THE BIRCH REDUCTION OF 2-ACYLTHIOPHENES.
## SYNTHESIS OF 1,3-DIENYL KETONES FROM 2-ACYLTHIOPHENES

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The Birch reduction of 2-acyl or 2-acyl-5-alkylthiophenes and
subsequent alkylation by alkyl halides gave 2-acyl-2-alkyl or 2-acyl-
2,5-dialkyl-2,5-dihydrothiophenes in good yields. Further, 1,3-dienyl
ketones were obtained in good yields by the thermolysis of 2,5-
dihydrothiophene 1,1-dioxides which were obtained by the oxidation of
resulted dihydrothiophene derivatives with m-chloroperbenzoic acid.

1,3-Dienes are valuable intermediates[1] for the synthesis of many types of natural
products such as antibiotics and terpenes, and it is well known that the thermolysis
of 2,5-dihydrothiophene 1,1-dioxides[2], which are obtained easily by the oxidation of
2,5-dihydrothiophenes, give 1,3-diene derivatives in good yields.

Although a variety of useful methods for the preparation of 2,5-dihydrothiophene
derivatives[3] exist, there is a few reports which state that thiophene derivatives
can be the starting materials, because the Birch reduction of thiophene derivatives[4]
results in the formation of many products such as 2,5-dihydrothiophene, 2,3-dihydro-
thiophene and ring opening compounds, except for the case of the Birch reduction of
thiophene-2-carboxylic acid. Joullié and his co-workers reported[5] that the Birch
reduction of thiophene-2-carboxylic acid formed 2,5-dihydrothiophene-2-carboxylic
acid in good yield.

Now, we describe herein a new synthetic route leading to 1,3-dienyl ketones(4)
from 2-acylthiophene derivatives(1) using the Birch reduction as shown in the
following Scheme.
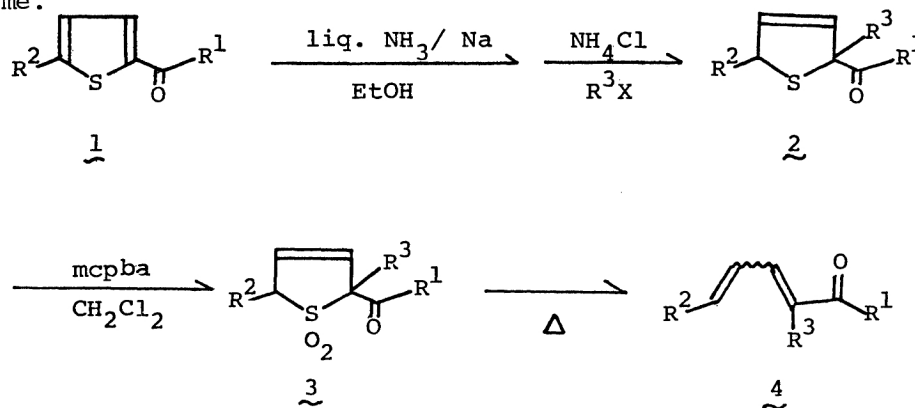
Scheme

At first, $2(R^2=H)$ was obtained by the reduction of 2-acylthiophenes$(1, R^2=H)$ with sodium in liquid ammonia in the presence of ethanol and subsequent addition of ammonium chloride and excess amounts of alkyl halides[6]. The results are summarized in Table I. As shown in Table I, 2-acyl-2-alkyl-2,5-dihydrothiophenes were obtained selectively without the formation of 2,5-dialkylated dihydrothiophene or double bond isomerized dihydrothiophenes by the above mentioned procedure. Further, $2(R^2=alkyl)$ were also obtained by similar procedures starting from 2-acyl-5-alkylthiophenes $(1, R^2=alkyl)$ in good yields (Run 2 i-k).

Table I.　The Birch reduction and alkylation of 2-acylthiophenes(1)

Run	R^1	R^2	R^3X(eq.)	Product[a] (2)	Yield(%)[b]
1a	Me	H	$PhCH_2Br$(2.1)		73
b	n-Pr	H	$PhCH_2Br$(2.1)		82
c	n-Pr	H	MeI(4.4)		72
d	n-Pr	H	⬳Br(3.2)		68
e	n-Pr	H	$n-C_4H_9Br$(3.1)		55
f	$n-C_9H_{19}$	H	$PhCH_2Br$(2.1)		61
g	cyclohexyl	H	$PhCH_2Br$(2.1)		80
h	-OH	H	$PhCH_2Br$(2.1)		68
i	n-Pr	Me	$PhCH_2Br$(2.1)		67
j	n-Pr	$n-C_4H_9$	$PhCH_2Br$(2.1)		76
k	$n-C_7H_{15}$	Me	MeI(4.5)		44

a) These products are characterized by nmr, ir, mass spectra and elemental analysis.
b) All products were isolated by column chromatography.

The reason for the selective formation of 2,5-dihydrothiophene derivatives is as follows; the addition of the ammonium chloride forms cyclic allyl anion by the protonation of dianion, which is produced initially by the Birch reduction. The resulted allyl anion is alkylated by the reaction of alkyl halide onyl at the 2 position to form 2,5-dihydrothiophene derivatives because the 2 position has highest electron density in the allyl anion by the effect of two electron attracting groups, that is, the acyl group of the 2 position and sulfur atom of the 1 position.

A typical procedure for the Birch reduction is as follows; into a solution of 2-butyrylthiophene (3.08 g, 20.0 mmol) in the mixed solvent, 3 ml of ether, 4 ml of ethanol and ca. 100 ml of liquid ammonia, sodium (1.06 g, 46.0 mmol) was added in small pieces over a period of several minutes. After stirring for 1 h, solid ammonium chloride (1.30 g, 24.3 mmol) was added and then the mixture was stirred for an additional 30 min. Then, benzyl bromide (5 ml, 42 mmol) was added slowly into the reaction mixture and was stirred for 1 h. Ammonia was evaporated and the residual mixture was quenched with 10% hydrochloric acid. The organic layer was extracted with diethyl ether and the ethereal layer was dried over magnesinm sulfate. After removal of the solvent, the residual oil was chromatographed on silica gel to give 4.04 g(82%) of 2-butyryl-2-benzyl-2,5-dihydrothiophene.

Oxidation of 2,5-dihydrothiophene derivatives(2b,i,j and k) to 2,5-dihydro-thiophene 1,1-dioxides(3) were carried out by treating with 2.5 eq. of m-chloroperbenzoic acid in dichloromethane. These results are summarized in Table II.

Next, thermal decomposition of 3b and 3i was performed in refluxing xylene for 6 h in the presence of 2,6-di-tert-butyl-4-methylphenol (BHT) in order to stabilize the resulted dienes giving desired 1,3-dienyl ketones(4b,i) in good yields.

Table II.   Oxidation of 2 and thermal decomposition of 3

Run	Yield of 3(%) [a)b)]	Product(4) [a)]	Yield of 4(%) [b)]	Total Yield(%) [d)]
2b	86		82	56
i	81		66	36
j	84		73[c)]	47
k	92		88[c)]	36

a) These products are characterized by nmr, ir, mass spectra and elemental analysis.
b) All products were isolated by column chromatography. c) These products were obtained by the thermolysis at 340 °C as mentioned above. These yields are based on recoverd starting materials; the amounts of recoverd starting materials were 3j 49% and 3k 39%. d) Total yields are calculated from 2-acyl-5-alkylthiophenes.

However, the thermal decomposition of 3j and 3k, which have rather long side chains at the 2 or 5 position, in refluxing xylene gave trace amounts of 1,3-dienyl ketones 4j and 4k and the starting materials were recoverd.   Then, the thermolysis of 3j and 3k were carried out by distillation at reduced pressure (2 mmHg) through the horizontally mounted glass tube (inner diameter 8 mm) preheated to 340 °C to give 4j and 4k in good yields.   These results are also summarized in Table II.

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6) Excess amounts (2.1-4.5 eq.) of alkyl halides must be added to complete the reaction, because a part of alkyl halides consumed by liquid ammonia.