

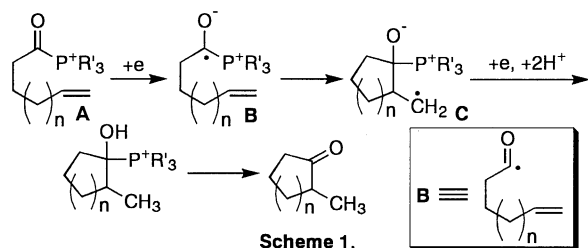
## Generation of Acyl Radical Equivalents by Cathodic Reduction of Acyl Tributylphosphonium Ions

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The species generated by one-electron transfer to acyl tributylphosphonium ions has proved to be potent acyl radical equivalents by the results that unsubstituted and 6-phenyl-substituted 5-hexenoic acids were transformed into cyclopentanones by the electrolysis in the presence of Bu<sub>3</sub>P in an undivided cell, although the yields were not satisfactory due to the formation of 5-hexen-1-als *via* further one-electron reduction of the radicals before their cyclization.

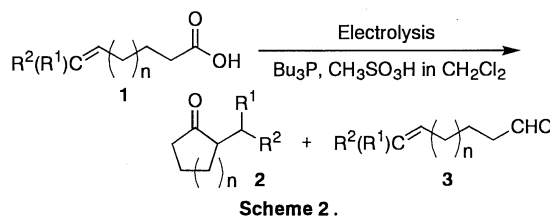
Recently, we have found that the partial reduction of carboxylic acids to the corresponding aldehydes can be achieved by constant current electrolysis of the acids in the presence of Ph<sub>3</sub>P<sup>1,2</sup> or Bu<sub>3</sub>P<sup>3</sup> in an undivided cell. Based on the proposed mechanism<sup>2,3</sup> as well as the finding that an  $\alpha$ -hydroxymethyl phosphonium moiety is equivalent to a carbonyl group, it was expected that a novel acyl radical equivalent would be generated directly from a carboxylic acid itself by the above unique electrolysis: that is, formation of cycloalkanones from carboxylic acids bearing an olefin at a proper position can be accomplished through cyclization of the acyl radical equivalent (radical **B**) generated by one-electron reduction of the acyl phosphonium ion (**A**) produced at the anode (Scheme 1).



The hypothesis is of great interest by the following reasons: (a) the electrochemical method will provide an easy access to novel acyl radical equivalents from easily available carboxylic acids without any tedious steps such as derivatization and deprotection usually required for the generation of hitherto reported acyl radical equivalents,<sup>4</sup> and nevertheless the latter have been recognized to be useful for C-C bond formation as acyl radicals themselves;<sup>5,6</sup> (b) the chemistry of carbon centered radicals adjacent to a phosphorus atom has been unexplored as far as we are aware. In this paper, we describe the possibility of acyl phosphonium ions as precursors of acyl radical equivalents.

As the model compounds, 5-hexenoic acid (**1a**), 8-phenyl-5-octenoic acid (**1b**), and 6-phenyl-5-hexenoic acid (**1c**) were chosen and prepared by a Wittig reaction of 5-carboxybutyl triphenylphosphonium bromide and the corresponding aldehydes with NaH in DMSO.<sup>7</sup> The electrolysis was carried out as follows. A solution of **1** (3 mmol), Bu<sub>3</sub>P (9 mmol), CH<sub>3</sub>SO<sub>3</sub>H (6 mmol), and Bu<sub>4</sub>NBr (3 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (30 ml)

was placed in an undivided cell equipped with two graphite plates (12.5 cm<sup>2</sup> each) as an anode and a cathode. Constant electric current (30 mA) was applied under a nitrogen atmosphere.<sup>8</sup> After 4.0 F/mol of electricity on **1** had been consumed, work-up with aqueous 10% K<sub>2</sub>CO<sub>3</sub> followed by column chromatography on SiO<sub>2</sub> eluting with benzene gave the products (Scheme 2 and Table 1).



On electrolysis of **1a**, the cyclized product **2a** was afforded in a 11% yield along with the aldehyde **3a** in a 64% yield, while **1b** was transformed only into the aldehyde **3b** in a 68% yield (runs 1 and 2 in Table 1). The electrochemical reaction allowed the conversion of **1c** into the cyclized product **2c** more effectively (37%) although **3c** was still formed in a 59% yield (run 3). These results suggest that the neutral radical **B** (Scheme 1), generated by one-electron reduction of the acyl phosphonium ion, can function as an acyl radical equivalent, but its intramolecular cyclization is in competition with its another one-electron reduction to an  $\alpha$ -oxy ylide leading into the formation of **3**.<sup>9</sup> An alternative cyclization mode initiated by cathodic reduction of the olefin moiety in **A** was ruled out by the following voltammetric results: each 5-hexenoic acid examined here showed no cathodic peak before the discharge of the solvent under the conditions of preparative electrolysis while acyl tributylphosphonium ions chemically formed from simple aliphatic acid chlorides and Bu<sub>3</sub>P exhibit cathodic peaks around -0.8~-0.9 V vs. Ag wire,<sup>3</sup> indicating that an electron transfer to the olefin moiety in **A** in preference to the phosphonium group is unlikely. As shown in Scheme 1, the neutral radical **C** formed after the cyclization seems to undergo another one-electron reduction instead of hydrogen abstraction from the solvent since no deuterated **2c** was obtained when the electrolysis of **1c** was carried out in CD<sub>2</sub>Cl<sub>2</sub> in the absence of CH<sub>3</sub>SO<sub>3</sub>H.<sup>10</sup>

Then, our attention was turned to the study on the steric and electronic effects of the internal olefin moiety upon the acyl radical cyclization since it would give a useful information to make the present methodology more synthetically valuable. First, the origin of the observed decrease in the *trans/cis* ratios during the transformation of **1c** to **3c** (see run 3) was investigated. Two explanations can be envisaged: (1) the acyl radical equivalent generated from *trans*-**1c** can cyclize faster than that from *cis*-**1c**; (2) the cyclization of the radical is a reversible process, allowing the *trans/cis* ratio in the neutral radical **B** to change, which will then reflect on the isomer ratio

**Table 1.** Results of the electrolysis of 5-hexenoic acids (**1**) in the presence of Bu<sub>3</sub>P<sup>a</sup>

Run		Substrate			Yield/% <sup>b</sup> of		
		R <sup>1</sup>	R <sup>2</sup>	n	<i>trans/cis</i>	<b>2</b>	<b>3</b> <sup>c</sup>
1	<b>1a</b>	H	H	1	—	11 <sup>d</sup>	64 <sup>d</sup>
2	<b>1b</b>	PhCH <sub>2</sub> CH <sub>2</sub>	H	1	— <sup>e</sup>	0	68 <sup>e</sup>
3	<b>1c</b>	Ph	H	1	1.04	37	59 (0.69)
4	"	"	"	"	8.09	49	38 (6.69)
5	<b>1d</b>	<i>p</i> -CH <sub>3</sub> -Ph	H	1	2.03	27	67 (0.82)
6	"	"	"	"	11.5	33	53 (8.09)
7	<b>1e</b>	<i>p</i> -MeO-Ph	H	1	3.76	26	68 (2.57)
8	"	"	"	"	only <i>trans</i>	31	61 (only <i>trans</i> )
9	<b>1f</b>	<i>p</i> -Cl-Ph	H	1	2.85	44	45 (1.94)
10	"	"	"	"	9.00	49	44 (6.14)
11	<b>1g</b>	<i>m</i> -Br-Ph	H	1	1.63	40	39 (0.89)
12	"	"	"	"	6.14	47	43 (4.26)
13	<b>1h</b>	Ph	Ph	1	—	11	77
14	<b>1i</b>	Ph	H	2	— <sup>e</sup>	0	93 <sup>e</sup>

<sup>a</sup>Yields are not optimized. <sup>b</sup>Isolated yield. <sup>c</sup>The number in parentheses shows the ratio between *trans*- and *cis*-isomers. <sup>d</sup>Isolated as its 2,4-dinitrophenylhydrazone derivative. <sup>e</sup>The isomer ratio was not determined.

in **3c**. In order to examine the possibility of the former, *trans*-enriched **1c** was synthesized by a similar Wittig reaction with (Me<sub>3</sub>Si)<sub>2</sub>NNa in THF.<sup>7</sup> The electrolysis of thus obtained **1c** with *trans/cis* = 8.09 gave **2c** in a 49% yield (run 4), which is a better result than that from **1c** with *trans/cis* = 1.04. The aldehyde **3c** was also formed but in a smaller amount, and the amount of *cis*-isomer again increased as compared with that of the starting acid.

The electrolysis was also applied to **1d**~**1g** with a substituent on the benzene ring of the styrene moiety. As apparent from the results in runs 5~12 in Table 1, the cyclized products were obtained in better yields from the *trans*-isomer enriched acids and the *trans/cis* ratio of the product **3** became smaller than that of the starting substrate as observed in the case of **1c**. Only *trans*-**3e** was obtained from pure *trans*-**1e**, indicating that a reversible cyclization of the radical (the possibility (2)) is unlikely. Thus, the finding that each neutral radical **B** derived from *trans*-**1c**~**1g** cyclizes faster than those from *cis*-ones can be ascribed to the difference in the steric interactions between the benzene ring and phosphorus moiety in the transition state. Importance of steric effects in the present cyclization was also shown by the results for 6,6-diphenyl-5-hexenoic acid (**1h**). The transformation of **1h** to the desired cyclized product **2h** resulted in a much poorer yield than the case of **1c**, although the olefin in **1h** seemed to be

more electrophilic (see below) than that in **1c** (run 13).

Although the electronic effects on the cyclization should be estimated from the results obtained for **1c**~**1g** with the same *trans/cis* ratio, the comparison of the results in runs 4, 6, 8, 10, and 12 has led to the conclusion that introduction of an electron-donating substituent on the aromatic ring induces the decrease in the cyclization rate of the acyl radical equivalent **A**, which shows that the present acyl radical equivalents are nucleophilic in nature.

In contrast to the case of **1c**, the electrolysis of 7-phenyl-6-hexenoic acid **1i** gave only the corresponding aldehyde **3i** without any formation of the desired cyclohexanone (run 14). This result, which is in line with the fact that cyclization of 6-heptenoyl radicals is slower than that of 5-hexenoyl radicals,<sup>6b</sup> also supports the radical character of the present reaction.

The results described so far confirm our initial hypothesis that acyl tributylphosphonium ions are potential precursors of acyl radical equivalents when subjected to electrochemical reduction. In spite of the limitations in preparing cyclopentanones, further work to investigate the chemical as well as electrochemical conditions for the highly selective one-electron reduction of the acyl phosphonium ions over their two-electron reduction will establish the generality and the synthetic utility of the present methodology, since the phosphonium ions can be chemically prepared from Bu<sub>3</sub>P and acid halides.<sup>11</sup>

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- The cell voltage during the electrolysis was about 5 V.
- Further proof for the existence of **B** might be given by the formation of a product derived from the homocoupling of **B**, but such a product was not obtained at all.
- 2c** and **3c** were formed in 25 and 8% yields, respectively.
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