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$_2$O or CF$_3$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$^1$ 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 particularly valuable for C-C bond formation.$^4$ For instance, allylsilanes react with p-quinones to give allyl-substi-

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§Dedicated to Professor Emeritus Masatomo Hamana on the occasion of his 75th birthday.
Scheme 1

\[
\begin{align*}
\text{MeO} & \quad \text{MeO} \\
\text{C}_6\text{H}_5\text{CH}_2^+ & \quad \text{MeOH} \\
\text{NH} & \quad \text{MeO} \\
\text{H} & \quad \text{NCOCF}_3 \\
\text{MeO} & \quad \text{MeO} \\
\text{HO} & \quad \text{MeO} \\
\text{C}_6\text{H}_5\text{CH}_2^+ & \quad \text{MeO} \\
\text{NH} & \quad \text{NMe} \\
\end{align*}
\]

Scheme 2

\[
\begin{align*}
\text{MeO} & \quad \text{MeO} \\
\text{HO} & \quad \text{MeO} \\
\text{C}_6\text{H}_5\text{CH}_2^+ & \quad \text{MeO} \\
\text{NH} & \quad \text{NMe} \\
\end{align*}
\]

Table

<table>
<thead>
<tr>
<th>Solvent^a</th>
<th>Acid</th>
<th>Reaction temp.</th>
<th>Time (h)</th>
<th>Product (%)^b</th>
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<tbody>
<tr>
<td>CH\textsubscript{2}Cl\textsubscript{2}</td>
<td>BF\textsubscript{3} Et\textsubscript{2}O</td>
<td>r.t.\textsuperscript{c}</td>
<td>2</td>
<td>22.4</td>
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<tr>
<td>CH\textsubscript{2}Cl\textsubscript{2}</td>
<td>BF\textsubscript{3} Et\textsubscript{2}O</td>
<td>0\textdegree C</td>
<td>2</td>
<td>12.7</td>
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<tr>
<td>CH\textsubscript{2}Cl\textsubscript{2}</td>
<td>CF\textsubscript{3}COOH</td>
<td>r.t.\textsuperscript{c}</td>
<td>2</td>
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<tr>
<td>MeCN</td>
<td>BF\textsubscript{3} Et\textsubscript{2}O</td>
<td>r.t.\textsuperscript{c}</td>
<td>2</td>
<td>10.2</td>
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<tr>
<td>MeCN</td>
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<td>0\textdegree C</td>
<td>3</td>
<td>20.0</td>
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<tr>
<td>MeCN</td>
<td>CF\textsubscript{3}COOH</td>
<td>r.t.\textsuperscript{c}</td>
<td>3</td>
<td>7.5</td>
</tr>
</tbody>
</table>

\^a 10 ml of solvent was used.

\^b Yield from corypalline (2a) (100 mg).

\^c Room temperature.
tuted hydroquinones and p-quinone methides bearing an allylsilyl moiety react intramolecularly to afford cyclized products. 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 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, was not purified but was dissolved in dichloromethane containing allyltrimethylsilane (1.5 eq.). Then, boron trifluoride etherate (BF$_3$·Et$_2$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), mp 112-113°C, in 22.4% yield. Other reaction conditions 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) followed by debenzylation gave N-trifluoroacetylcorpylline (5). By successive reactions (O-allylation, N-deprotection and N-methylation) the phenol (5) was transformed to O-allylcorypalline (6), 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$_3$·Et$_2$O at 0°C followed by the similar purification as above produced 4-allylcorypalline (7), 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 cornyplines (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, 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 organo-silicon reagents is now in progress.

ACKNOWLEDGEMENT

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REFERENCES AND NOTES

8. All new compounds gave satisfactory $^1$H-nmr and high resolution mass spectral or microanalytical data.
9. Titanium tetrachloride as acid was not used because of producing 8-chlorocorpalline. $^{2c}$

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