REISSERT COMPOUND STUDIES. LIII. A NEW SYNTHESIS OF REISSERT
COMPOUNDS USING TRI-n-BUTYL Tin CYANIDE

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Abstract - Reissert compounds were prepared by the reaction of
the heterocyclic base and acyl halide with tri-n-butyltin
cyanide in methylene chloride.

Reissert compounds (N-acyldihydroazaaromatic-α-nitriles)\(^1\) have been widely used
for the synthesis of various heterocyclic compounds. Many methods have been
reported for the synthesis of Reissert compounds. The formation of Reissert
compounds by the reaction of the heterocyclic base with potassium cyanide and an
acyl chloride in methylene chloride-water\(^2\) (occasionally with a phase transfer
catalyst\(^3\)) is the general method of choice. The reaction of the heterocyclic
base and acyl chloride with trimethylsilyl cyanide\(^4\) in anhydrous methylene chloride
(sometimes with an aluminum chloride catalyst) offers certain advantages in some
situations.\(^5\) We now wish to report the use of a convenient new cyanide source in
Reissert compound preparation. In a typical experiment, 5 mmole of isoquinoline
and 10 mmole of tri-n-butyltin cyanide and a trace of anhydrous aluminum chloride
were stirred in 20 ml of anhydrous methylene chloride. A solution of 10 mmole of
benzoyl chloride in 5 ml of anhydrous methylene chloride was slowly added and the
mixture was stirred at room temperature for 1.5 h. The methylene chloride solu-
tion was washed with water, dilute hydrochloric acid, water, dilute sodium
hydroxide, and water. The dried (\(\text{MgSO}_4\)) methylene chloride solution was evapo-
rated and the residue washed with ethanol to give a 96% yield of the isoquinoline
Reissert compound (2-benzoyl-1,2-dihydroisoquinaldonitrile) identical in all
respects with a pure authentic sample. The reactions shown in the Table were
carried out in a similar manner.
Table. Reaction of Benzoyl Chloride and Tri-n-butyltin Cyanide with Heteroaromatic Compounds

<table>
<thead>
<tr>
<th>Heterocyclic compound used</th>
<th>Ratio of reactants</th>
<th>AlCl₃</th>
<th>Time</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoquinoline</td>
<td>Het. Cpd. Bu₃SnCN PhCOCl</td>
<td>yes</td>
<td>1.5</td>
<td>68</td>
</tr>
<tr>
<td>Isoquinoline</td>
<td>1 1 1</td>
<td>yes</td>
<td>1.5</td>
<td>96</td>
</tr>
<tr>
<td>Isoquinoline</td>
<td>1 2 2</td>
<td>yes</td>
<td>1.5</td>
<td>83</td>
</tr>
<tr>
<td>Phthalazine</td>
<td>1 1.2 1.4</td>
<td>no</td>
<td>1.5</td>
<td>79</td>
</tr>
<tr>
<td>Phthalazine</td>
<td>1 1.2 1.4</td>
<td>no</td>
<td>18</td>
<td>91</td>
</tr>
<tr>
<td>Phthalazine</td>
<td>1 1.2 1.4</td>
<td>yes</td>
<td>1.5</td>
<td>85</td>
</tr>
<tr>
<td>Phthalazine</td>
<td>1 2 2</td>
<td>yes</td>
<td>3</td>
<td>95</td>
</tr>
<tr>
<td>Quinoline</td>
<td>1 1.2 1.4</td>
<td>no</td>
<td>18</td>
<td>75</td>
</tr>
<tr>
<td>Quinoline</td>
<td>1 1.2 1.4</td>
<td>no</td>
<td>2</td>
<td>65</td>
</tr>
<tr>
<td>Quinoline</td>
<td>1 1.2 1.4</td>
<td>yes</td>
<td>18</td>
<td>82</td>
</tr>
<tr>
<td>Quinoline</td>
<td>1 2 2.5</td>
<td>yes</td>
<td>18</td>
<td>83</td>
</tr>
<tr>
<td>Phenanthridine</td>
<td>1 1.2 1.4</td>
<td>no</td>
<td>18</td>
<td>91</td>
</tr>
</tbody>
</table>

Reaction of pyridine, tri-n-butyltin cyanide and ethyl chloroformate in a 1 to 1.2 to 1.4 molar ratio for 2 h in the absence of aluminum chloride gave an 89% yield of the Reissert analog. The use of tri-n-butyltin cyanide is thus shown to be a very effective source of cyanide for the preparation of Reissert compounds in very good yield. A wide variety of reaction conditions appear to give almost equally good results. It is anticipated that this reagent will prove to be at least as useful as tri-methylsilyl cyanide in the preparation of Reissert compounds from some of the more difficult heterocyclic systems.
REFERENCES


5. See for example many recent papers by F.D. Popp and co-workers and B.C. Uff and co-workers on Reissert compounds from diaza systems.


Received, 7th May, 1985