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Lithiation of 1*H*-Pyrazolo[3,4-*d*]pyrimidine Derivative Using Lithium Alkanetellurolate

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Abstract: 4-Chloro-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine was converted into alkyl 1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl telluride, which was lithiated using alkyllithium followed by the reaction with electrophiles.

Keywords: lithiation, pyrimidines, tellurium and compounds

The halogen-metal exchange reaction is widely used for the introduction of electrophiles in aromatic compounds. In some π-deficient heterocycles, treatment with an organolithium reagent gives multiproducts derived from some side reactions. Very low temperature is required for the metallation of π-deficient heterocycles. For example, it has been reported that 7-iodo-3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidine is lithiated at the 7-position [1], but this reaction requires a temperature of -105 °C, and produces some byproducts. Similarly, the reaction of 4-iodo-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine with *n*-butyllithium in THF at -78 °C gave multispots in Thin Layer Chromatography. We examined the lithiation of π-deficient heterocycles under mild conditions.

Recently, lithiation via a tellurium-lithium exchange reaction has been reported[2,3,4]. As regards π-deficient heterocycles, the lithiation of 2-bromopyridine using *n*-butyllithium via *n*-butyl 2-pyridyl telluride was reported by Kondo [5]. This method can avoid some side reactions which occur due to the superiority of the halogeno group as a leaving group. Thus, we applied the method to the lithiation of 4-chloro-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine.

Reaction of 4-chloro-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**1**) with lithium *n*-butanetellurolate, which was obtained from the reaction of tellurium and *n*-butyllithium, proceeded smoothly to give *n*-butyl 1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl telluride (**2**) in 90% yield. Then **2** was converted into the product **4** using *n*-butyllithium and pivalaldehyde

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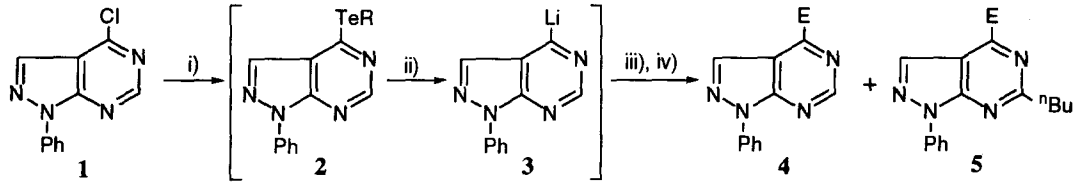
in 52 % yield. Because the telluride **2** is slightly unstable, conversion of **2** into **4** does not proceed in good yield.

Next, the results of the one-pot lithiation without isolating the telluride **2** are shown in Table 1. When the lithiating time was extended to 90 min, the yield of the product **4** showed a slight decline. Even at -78 °C, hence, 4-lithio derivative **3** seems to be unstable. Upon using methyllithium or phenyllithium instead of *n*-butyllithium, we found that the kind of alkyllithium affects the yield of the product **4**. It should be noted that treatment of **2**, generated *in situ* from **1**, with excess molar of *n*-butyllithium gives the product **5**, which is derived from the nucleophilic attack of *n*-butyllithium at the 6-position of the 4-lithio derivative **3** (entry 3 in Table 1). The introduction of some electrophiles at the 4-position in 1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine was accomplished in good to fair yields under the best conditions we examined.

Table 1



reagents and conditions: i) RTeLi (1.1 eq) / THF / rt; ii) RLi / -78 °C; iii) electrophile (5.0 eq) / -78 °C to rt; iv) H_3O^+ / rt

Entry	Alkyllithium (RLi) R	Amount	Time	Electrophile	-E	Yield 4	5
1	^{n}Bu	1.1 eq	10 min	^{t}BuCH=O	-CH(OH)^{t}Bu	74 %	
2	^{n}Bu	1.1 eq	90 min	^{t}BuCH=O	-CH(OH)^{t}Bu	50 %	
3	^{n}Bu	3.0 eq	10 min	^{t}BuCH=O	-CH(OH)^{t}Bu	43 %	14 %
4	Me	1.1 eq	10 min	^{t}BuCH=O	-CH(OH)^{t}Bu	48 %	
5	Ph	1.1 eq	10 min	^{t}BuCH=O	-CH(OH)^{t}Bu	16 %	
6	^{n}Bu	1.1 eq	10 min	PhCH=O	-CH(OH)Ph	61 %	
7	^{n}Bu	1.1 eq	10 min	Me_2NCH=O	-CH=O	60 %	

In conclusion, we have accomplished the lithiation of pyrazolo[3,4-*d*]pyrimidine derivative using lithium alkanetellurolate. We hope that this method can be applied to other π-deficient heterocycles.

References

[1] K. Tanji, H. Kato, and T. Higashino, *Chem. Pharm. Bull.*, **39** (11), 2793-6 (1991).

[2] T. Hiiro, Y. Morita, T. Inoue, N. Kambe, A. Ogawa, I. Ryu, and N. Sonoda, *J. Am. Chem. Soc.*, **112**, 455-457 (1990).

[3] T. Hiiro, N. Kambe, A. Ogawa, N. Miyoshi, S. Murai, and N. Sonoda, *Angew. Chem. Int. Ed. Engl.*, **26**, 1187-1188 (1987).

[4] T. Hiiro, T. Mogami, N. Kambe, S. Fujiwara, and N. Sonoda, *Synth. Commum.*, **20**, 703-711 (1990).

[5] Y. Kondo, M. Shilai, M. Uchiyama and T. Sakamoto, *J. Chem. Soc., Perkin Trans. 1*, 1781-2 (1996).