

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% yield⁷⁾ 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-alkylpyridine²⁾ 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-dithiane⁴⁾ 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).

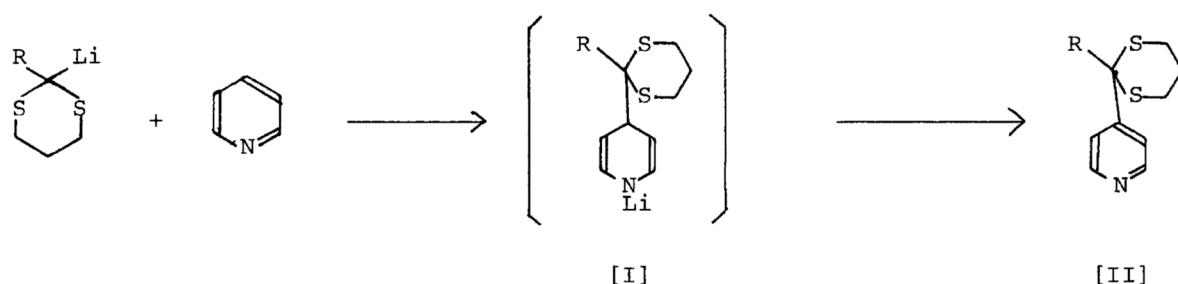
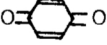


Table I. Yields of 2-Alkyl-2-(4-pyridyl)-1,3-dithiane by the Reactions of 2-Alkyl-2-lithio-1,3-dithiane with Pyridine

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 ₆ H ₅ CH ₂	"		7	156
H			69	
CH ₃	"		69	
C ₆ H ₅ CH 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 TiCl₄-LiAlH₄ 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.

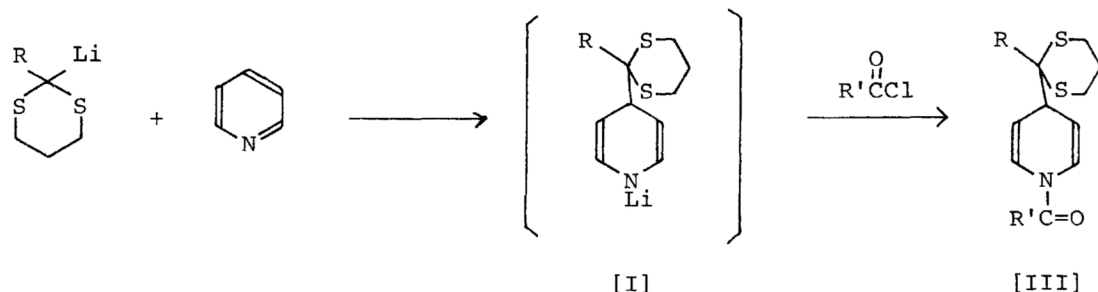


Table II shows the yields of N-acyl-1,4-dihydropyridine derivatives.

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

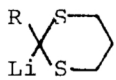
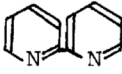
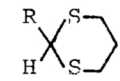
R	Addition Temp.	Conditions Time (hr)	$\text{R}'\overset{\text{O}}{\parallel}\text{CCl}$	[III] Yield (%)	m.p. (°C)
H	r.t.	3.5	$\text{C}_2\text{H}_5\overset{\text{O}}{\parallel}\text{CCl}$	72	66-69
CH_3	r.t.	3.5	$\text{C}_6\text{H}_5\overset{\text{O}}{\parallel}\text{CCl}$	78	88-89
$\text{C}_6\text{H}_5\text{CH}_2$	r.t.	24	$\text{C}_2\text{H}_5\overset{\text{O}}{\parallel}\text{CCl}$	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 confirmed 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% yield⁷⁾ 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)