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Tetrakis(trimethylsilyl)silane-Mediated Photochemical Alkylation of Heteroaromatic Bases with Alkyl Halides

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Alkyl halides reacted with protonated heteroaromatic bases in the presence of tetrakis(trimethylsilyl)silane (TTMS) under irradiation with high pressure mercury lamp to give the corresponding alkylated heteroaromatic bases. This is the first report on the photochemical use of TTMS for organic synthesis.

The nucleophilic radical alkylation of heteroaromatic bases is very important for organic synthesis due to their high regio- and chemoselectivities, and especially due to a selectivity opposite to that of Friedel-Crafts type reactions.1) To date, the alkylation of heteroaromatic bases has been studied in detail by Minisci et al.2) with alkyl iodides under oxidative conditions. However, these reactions require peroxides and alkyl iodides. As a part of our study to prepare the alkylated heteroaromatic bases under non-oxidative conditions,3) here we present an initial success of the radical alkylation onto heteroaromatic bases with alkyl halides by using tetrakis(trimethylsilyl)silane (**1a**, TTMS), which is a non-oxidative, simple, and harmless reagent. Since the first preparation of **1a** by Gilman,4) it has been used for the reactions with Lewis acids and alkyllithiums, and as a standard material for NMR measurement in solid state.5) However, **1a** has never been used for the carbon-carbon bond formation under photochemical conditions inspite of active study on the photochemistry of polysilanes.

At first, we studied the alkylation of the heteroaromatic bases **3** with alkyl halides **2** in the presence of bis(tributyltin) (**1c**) under irradiation with high pressure mercury lamp. In the reactions among alkyl iodides, **3**, and **1c**, the corresponding alkylated heteroaromatic bases **4** were obtained in good yields as shown in Table (Entries 1, 3, and 6). However, **1c** is a toxic substance and the reaction with alkyl bromides didn't proceed effectively (Entry 2). Therefore, we then studied the reaction with hexamethyldisilane (**1b**) and **1a** because tris(trimethylsilyl)silyl radical, which was generated from tris(trimethylsilyl)silane, had been reported to react with alkyl halides forming reduction and addition products.6) The yield of **4** in the reactions of alkyl iodides with **1a** was good (Entries 1, 3, and 6), while that of **4** with **1b** was poor (Entry 1). Surprisingly, **4** could be also obtained by using alkyl bromides instead of alkyl iodides. Thus, the alkylation of heteroaromatic bases in the presence of TTMS proceeded not only with alkyl iodides but also with alkyl bromides in moderate yields, though alkyl chlorides didn't react at all. Recently, we reported the alkylation of heteroaromatic bases with oxalic acid monoalkyl esters in the presence of [bis(trifluoroacetoxy)iodo]benzene.7) However, the present method gave the products in higher yields than those with the previous method and doesn't require the excess of alkylation agents. Thus TTMS acts as a non-toxic and non-oxidative radical initiator to give the alkylated heteroaromatic bases under photochemical conditions. Similar reaction of alkyl halides with TTMS didn't proceed at all under thermal conditions because of the thermal stability of TTMS. The detailed reaction mechanism and the further applications are underway in this labotatory.

Table 1. Alkylation of Heteroaromatic Bases with TTMS[a]

Entry	RX (2)	Heteroaromatic base (3)	Product (4)	Yield/%
1	1-AdI	Lepidine	2-(1-Adamantyl)-4-methylquinoline	87 (17)[b] (74)[c]
2	1-AdBr	"	"	71 (16)[c]
3	$c\text{-}C_6H_{11}I$	"	2-Cyclohexyl-4-methylquinoline	63 (81)[c]
4	$c\text{-}C_6H_{11}Br$	"	"	61
5	$c\text{-}C_6H_{11}Cl$	"	"	<1
6	$n\text{-}C_8H_{17}I$	"	4-Methyl-2-octylquinoline	40 (59)[c]
7	$n\text{-}C_8H_{17}Br$	"	"	39
8	1-AdBr	Benzothiazole	2-(1-Adamantyl)benzothiazole	78
9	$c\text{-}C_6H_{11}Br$	"	2-Cyclohexylbenzothiazole	71
10	$HOCH_2CH_2Br$	Lepidine	2-(2-Hydroxyethyl)-4-methylquinoline	32
11	1-AdBr	Pyridine	2- and 4-(1-Adamantyl)pyridines	32 (α:γ=1:1)

a) The reaction was performed with **1a** by the following molar ratio: 2/3/1a = 0.5/2.5/0.5 for Entries 1, 2, 3, 5, and 6; 0.5/2.5/1.0 for Entries 4, 7, 8, 9, 10, and 11. The yield was calculated based on **2**. b) **1b** was used instead of TTMS (2/3/1b = 0.5/2.5/1.5). c) **1c** was used instead of TTMS (2/3/1c = 0.5/2.5/1.5) and 2-butyl-4-methylquinoline was obtained in 5-7% yield as a by-product.

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