mixture of allylation and cyclisation products. It is of note that the use of allyltriisopropylsilane with this substrate had no influence on the chemoselectivity.

Based on these results, we considered that the formation of oxazinones **3** and **4** in the case of substrates **1a**–**e** could not be ascribed to the peculiar nucleophilicity of the *N*-Boc group which has been implicated elsewhere in unexpected nucleophilic displacements.[7,9] We concluded that formation of oxazinones in the case of *N*-Boc derivatives was the consequence of the final irreversible loss of 2-methylpropene. In the case of the isopropoxycarbamate derivative, a similar cleavage, albeit more surprising, of the alkoxy group followed by evolution of propene, would explain the partial formation of oxazinone **3a**. However, it is still unclear why the use of allyltriisopropylsilane was unable to improve the chemoselectivity of the reaction. Intermediates analogous to **C** were likely to be generated in the case of other carbamates but were unable to form into oxazinones owing to the lack of a similar driving force. As a consequence, these carbamates only afforded homoallylic amines through a classical pathway.

In conclusion, we have discovered a new reaction of

¶ T. Shono *et al.*[5] have submitted substrate **1e** to similar reaction conditions and reported the isolation of compound **2e** exclusively with a comparable yield (35%).

‖ In most cases, reactions usually proceeded cleanly except for substrates **1c** and **1e**. Unidentified by-products detected in these cases are probably responsible for these moderate yields.

α-methoxycarbamates which leads to new silylated oxazinones. Our results constitute a new illustration of the original properties of the *N*-Boc group which was shown to be able to intercept β-silyl stabilised carbocations. Further evaluation of the synthetic potential of the prepared oxazinones is underway in our laboratory.

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