REGIOSELECTIVE ALLYLATION TO A TETRAHYDROISOQUINOLINE§

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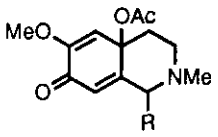
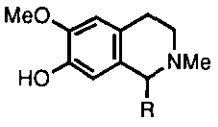
Abstract---- The *p*-quinol acetate (**1a**) reacted with allyltrimethylsilane in dichloromethane in the presence of acid (BF_3·Et_2O or CF_3COOH) to give 8-allylcorypalline (**3**), while in acetonitrile to give 4-allylcorypalline (**7**), regioselectively. Plausible pathway on formation of **3** and **7** is described.

The *p*-quinol acetates (**1**), derived from tetrahydroisoquinolin-7-ol (**2**), are highly reactive to nucleophiles in the presence of acid[1] and are versatile compounds for synthesis of isoquinoline alkaloids. We have already reported syntheses of various isoquinoline alkaloids and their derivatives by use of the *p*-quinol acetates (**1**) as key compounds.[2] Especially, application of this nucleophilic reactions to C-C bond formation serves for synthesis of tetracyclic alkaloids[2a] by intramolecular cyclization and for intermolecular construction of biaryls.[2b]

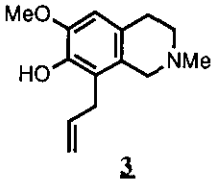
At present silicon reagents should be indispensable for organic synthesis.[3] Among them, allylsilanes are paticularly valuable for C-C bond formation.[4] For instance, allylsilanes react with *p*-quinones to give allyl-substi-



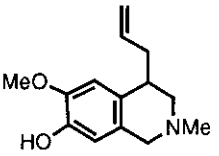
1
1a : R=H



2
2a : R=H



3



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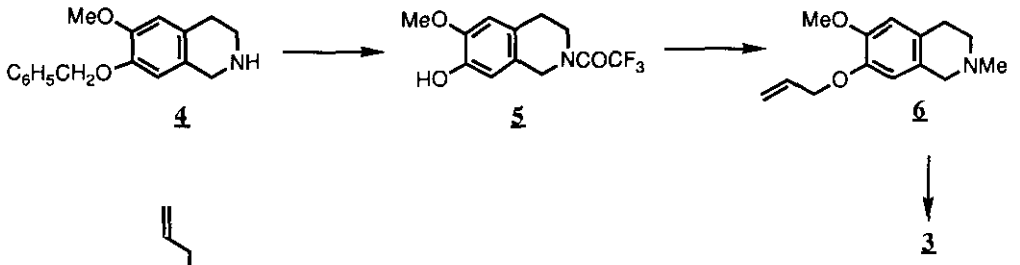
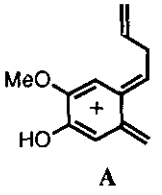
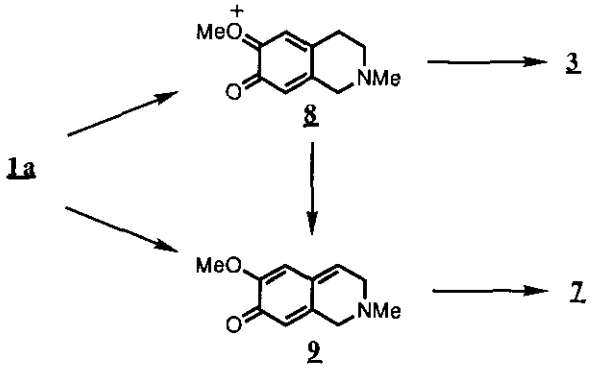
§Dedicated to Professor Emeritus Masatomo Hamana on the occasion of his 75th birthday.

Scheme 1





Scheme 2



Table

Solvent[a]	Acid	Reaction temp.	Time (h)	Product (%)[b] 3	7
CH_2Cl_2	BF_3 Et_2O	r.t.[c]	2	22.4	-----
CH_2Cl_2	BF_3 Et_2O	0°C	2	12.7	-----
CH_2Cl_2	CF_3COOH	r.t.[c]	2	6.5	-----
MeCN	BF_3 Et_2O	r.t.[c]	2	-----	10.2
MeCN	BF_3 Et_2O	0°C	3	-----	20.0
MeCN	CF_3COOH	r.t.[c]	3	-----	7.5

[a] 10 ml of solvent was used.

[b] Yield from corypalline (2a) (100 mg).

[c] Room temperature.

tuted hydroquinones[5] and *p*-quinone methides bearing an allylsilyl moiety react intramolecularly to afford cyclized products.[6] Those results suggested that the *p*-quinol acetate (**1a**) in the presence of acid could react with allylsilane. Here we wish to report a regioselective allylation[7] to a 1,2,3,4-tetrahydroisoquinoline, corypaline (**2a**), by use of allyltrimethylsilane as a nucleophile.

The *p*-quinol acetate (**1a**), prepared from corypalline (**2a**) by the similar reaction as reported previously,[2] was not purified but was dissolved in dichloromethane containing allyltrimethylsilane (1.5 eq.).

Then, boron trifluoride etherate ($BF_3 \cdot Et_2O$) (1.5 eq.) was added to the stirred mixture at room temperature and stirring was continued for 1.5 h. Work-up as usual gave an oily product, which was purified by preparative tlc to give rise to 8-allylcorypalline (**3**),[8] mp 112-113°C, in 22.4% yield. Other reaction conditions[9] decreased yield of the product. The results are shown in Table.

Structure of the product (**3**) was determined as follows (Scheme 1). *N*-Trifluoroacetylation of a tetrahydroisoquinoline (**4**)[10] followed by debenzylation gave *N*-trifluroacetylcorypalline (**5**).[8] By successive reactions (*O*-allylation, *N*-deprotection and *N*-methylation) the phenol (**5**) was transformed to *O*-allylcorypalline (**6**),[8] the Claisen rearrangement (reflux in *N*, *N*-dimethylaniline) of which gave rise to an allylphenol (**3**) (29%) being identical with the product derived from the *p*-quinol acetate (**1a**).

On the other hand, when acetonitrile was used as the more polar solvent instead of dichloromethane, direction of the substitution was dramatically changed (see Table). Namely, similar reaction of **1a** in acetonitrile in the presence of $BF_3 \cdot Et_2O$ at O°C followed by the similar purification as above produced 4-allylcorypalline (**7**),[8] mp 74-75°C, in 20% yield, structure of which was established spectroscopically. ^{1}H-Nmr spectrum of **7** showed two aromatic protons (δ 6.50 and 6.65, each singlet) and methylene protons on 1-position (δ 3.31 and 3.53, each doublet, J=12.9 Hz). Those spectral data suggested an allyl group to be introduced 3 or 4 position. However, introduction to the 3-position was excluded because a characteristic fragment ion (**A**) (*m/z* 190) due to 1,2,3,4-tetrahydroisoquinoline bearing an allyl substituent at 4-position appeared in the mass spectrum.

As for formation of two allyl-substituted corypallines (**3** and **7**), pausible pathway could be proposed as shown in Scheme 2. Namely, *o*-quinonoid cation (**8**) was generated in dichloromethane solution, which was similar to that in C-C bond formation reported previously,[2] while in acetonitrile solution *p*-quinone methide (**9**) was formed *via* **8** or directly from **1a**. Then both intermediates reacted with allyl anion to give 8-(**3**) or 4-allylcorypalline (**7**), respectively. It was noticed that the allylation reaction gave a sole product being dependent on solvent.

In order to investigate scope and limitation of this regioselectivity, reaction of other substrates with organosilicon reagents is now in progress.

ACKNOWLEDGEMENT

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