

REGIOSELECTIVE ALLYLATION TO A TETRAHYDROISOQUINOLINE<sup>§</sup>

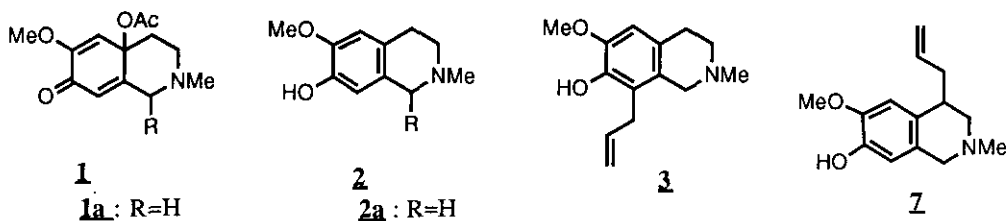
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*Abstract*--- The *p*-quinol acetate (**1a**) reacted with allyltrimethylsilane in dichloromethane in the presence of acid (BF<sub>3</sub>·Et<sub>2</sub>O or CF<sub>3</sub>COOH) to give 8-allylcorypalline (**3**), while in acetonitrile to give 4-allylcorypalline (**7**), regioselectively. Plausible pathway on formation of **3** and **7** is described.

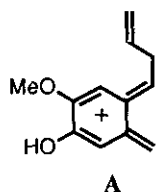
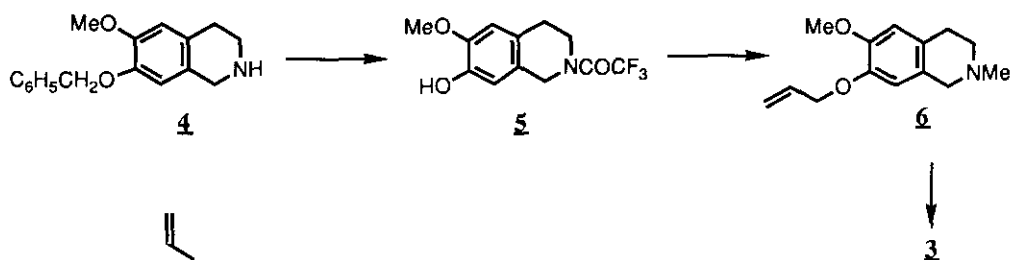
The *p*-quinol acetates (**1**), derived from tetrahydroisoquinolin-7-ol (**2**), are highly reactive to nucleophiles in the presence of acid<sup>1</sup> and are versatile compounds for synthesis of isoquinoline alkaloids. We have already reported syntheses of various isoquinoline alkaloids and their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

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

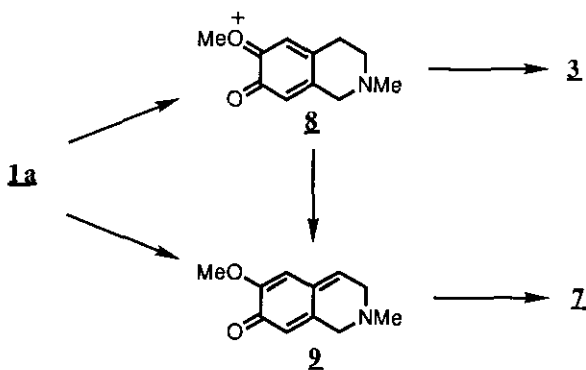


<sup>§</sup>Dedicated to Professor Emeritus Masatomo Hamana on the occasion of his 75th birthday.

Scheme 1



Scheme 2



Table

Solvent <sup>a</sup>	Acid	Reaction temp.	Time (h)	Product (%) <sup>b</sup>	
				3	7
CH <sub>2</sub> Cl <sub>2</sub>	BF <sub>3</sub> Et <sub>2</sub> O	r.t. <sup>c</sup>	2	22.4	-----
CH <sub>2</sub> Cl <sub>2</sub>	BF <sub>3</sub> Et <sub>2</sub> O	0°C	2	12.7	-----
CH <sub>2</sub> Cl <sub>2</sub>	CF <sub>3</sub> COOH	r.t. <sup>c</sup>	2	6.5	-----
MeCN	BF <sub>3</sub> Et <sub>2</sub> O	r.t. <sup>c</sup>	2	-----	10.2
MeCN	BF <sub>3</sub> Et <sub>2</sub> O	0°C	3	-----	20.0
MeCN	CF <sub>3</sub> COOH	r.t. <sup>c</sup>	3	-----	7.5

<sup>a</sup> 10 ml of solvent was used.

<sup>b</sup> Yield from corypalline (**2a**) (100 mg).

<sup>c</sup> Room temperature.

tuted hydroquinones<sup>5</sup> and *p*-quinone methides bearing an allylsilyl moiety react intramolecularly to afford cyclized products.<sup>6</sup> 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<sup>7</sup> to a 1,2,3,4-tetrahydroisoquinoline, corypalline (**2a**), by use of allyltrimethylsilane as a nucleophile.

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

Then, boron trifluoride etherate (BF<sub>3</sub>·Et<sub>2</sub>O) (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**),<sup>8</sup> mp 112-113°C, in 22.4% yield. Other reaction conditions<sup>9</sup> 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**)<sup>10</sup> followed by debenzoylation gave *N*-trifluoroacetylcorypalline (**5**).<sup>8</sup> By successive reactions (*O*-allylation, *N*-deprotection and *N*-methylation) the phenol (**5**) was transformed to *O*-allylcorypalline (**6**),<sup>8</sup> 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<sub>3</sub>·Et<sub>2</sub>O at 0°C followed by the similar purification as above produced 4-allylcorypalline (**7**),<sup>8</sup> mp 74-75°C, in 20% yield, structure of which was established spectroscopically. <sup>1</sup>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**), plausible 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,<sup>2</sup> 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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