CHEMISTRY LETTERS, pp. 1307-1310, 1973. Published by the Chemical Society of Japan

REACTIONS OF 2-ALKYL-2-LITHIO-1,3-DITHIANES WITH PYRIDINE

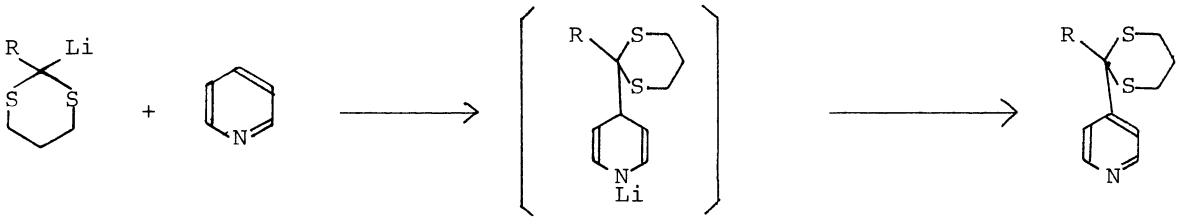
Takeo TAGUCHI, Mineo NISHI, Kenzo WATANABE, and Teruaki MUKAIYAMA
Laboratory of Organic Chemistry, Tokyo Institute of Technology
Ookayama, Meguro-ku, Tokyo 152

It was found that 2-alkyl-2-(4-pyridyl)-1,3-dithiane [II] is obtained in fairly good yield by the reaction of 2-alkyl-2-lithio-1,3-dithiane with pyridine followed by the subsequent oxidation with p-benzoquinone or air. N-Acyl-1,4-dihydropyridine derivative [III] was isolated by treating the adduct [I] of 2-alkyl-2-lithio-1,3-dithiane and pyridine with acyl chloride. Further, it was found that 2,2'-dipyridyl is obtained in 74% yield(7) by refluxing 2-benzyl-2-lithio-1,3-dithiane with excess amount of pyridine in tetrahydrofuran.

Many works have been reported on the reactions of organometals with pyridine;(1) for example, alkyllithium reacts with pyridine to afford 2-alkylpyridine(2) through 1,2-addition reaction and by the subsequent oxidation, and 4-alkylpyridine was obtained from a Grignard reagent and pyridine in poor yield along with the 2-isomer.(3)

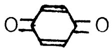
In the present investigation, it was established that 2-alkyl-2-(4-pyridyl)-1,3-dithiane is obtained in fairly good yield by the reaction of 2-alkyl-2-lithio-1,3-dithiane(4) with pyridine in tetrahydrofuran at room temperature, followed by hydrolysis and air oxidation. For example, 2-(4-pyridyl)-1,3-dithiane was obtained in 46% yield by treating 2-lithio-1,3-dithiane with 5 molar equivalents pyridine in tetrahydrofuran at room temperature for 3.5 hr under argon atmosphere, followed by hydrolysis by addition of 3 ml of water and air oxidation. Similarly, 2-alkyl-2-(4-pyridyl)-1,3-dithianes were obtained by the reactions of the lithium salts of 2-methyl-1,3-dithiane and 2-benzyl-1,3-dithiane with pyridine. These results are listed in table I.

On the consideration that 1,4-dihydropyridine derivative would be readily hydrolyzed to afford the corresponding 1,5-dicarbonyl compound,5) it was expected that the yield of 2-alkyl-2-(4-pyridyl)-1,3-dithiane [II] would be increased when the intermediate [I], the adduct of lithium salt and pyridine, is oxidized under strictly anhydrous conditions. Thus the final oxidation reaction was carried out by the utilization of p-benzoquinone as an oxidant. For example, 2-(4-pyridyl)-1,3-dithiane was obtained in 69% yield by treating the adduct [I] formed in a similar way as above mentioned with an equimolar amount of p-benzoquinone in tetrahydrofuran at 0°C for 1 hr (Table I).



[I] [II]

Table I. Yields of 2-Alkyl-2-(4-pyridyl)-1,3-dithiane by the Reactions of 2-Alkyl-2-lithio-1,3-dithiane with Pyridine

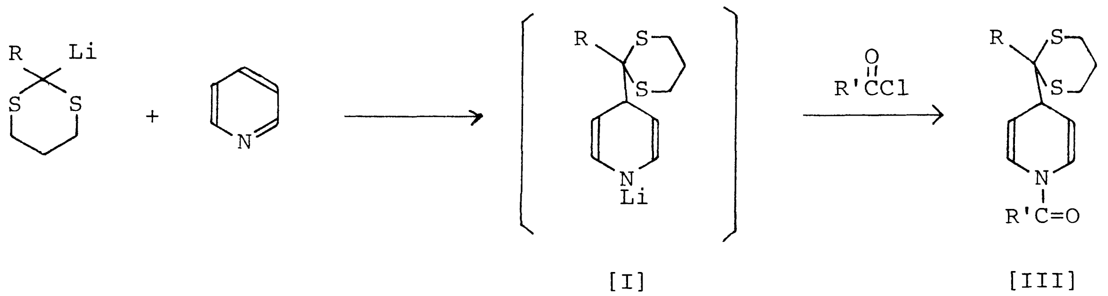
R	Oxidizing Reagent	[II] a) Yield (%)	m.p. (b.p. mmHg) °C
H	air	46 b)	107 – 108
CH_3	"	42	45 – 48.5 (134/1.2)
$C_6H_5CH_2$	"	7	156
H		69	
CH_3	"	69	
$C_6H_5CH_2$	"	47	

a) The structures of these materials are supported from the data of elemental analysis, n.m.r. spectrum and gas chromatograph analysis.

b) By reductive desulfurization by the use of $TiCl_4$-$LiAlH_4$ system of this material, only 4-picoline was detected by gas chromatographic analysis.6)

Further, adduct [I] was treated with acyl chloride to afford N-acyl-1,4-dihydropyridine derivatives in good yields. For example, when the adduct of 2-

lithio-1,3-dithiane and pyridine formed in a similar way mentioned above was treated with ethyl chloroformate in tetrahydrofuran at -78°C for 1 hr, the corresponding N-ethoxycarbonyl-1,4-dihydropyridine was obtained in 72% yield.



[I] [III]

Table II shows the yields of N-acyl-1,4-dihydropyridine derivatives.

Table II. Yields of N-Acyl-1,4-dihydropyridine Derivatives

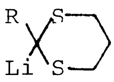
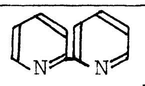
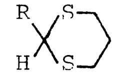
R	Addition Conditions Temp.	Addition Conditions Time(hr)	$\mathrm{R'\overset{O}{C}Cl}$	[III] Yield (%)	m.p.(°C)
H	r.t.	3.5	$\mathrm{C_2H_5O\overset{O}{C}Cl}$	72	66-69
CH_3	r.t.	3.5	$\mathrm{C_6H_5\overset{O}{C}Cl}$	78	88-89
$C_6H_5CH_2$	r.t.	24	$\mathrm{C_2H_5O\overset{O}{C}Cl}$	70	124-126

Furthermore, it is found that 2,2'-dipyridyl is obtained when 2-alkyl-2-lithio-1,3-dithiane was refluxed in tetrahydrofuran with excess pyridine (10 molar equivalents) and at the same time 2-alkyl-1,3-dithiane, one of the starting materials, is recovered. In a typical procedure, the treatment of 2-benzyl-2-lithio-1,3-dithiane with 10 molar equivalents of pyridine in boiling tetrahydrofuran for 2 hr under argon atmosphere, followed by hydrolysis and air oxidation afforded 2,2'-dipyridyl in 74% yield7) and 2-benzyl-1,3-dithiane was recovered in 91%. The structure of 2,2'-dipyridyl thus obtained was comfirmed by comparing with an authentic sample. A similar result was obtained by the reaction of the lithium salt of 2-n-octyl-1,3-dithiane with pyridine. On the other hand, when 2-

methyl-2-lithio-1,3-dithiane was allowed to react with pyridine under the same condition, 2,2'-dipyridyl was obtained in 26% yield[7] and at the same time 2-methyl-2-(4-pyridyl)-1,3-dithiane was isolated in 16% yield.

These results are summarized in Table III.

Table III. Yield of 2,2'-Dipyridyl Formed by the Reaction of 2-Alkyl-2-lithio-1,3-dithiane with Pyridine

	 Yield (%)[7]	 Recovery (%)
$C_6H_5CH_2$	74	91
n-C_8H_{17}	72	97
CH_3[3]	26	45

a) In this case 2-methyl-2-(4-pyridyl)-1,3-dithiane was obtained in 16% yield.

In summary, it is noted that 2-alkyl-2-(4-pyridyl)-1,3-dithiane is obtained in good yield by the reaction of the lithium salt of 2-alkyl-1,3-dithiane with pyridine in tetrahydrofuran at room temperature. Further, it was established that 2,2'-dipyridyl is formed by refluxing the lithium salt of 2-alkyl-1,3-dithiane in tetrahydrofuran with pyridine.

REFERENCES

1) U. Eisner and J. Kuthan, Chem. Rev., 72, 1 (1972).
2) W. Von E. Doering and V. Z. Pasternak, J. Amer. Chem. Soc., 72, 143 (1950).
3) R. A. Benkeser and D. S. Holtar, J. Amer. Chem. Soc., 73, 5861 (1951).
4) D. Seebach, Synthesis, 1, 17 (1969).
5) a) B. D. Shaw, J. Chem. Soc., 125, 1930 (1924), b) B. D. Shaw, ibid., 127, 215 (1925), c) S. Danishefsky and A. Nagel, J. Amer. Chem. Soc., 90, 520 (1968).
6) T. Mukaiyama, M. Hayashi, and K. Narasaka, Chem. Lett., 291 (1973).
7) The Yield of 2,2'-dipyridyl was based on that 2 molar equivalents of the lithium salt of 2-alkyl-1,3-dithiane affords one mole equivalent 2,2'-dipyridyl.

(Received September 10, 1973)