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N-CARBOXYLATE ION EQUIVALENT. II. NOVEL TRANSFORMATIONS OF N-BENZYLOXYCARBONYL (Z) GROUP AND N-ALLYLOXYCARBONYL GROUP INTO N-t-BUTYLDIMETHYLSILYLOXYCARBONYL INTERMEDIATE

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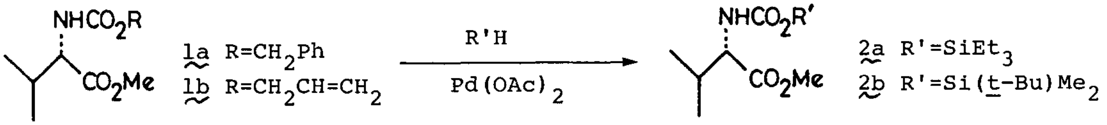
SUMMARY: N-Benzyloxycarbonyl compounds and N-allyloxycarbonyl compounds were efficiently converted to the corresponding t-butyldimethylsilyloxycarbonyl compounds by t-butyldimethylsilane in the presence of Pd(II) catalyst.

In the previous paper,[1] we described a novel transformation of the N-t-butoxycarbonyl (t-Boc) group into the N-t-butyldimethylsilyloxycarbonyl group (eq 1, a). The significant importance of this intermediate was well demonstrated by its conversion into the other N-ester groups such as N-benzyloxycarbonyl (Z) group, one of the most common amino protecting groups, under the mild conditions (eq 1, b). Therefore, the synthesis of an N-carboxylate ion equivalent (t-butyldimethylsilyloxycarbonyl intermediate) from the other ester type amino protecting groups seemed to serve an important method in organic synthesis. Described herein are the syntheses of N-t-butyldimethylsilyloxycarbonyl compounds from N-Z compounds as well as N-allyloxycarbonyl compounds via a Pd(II) catalysis (eq 1, c).

$$\mathrm{RNHCO_2\text{-}\underline{t}\text{-}Bu} \xrightarrow{\ a\ } \mathrm{RNHCO_2Si(\underline{t}\text{-}Bu)Me_2} \underset{c}{\overset{b}{\rightleftarrows}} \underset{(R'=CH_2Ph,\ CH_2CH=CH_2)}{\mathrm{RNHCO_2R'}} \qquad \text{(eq 1)}$$

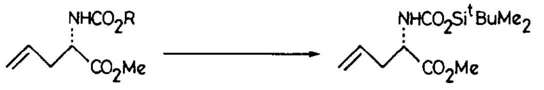
In 1961, Birkofer et al. reported that the N-Z group was removed by triethylsilane (Et_3SiH)/$PdCl_2$ to give an amine via an N-triethylsilyl (N-$SiEt_3$) intermediate.[2] Following their procedures, however, we observed the formation of the triethylsilyloxycarbonyl compound [**1a** → **2a**; IR(film) 1750, 1704 cm^{-1}; MS (EI method, m/z) 290 $(M+H)^+$], where the benzyl group was replaced by the triethylsilyl group. Since the triethylsilyl moiety of **2a** was partly removed during the extractive work-up, we have examined the conversion of an N-Z group into the N-t-butyldimethylsilyl group. This was achieved by the use of t-butyldimethylsilane ($\underline{t}$-$BuMe_2SiH$)[3] in the presence of 0.05 equiv of palladium(II) acetate ($Pd(OAc)_2$).[4]



The N-*t*-butyldimethylsilyloxycarbonyl compounds **2b**, **4**[5], **5b**, and **6b** were obtained from the corresponding Z-amino acid derivatives in nearly quantitative yields.[6]

The typical experimental procedure is as follows: A suspension of *t*-BuMe$_2$-SiH (0.28 ml, 1.7 mmol), Pd(OAc)$_2$ (13 mg, 0.06 mmol), and triethylamine (0.025 ml, 0.18 mmol) in dry dichloromethane (2.0 ml) at room temperature under argon was stirred for 15 min. To this mixture was added a solution of N-Z-valine methyl ester **1a** (300 mg, 1.1 mmol) in dichloromethane (2.0 ml). The resulting mixture was stirred for 8 h, quenched with saturated ammonium chloride solution, and extracted with ether several times. The combined organic layers were washed with brine, dried over magnesium sulfate, and concentrated in vacuo to give the spectroscopically (^{1}H NMR) pure **2b** (342 mg, 100%) as an oil; MS (EI method, m/z) 290 (M+H)$^+$. For an additional example, N$^\alpha$-*t*-Boc-N$^\varepsilon$-Z-lysine methyl ester **7** was converted to the N$^\varepsilon$-silyloxycarbonyl compound **8a** (90%; *t*-BuMe$_2$SiH/Pd(OAc)$_2$) and N$^\alpha$-silyloxycarbonyl compound **8b** (99%; *t*-BuMe$_2$SiOSO$_2$CF$_3$/2,6-lutidine), respectively.

On the other hand, the present method was found to be effective for the conversion of the allyloxycarbonyl compounds to the N-*t*-butyldimethylsilyloxycarbonyl compounds (**1b**→**2b** and **3b**→**4**) in quantitative yields.[6] In addition to above transformations, it is interesting to test the conversion of benzyl ester into its silyl ester. Thus, treatment of the benzyl ester **9a** with *t*-BuMe$_2$SiH/Pd(OAc)$_2$ provided the silyl ester **9b** (100%).[6] However, benzyl ether **9c** did not react under the present reaction conditions. Further studies related to the N-carboxylate ion equivalent are in progress.



3a R=CH$_2$Ph[5]
3b R=CH$_2$CH=CH$_2$

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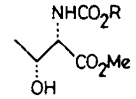
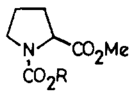
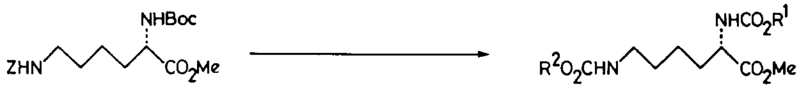


5a R=CH$_2$Ph
5b R=Si(*t*-Bu)Me$_2$



6a R=CH$_2$Ph
6b R=Si(*t*-Bu)Me$_2$



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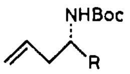
8a R^1=*t*-Bu, R^2=Si(*t*-Bu)Me$_2$
8b R^1=Si(*t*-Bu)Me$_2$, R^2=CH$_2$Ph



9a R=CO$_2$CH$_2$Ph
9b R=CO$_2$Si(*t*-Bu)Me$_2$
9c R=CH$_2$OCH$_2$Ph

REFERENCES AND FOOTNOTES

1. M.Sakaitani and Y.Ohfune, Tetrahedron Lett., 5543 (1985).
2. L.Birkofer, E.Bierstein, and F.Ritter, Chem. Ber., 94, 821 (1961).
3. T.J.Barton and C.R.Tully, J. Org. Chem., 43, 3649 (1978).
4. Other Pd(II) catalysts required longer reaction times resulting in decreased yields.
5. In the case of **3a** to **4**, 38% of the starting material was recovered.
6. Satisfactory spectroscopic data were obtained for the compounds described in the text.

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