Synthesis of 2-Alkylfurans via the Reaction of Iodine with the Ate-Complexes Obtained from 2-Furyllithium and Trialkylboranes

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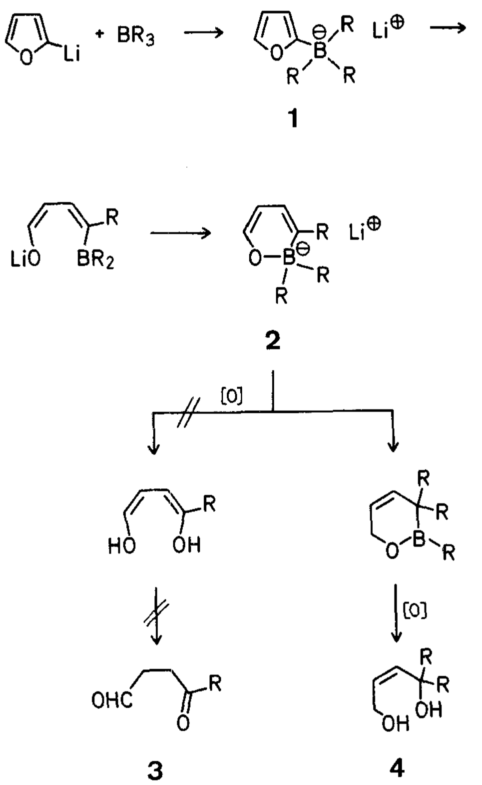
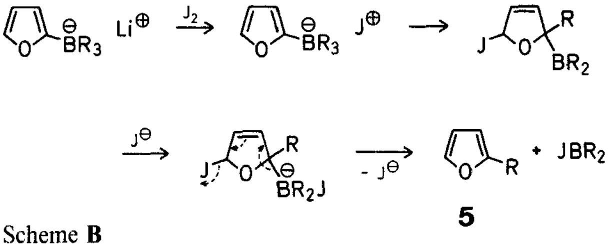
Previously, we have examined the reaction of trialkylboranes with 2-furyllithium in an attempt to find a new synthetic procedure of 4-oxoalkanals **3** through the following reaction path (Scheme A). Contrary to the expectation, it was found that the actually obtained products were not the ketoaldehydes **3** but the corresponding 4,4-dialkyl-2-buten-1,4-diols **4** derived from the intermediates **2** via the reaction route indicated[1].



Scheme A

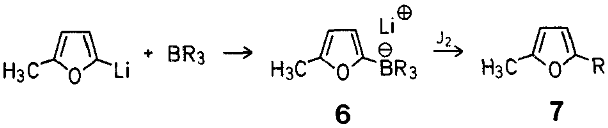
We wish to report here a synthetic procedure for 2-alkylfurans via the reaction of iodine with ate-complexes **1** formed from 2-furyllithium and trialkylboranes. Addition of an equimolar amount of furan in ether containing tetramethylethylenediamine (TMEDA) to *n*-butyllithium in ether at −20° resulted in quantitative metallation to give 2-lithiofuran, which was then treated at 0° with a solution of tricyclopentylborane in tetrahydrofuran. The reaction of the resultant solution of the ate-complex **1** thus obtained with iodine, followed by the usual alkaline hydrogen peroxide oxidation provided 2-cyclopentylfuran in a yield of 95%. The results of reactions with representative trialkylboranes are summarized in Table 1.

In the present reaction, trialkylboranes with bulky alkyl groups such as *iso*-butyl, *sec*-butyl, and cyclopentyl seem to give high yields of corresponding 2-alkylfurans **5**. On the other hand, the opposite tendency was observed in the reaction of organoboranes with 2-lithiofuran in the absence of iodine[1]. Consequently, the present reaction, although not clear, could be considered to proceed via a different type of mechanism, for example, as shown in Scheme **B**.



Scheme **B**

The reaction can be extended for the synthesis of 2,5-dialkylfurans (**7**) (Scheme C). Thus, results of the reaction of trialkylboranes with 2-lithio-5-methylfuran are summarized in Table 2.



Scheme C

Probably the most general procedure previously available for the synthesis of 2-alkylfurans involves the reaction of 2-furyllithium with alkyl halides[2]. However, this synthesis is really satisfactory only for alkyl halides with primary alkyl groups[3], which readily undergo nucleophilic substitution reactions. In the case of *sec*-alkyl halides, it may involve a competitive elimination reaction[4]. On the other hand, the present synthesis is free of this limitation. Secondary groups appear to be introduced rather more readily than primary groups, as shown in Tables 1 and 2.

Ring opening reactions[5, 6, 7] of 2-alkylfurans and 2,5-dialkylfurans obtained by this method can provide synthetic routes to 4-oxoalkanals and 1,4-diketones. Thus, a synthetic procedure of 1,4-dicarbonyl compounds from organoboranes, though an indirect one, is now available. The following procedures are representative of the reactions described in this communication.

2-*sec*-Butylfuran (5d; R = *sec*-C_4H_9):

A dry 100 ml-flask equipped with a reflux condenser, a septum inlet, and a magnetic stirring bar is flushed with nitrogen. In the flask is placed furan (20.0 mmol, 1.5 ml) and anhydrous ether (15.0 ml). Then, *n*-butyllithium (20.0 mmol, 14.3 ml of 1.4 molar solution in ether) is added at −20°. The mixture is allowed to warm to room temperature and then refluxed for 4 h. After metallation is complete, tri-*sec*-butylborane (20.0 mmol, 10 ml of 2 molar solution in tetrahydrofuran) is added at 0° and stirred for 2 h. Finally, a solution of iodine (20.0 mmol, 5.08 g in 20 ml of tetrahydrofuran) is added at −78°. The solution is allowed to warm to room temperature and stirred over night. The reaction mixture is treated with 3 normal aqueous sodium hydroxide (13.4 ml) followed by dropwise addition of 30% hydrogen peroxide (4 ml). The product is extracted three times with ether and the combined organic layer is dried over magnesium sulfate. G.L.C. analysis (15% Silicon DC 550 on Uniport B, 150°) reveals 84% of 2-*sec*-butylfuran (**5d**). After evaporation of the solvent, the residue is distilled to give pure **5d**; yield: 1.6 g (65%); b.p. 30–32°/12 torr.

2-*sec*-Butyl-5-methylfuran (7d; R-*sec*-C_4H_9):

The ate complex **6d** is first prepared from 2-methylfuran (20.0 mmol, 1.8 ml in 15 ml of anhydrous ether), *n*-butyllithium (20.0 mmol, 14.3 ml of 1.4 molar solution in ether), and tri-*sec*-butylborane (20.0 mmol, 10 ml of 2 molar solution in tetrahydrofuran) under the same conditions mentioned above. A solution

0039-7881/79/0232-0146 $ 03.00

Table 1. Synthesis of 2-Alkylfurans 5 by the Reaction of Ate-complexes 1 with Iodine (Scheme B)

Product	R	Yield [%][a]	n_D^{20}	Lit. n_D (temp.)	Molecular formula[c]	Mass spectra *m/e*	b.p./torr
5a	n-C_3H_7	64	1.4419	1.4410 (25°)[8]	$C_7H_{10}O$ (110.2)	110 (M^+)	
5b	n-C_4H_9	76	1.4460	1.4460 (25°)[8]	$C_8H_{12}O$ (124.2)	124 (M^+)	
5c	*iso*-C_4H_9	92	1.4278	1.4425 (25°)[8]	$C_8H_{12}O$ (124.2)	124 (M^+)	
5d	*sec*-C_4H_9	84 (65)[b]	1.4359	1.4440 (14°)[9]	$C_8H_{12}O$ (124.2)	124 (M^+)	30–32°/12
5e	n-C_6H_{13}	66	1.4507		$C_{10}H_{16}O$ (152.2)	152 (M^+)	
5f	*cyclo*-C_5H_9	95	1.4838		$C_9H_{12}O$ (136.2)	136 (M^+)	

[a] G.L.C. analysis based on the organoborane used.
[b] Preparative yield by distillation.
[c] All products gave satisfactory microanalyses (C ±0.26 %, H ±0.11 %).

Table 2. Synthesis of 2-Alkyl-5-methylfurans 7 by the Reaction of Ate-complexes 6 with Iodine (Scheme C)

Product	R	Yield [%][a]	n_D^{20}	Lit. n_D (temp.)	Molecular formula[c]	Mass spectra *m/e*	b.p./torr
7a	n-C_4H_9	21	1.4482	1.4560 (25°)[8]	$C_9H_{14}O$ (138.2)	138 (M^+)	
7b	n-C_6H_{13}	26	1.4539		$C_{11}H_{18}O$ (166.2)	166 (M^+)	
7c	*iso*-C_4H_9	83	1.4423		$C_9H_{14}O$ (138.2)	138 (M^+)	
7d	*sec*-C_4H_9	97 (71)[b]	1.4501		$C_9H_{14}O$ (138.2)	138 (M^+)	74–75°/50
7e	*cyclo*-C_5H_9	93	1.4820		$C_{10}H_{14}O$ (150.2)	150 (M^+)	

[a] G.L.C. analysis based on the organoborane used.
[b] Preparative yield by distillation.
[c] All products gave satisfactory microanalyses (C ±0.22 %, H ±0.15 %).

of iodine (20.0 mmol, 5.08 g in 20 ml of tetrahydrofuran) is added to the mixture at −78°. The solution is allowed to warm to room temperature and stirred over night. The organic layer is oxidized with 3 normal aqueous sodium hydroxide (13.4 ml) and 30 % hydrogen peroxide (4 ml). The product is extracted with ether and dried over magnesium sulfate. Analysis by G.L.C. (15 % Silicon DC 550 on Uniport B, 160°) shows that 2-*sec*-butyl-5-methylfuran (**7d**) has been formed in a 97 % yield. Pure material of **7d** is obtained by distillation; yield: 2.0 g (71 %); b.p. 74–75°/50 torr.

Received: September 26, 1978

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0039-7881/79/0232-0147 $ 03.00