

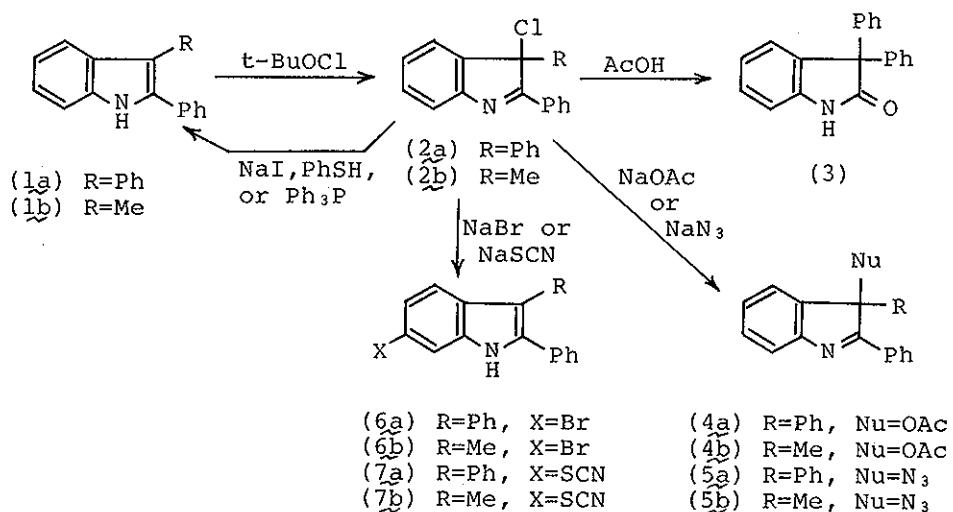
REACTIONS OF 3-CHLOROINDOLENINES WITH SOME NUCLEOPHILES<sup>1</sup>

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The behavior of 3-chloro-2,3-diphenyl- and 3-chloro-3-methyl-2-phenyl-indolenines towards some nucleophiles in acetic acid was examined. Nucleophiles such as  $N_3^-$  and  $AcO^-$  underwent irreversible nucleophilic attack, possibly by  $S_N1$  mechanism, at the 3-position of the 3-chloroindolenines to give 3-azido- and 3-acetoxy-indolenines, while the nucleophiles such as  $I^-$ ,  $PhSH$ ,  $Ph_3P$ ,  $Br^-$ , and  $SCN^-$  reverted the 3-chloro-indolenines to the parent indoles by attacking the chlorine atom. Bromine and thiocyanogen (or their equivalents) thus formed underwent further electrophilic attack at the 6-position of the indoles to give 6-bromo- and 6-thiocyanato-indoles, respectively. The above results are discussed in terms of the HSAB principle.

3-Haloindolenines undergo two types of heterolytic cleavage of the C-Hal bond to give either a carbonium ion and a halide



Scheme 1

anion, or an indole and a positive halogen, depending upon the substrates, solvents, acids or bases, and temperature.<sup>2</sup> In this paper we wish to report our preliminary studies which show that the reaction course of 3-haloindolenines is markedly affected by the softness of the nucleophiles.

The starting 3-chloro-2,3-diphenylindole (2a), mp 127-128°, was obtained in quantitative yield by the reaction of 2,3-diphenylindole (1a) with tert-butyl hypochlorite in methylene chloride.<sup>2c</sup> Similarly, 3-chloro-3-methyl-2-phenylindole (2b) was obtained from 3-methyl-2-phenylindole (1b) as an oil.

The reactions of (2) (1 equiv) with nucleophiles (3 equiv) were generally carried out in glacial acetic acid at room temperature. Although (2a) slowly underwent an acid-catalyzed rearrangement to oxindole (3),<sup>2b-d</sup> this rearrangement was

Table 1. Reactions of 3-Chloroindolenines with Nucleophiles

3-Chloro-indolenine	Nucleophile	Product(s)	Time (hr)	Yield (%)	mp (°C)
(2a)	—	(3)	72	quant.	231-232 (lit. <sup>3</sup> 227-228)
(2a)	NaOAc	(4a) <sup>a</sup>	72	59	165-167 (lit. <sup>4</sup> 167-170)
(2a)	AgOAc	(4a)	5	quant.	165-167
(2b)	NaOAc	(4b) <sup>b</sup>	72	52	oil
(2a)	NaN <sub>3</sub>	(5a)	2	quant.	106-107 (lit. <sup>5</sup> 106-107)
(2b)	NaN <sub>3</sub>	(5b)	2	quant.	oil <sup>5</sup>
(2a)	NaI	(1a)+I <sub>2</sub> <sup>c</sup>	0.5	quant.	
(2a)	PhSH	(1a)+(PhS) <sub>2</sub>	0.5	quant.	
(2a)	Ph <sub>3</sub> P	(1a)+Ph <sub>3</sub> PO	0.5	quant.	
(2b)	Ph <sub>3</sub> P	(1b)+Ph <sub>3</sub> PO	0.5	quant.	
(2a)	NaBr	(6a)	2	quant.	112-114 (lit. <sup>6</sup> 116-117)
(2b)	NaBr	(6b)	2	quant.	145-146 (lit. <sup>6</sup> 147)
(2a)	NaSCN	(7a)	0.5	quant.	154-155 <sup>7</sup>
(2b)	NaSCN	(7b)	0.5	quant.	142-143 <sup>7</sup>

a) Other products were (1a) (3%), (3) (9%), and (2a) (4%).

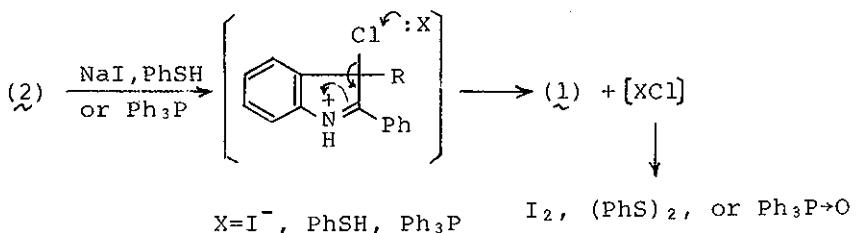
b) Other products were (1b) (trace), (2b) (trace), and resinous material.

c) Iodine was not isolated.

suppressed in the presence of a nucleophile. The results are summarized in Scheme 1 and Table 1.

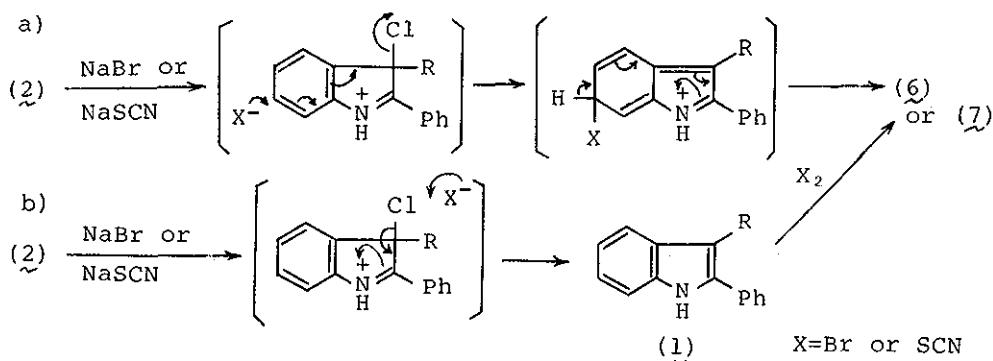
The formation of 3-acetoxy- (4) and 3-azido-indolenines (5) is straightforward and can be formulated as direct nucleophilic

substitution on  $\underline{(2)}$ , possibly by  $S_N1$  mechanism. Reaction with sodium iodide,<sup>2a</sup> thiophenol, and triphenylphosphine gave the parent indoles  $\underline{(1)}$  along with iodine, diphenyl disulfide, or triphenylphosphine oxide. This reaction may occur by a mechanism involving a direct attack of nucleophile on chlorine atom as illustrated in Scheme 2.



Scheme 2

The reaction of  $\underline{(2)}$  with sodium bromide or sodium thiocyanate gave 6-bromo-  $\underline{(6)}$  and 6-thiocyanato-indoles  $\underline{(7)}$ , respectively. In principle, two mechanisms could be considered as shown in Scheme 3: (a) direct nucleophilic substitution of  $\underline{(2)}$  at the 6-position by bromide or thiocyanate ions, or (b) initial formation of  $\underline{(1)}$  and bromine or thiocyanogen (or their equivalents) by the mechanism shown in Scheme 2, followed by electrophilic substitution of  $\underline{(1)}$  by  $\text{Br}^+$  or  $\text{SCN}^+$ . In an attempt to gain some insight into the process  $[(2) \rightarrow (6) \text{ or } (7)]$ , trapping experiments were carried out using *N,N*-dimethylaniline<sup>8</sup> which is more reactive to electrophiles than  $\underline{(1)}$ . Thus, when the reaction of  $\underline{(2a)}$  (1 equiv) with sodium bromide (3 equiv) was carried out in the presence of *N,N*-dimethylaniline (1 equiv), *p*-bromo-*N,N*-dimethylaniline (77%),  $\underline{(1a)}$  (93%), and  $\underline{(6a)}$  (trace) were obtained.



Scheme 3

Similarly, the reaction of (2a) with sodium thiocyanate in the presence of N,N-dimethylaniline gave p-thiocyanato-N,N-dimethylaniline<sup>9</sup> (81%), (1a) (86%), and (7a) (trace). These results, together with the fact that (1) undergo direct substitution by bromine<sup>6</sup> and thiocyanogen<sup>7</sup> to give (6) and (7), are compatible with the mechanism (b).

In view of these observations, it can be concluded that softness<sup>10</sup> of the nucleophiles may play an important role in determining the course of reaction; the harder nucleophiles (AcO<sup>-</sup> and N<sub>3</sub><sup>-</sup>) tend to undergo irreversible nucleophilic attack at the hard 3-position of (2), while the softer nucleophiles (I<sup>-</sup>, PhSH, Ph<sub>3</sub>P, Br<sup>-</sup>, and SCN<sup>-</sup>) revert (2) to the parent indoles (1) by attacking the soft chlorine atom. Bromine and thiocyanogen (or its equivalent) thus formed undergo further electrophilic attack on (1) to give (6) and (7).

#### REFERENCES AND FOOTNOTES

1. Dedicated to Professor Emeritus S. Sugasawa on the occasion

of his 80th birthday.

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