REISSERT COMPOUND STUDIES LXIII[1]: PREPARATION OF REISSERT COMPOUNDS USING DIETHYLALUMINUM CYANIDE

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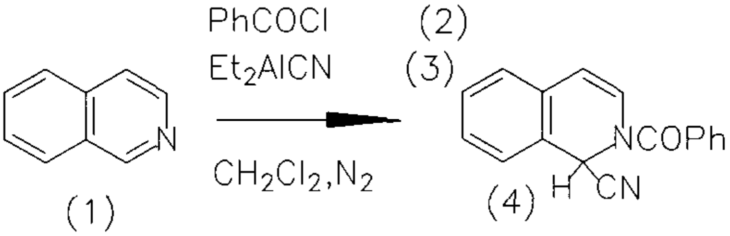
Abstract-Reissert compounds and analogs were synthesized from the reaction of an acid halide, heterocyclic base and diethylaluminum cyanide. This new method of Reissert compound synthesis gave yields comparable to other synthetic routes.

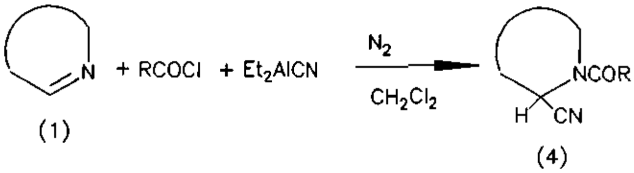
Reissert compounds have played a key role as intermediates for the synthesis of a variety of heterocyclic species.[2] Two general methods are most frequently used for the preparation of Reissert compounds. One method, a heterogeneous system, consists of reacting an acid halide, heterocyclic base, and potassium cyanide in a water and methylene chloride mixture.[3] The other method utilizes a homogeneous system using methylene chloride as the solvent and trimethylsilyl cyanide as the cyanide source.[4,5] These methods have been used to synthesize a variety of Reissert compounds and analogs in reported yields ranging from trace amounts to greater than 90%. We wish to report that diethylaluminum cyanide can also be used as the cyanide source, to give Reissert compounds in yields comparable to the previously reported methods. Table 1 summarizes yields of Reissert compound obtained from isoquinoline and benzoyl chloride by the variation of mole ratios of reactants and reaction times. A reaction time of almost 24 hours yielded no Reissert compound, but did give an inseparable polymer-like mixture of unknown material. Optimum conditions of the synthesis herein involved a reaction time of two hours and a mole ratio for isoquinoline, benzoyl chloride and diethylaluminum cyanide of 1:2:2, respectively. All subsequent runs of the other heterocyclic systems were thus kept at the forementioned mole ratios and maintained at ambient temperature under a nitrogen atmosphere.



mole ratio (1 : 2 : 3)			time (h)	yield (%) (4)
1	1	1	1·2	39
1	2	2	1·2	61–69
1	2	2	23	0
1	1·5	1·5	4	69
1	2	2	2	85

Table 1

Table 2 summarizes the yields of various Reissert compounds obtained utilizing a variety of heterocyclic bases and acid halides.



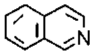
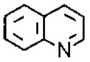
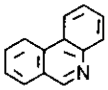
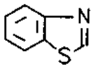
(1)	R	(4) yield (%)
	OEt	74
	Me	44
	p-$MeOC_6H_4$	96
	p-$NO_2C_6H_4$	30
	PhCH=CH (4E:1Z)	45
	MeCH=CH (1E:1Z)	58
	Me_2N	22
		76
	Ph	42
	Me	28
	Ph	45
	OEt	39

Table 2

A noteworthy entry in Table 2 is the reaction of p-nitrobenzoyl chloride and isoquinoline giving a 30% yield of the corresponding Reissert analog. This is a ten-fold increase of the reported yield of 3% using the aqueous-methylene chloride system. The use of diethylaluminum cyanide is thus been shown to be as an effective source of cyanide for the preparation of Reissert compounds. Application of this reagent to other heterocyclic systems is currently in the process of further investigation.

EXPERIMENTAL

Starting materials were commercially available and used without further purification. The diethylaluminum cyanide was obtained as a 1 M solution in toluene (Aldrich).

GENERAL PROCEDURE

Diethylaluminum cyanide (2 mmol) was slowly added, under a nitrogen atmosphere, to a methylene chloride solution (25 ml) containing the heterocyclic base (1 mmol) and the acid halide (2 mmol). The reaction mixture was stirred for the appropriate time, and poured onto 25 ml of 5% sodium hydroxide containing ice. The basic mixture was stirred until all of the ice had melted. An additional 25 ml of methylene chloride was added and the organic layer was separated. The organic phase was washed with 50 ml of water, 2 x 25 ml of 10% hydrochloric acid, 50 ml of water, followed by drying over anhydrous magnesium sulfate. Evaporation of the solvent under reduced pressure yielded a thick residue which was triturated with 95% ethanol to yield the appropriate Reissert compound as shown in Tables 1 and 2. The Reissert compounds were recrystallized to give constant melting points consistent with reported values.[6]

REFERENCES AND NOTES

1. Part LXII: B. C. Uff, Y.-P. Ho, D. S. Brown, I. Fisher, F. D. Popp, and J. Kant. J. Chem. Res. (S), 1989, 346; (M), 1989, 2652.
2. F. D. Popp, Adv. Heterocyclic, 1979, 24, 187; F. D. Popp and B. C. Uff, Heterocycles, 1985, 23, 731.
3. A phase transfer catalyst is occasionally used.
4. Aluminum chloride is used at times.
5. Tri-*n*-butyltin cyanide is another cyanide source that has been used.
6. A. Soto, J. Chem. Soc., 1963, 1760; J. Kant, Ph. D. Dissertation, University of Missouri, Kansas City, 1988, p. 176; J. Kant, F. D. Popp, and B. C. Uff, J. Heterocycl. Chem., 1985, 22, 1065; B. C. Uff, S. L. Anne, A. Cheng, Y. P. HO, F. D. Popp, and J. Kant, J. Chem. Soc., Chem. Commun., 1984, 1245.

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