Anodic Cleavage of Several Ketone N-Phenylsemicarbazones into Methyl N-Phenylcarbamate and the Corresponding Dimethyl Acetals

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GRAPHICAL ABSTRACT

$$-4e, \ -4H^+ \quad + \ 3\ MeOH \quad \longrightarrow \quad 45\text{-}98\ \% \quad + \quad 40\text{-}94\ \% \quad + \ N_2$$
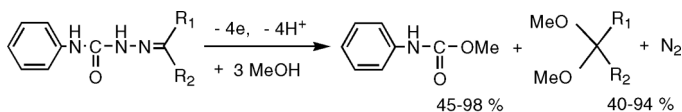
0.3 A const. current, 4.0-4.9 Fmol^{-1}, *ca.* 20°C R_1, R_2 = Alkyl or Aryl

Abstract *Several ketone* N-*phenylsemicarbazones were electrooxidized in the presence of potassium iodide and a base using methanol as the solvent to give nearly commensurate amounts of methyl* N-*phenylcarbamate and the corresponding dimethyl acetals. Continuous evolution of gaseous nitrogen was observed from the anolyte during the electrooxidation. The reactions were carried out under very mild reaction conditions and are presumed to proceed through a four-electron oxidation process, in which the iodide ion plays an important role as an electron carrier.*

INTRODUCTION

Aldehydes and ketones can be readily converted to the corresponding *N*-phenylsemicarbazones via condensation reactions using equivalent amounts of *N*-phenylsemicarbazide. The resulting semicarbazone derivatives are often used for identification of carbonyl compounds based on their known melting points.[1] The *N*-phenylsemicarbazone is the oxidized form of parent *N*-phenylsemicarbazide. Although a few reports are found regarding oxidation of ketone semicarbazones via typical chemical methods using oxidizing reagents,[2–9] to the best of our knowledge,

there are no reports on the oxidation of ketone *N*-phenylsemicarbazones via electrooxidative methods in MeOH.[10–12] Our studies focused on the electrooxidation of nitrogenous organic compounds, such as amines, enamines, and hydrazones, not only from the viewpoint of synthesis but also of the reactivities of the substrates.[13–21] During our investigation, we observed a novel and interesting behavior of ketone *N*-phenylsemicarbazone (**1**) under anodic conditions.

RESULTS AND DISCUSSION

At the beginning of the electrooxidation, almost all of substrate **1** existed as an insoluble fine powder in the anolyte because of its poor solubility in MeOH. Upon passage of electric current and under vigorous stirring, substrate **1** gradually dissolved into the anolyte. Interestingly, during the electrooxidation, continuous evolution of nitrogen gas from the anolyte was observed, which clearly indicates the decomposition of **1**. At the same time, gas–liquid chromatographic (GC) analysis of the anolyte indicated the immediate formation of methyl *N*-phenylsemicarbamate (**2**) and the corresponding dimethyl acetal (**3**). After the electric current passage of nearly 4 Fmol^{-1} of electrical current, most of **1** was dissolved, and the evolution of gaseous nitrogen ceased.

First, the optimal reaction conditions for the electrooxidative decomposition of **1** were determined using acetophenone semicarbazone (**1f**) as a model substrate. The types of the supporting electrolytes, along with the corresponding yields of **2** and acetophenone dimethylacetal (**3f**), are listed in Table 1.

Table 1. Anodic cleavage of acetophenone phenylsemicarbazone into methyl *N*-phenylcarbamate and acetophenone dimethyl acetal[a]
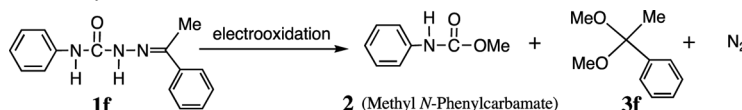
	Supporting electrolyte (mmol)		Yield (%)[b]	
Entry	Electrolyte	Mediator	**2**	**3f**
1	NaOMe (5.0)	None	11	26
2	None	KI (7.5)	95	94
3	NaOMe (2.5)	KI (7.5)	78	94
4	NaOMe (2.5)	NaI (7.5)	91	88
5	NaOMe (2.5)	KBr (7.5)	13	30
6	NaOMe (2.5)	KCl (7.5)	15	25
7	NaOAc (2.5)	KI (7.5)	90	83
8	NaOH (2.5)	KI (7.5)	91	94
9	KO(*t*-Bu) (2.5)	KI (7.5)	69	94
10	NaClO$_4$ (5.0)	None	12	20
11	LiClO$_4$ (5.0)	None	10	16
12	*p*-TsON(Et)$_4$ (5.0)	None	55	30

[a]**1f** (2.03 g, 8 mmol), MeOH (40 mL), constant current: 0.3 A, current passed: 4.2 Fmol^{-1}, rt (ca. 20 °C).
[b]Yields were determined by GC analysis using the internal standard (phenyl ether) method.

Remarkably, the use of merely 1 equivalent of KI (relative to **1f**) was the most effective in the formation of **2** and **3f** (95% and 94% yields, respectively, entry 2). One drawback, however, was that the terminal voltage tended to surpass 20 V during the first half step; this was easily resolved by the addition of NaOMe (ca. 0.3 equivalents relative to **1f**) without affecting the yield of **3f** (entry 3). However, the yield of **2** decreased from 95% to 78%. Substitution of KI with KBr (entry 5) or KCl (entry 6) resulted in poor yields of **2** and **3f** with unreacted **1** remaining within the electrolytic cell.
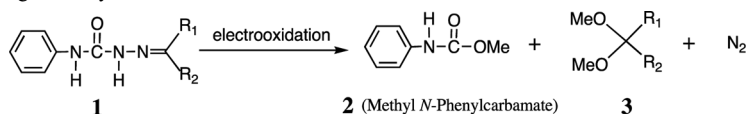
The use of a stronger base such as KO(*t*-Bu) (entry 9) resulted in a yield of **3f** (94%), comparable as that of NaOMe. The use of a weaker base such as NaOAc (entry 7) gave a somewhat lower yield of **3f** (83%). In regards to the mediator, the yields of **3f** were less than 30% for electrooxidation reactions that lacked KI (entries 1, 5, 6, and 10–12), illustrating the critical role of KI (source of iodide ions) in the decomposition reactions of **1f** (entries 2–4 and 7–9). Significant differences in the yields of **3f** were observed by varying the amounts of KI (5 mmol, 91%; 2 mmol, 70%; 1 mmol, 49%) and NaOMe (2.5 mmol, 94%; 10 mmol, 70%; 20 mmol, 49%). Immediately upon the start of the electrooxidation reactions, the yields of **2** and **3f** were proportional to the amount of current passed: 34% and 35% after the electric current passage of 1.5 F mol^{-1}, respectively and then 65% and 69% after 3.0 F mol^{-1}, respectively. In other words, these reactions are highly efficient (more than 86%) during the early stages. Theoretically, most of **1f** was consumed after a small excess amount of electric current (4.2 F mol^{-1}) was passed.

Based on the 50 results, the optimal reaction conditions were applied the electrooxidative cleavage of various ketone *N*-phenylsemicarbazones **1a–s**, as listed in Table 2. For alkyl ketone *N*-phenylsemicarbazones **1a–c, e**, the yields of the decomposed products varied between 68 to 85% of **2** and 58 to 67% of **3b, c**, and **e**, respectively. However, in the case of **1d**, the yields of **2** and **3d** unexpectedly decreased after the current passage of 3.0 F mol^{-1}. Compound **3a** could not be detected clearly by gas chromatography (GC) because of the low boiling point. For **1a–e**, the electrooxidations were carried out in the absence of NaOMe, which was found to decrease the yields of the products. Alkyl aryl ketones **1f–o** gave decomposed products in moderate to good yields (**2**, 64–95%, and **3**, 63–94%), except in the case of **1o**. For the benzophenone substrates, although good yields were obtained for **1p** (98% of **2** and 74% of **3p**), lower yields were observed for the substituted benzophenone *N*-phenylsemicarbazones **1q–s**, in which the parent substituted benzophenones were formed as the by-product in the yields of 20% to 36%. As a note, the solubilities of **1p–s**, which contain three aromatic rings, were improved using *t*-BuOH as a cosolvent with MeOH.

Following the electrooxidations, decomposed products **2** and **3** were readily isolated using silica-gel column chromatography. As a note, the phenyl-amido group (PhNHCO-) of **1** can be used repeatedly as a component of parent *N*-phenylsemicarbazide by refluxing isolated **2** with a small excess of hydrazinehydrate in EtOH.

Although the reaction pathway of these electrooxidiations still needs to be fully investigated, it is clear that iodide ions play an important role as electron carriers. As illustrated in Scheme 1, the anodic cleavage may involve the consumption of 3 equivalents of MeOH and elimination of four protons through a four-electron oxidation process.

In conclusion, the electrooxidation of ketone *N*-phenylsemicarbazone resulted in cleavage to methyl *N*-phenylsemicarbamate and the corresponding dimethyl acetal

Table 2. Anodic cleavage of ketone phenylsemicarbazones into methyl *N*-phenylcarbamate and the corresponding dimethyl acetals[a]

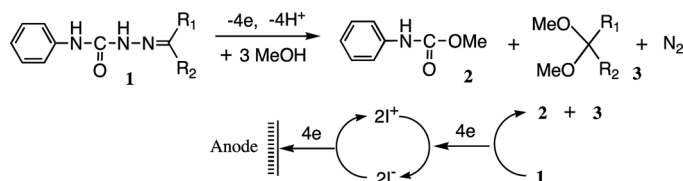| | | **1** | | **Yields (%)[b]** | |
Entry	R_1	R_2	Current passed ($Fmol^{-1}$)	**2**	**3**
a[c]	Me	Me	4.0	85	—
b[c]	-$(CH_2)_5$-		4.2	82	66
c[c]	-$(CH_2)_2$ -CH(t -C_4H_9)-$(CH_2)_2$-		4.2	84	58
d[c]	n-C_3H_7	n-C_3H_7	3.0	52	52
e[c]	Me	n-C_6H_{13}	4.2	68	67
f	Me	Ph	4.2	95	94
g	Me	p-Me C_6H_4	4.2	88	86
h	Me	p-MeO C_6H_4	4.2	80	77
i	Me	p-Cl C_6H_4	4.2	64	91
j	Et	p-Me C_6H_4	4.2	85	85
k	i-Pr	Ph	4.2	78	79
l	i-Bu	p-MeO C_6H_4	4.2	68	63
m	n-Bu	Ph	4.2	64	84
n	Me	3-Pyridyl	4.2	83	75
o[c]	Me	2-Furyl	4.1	45	40
p[d]	Ph	Ph	4.9	98	74
q[d]	p-Me C_6H_4	p-Me C_6H_4	4.9	93	55
r[d]	p-MeO C_6H_4	p-MeO C_6H_4	4.9	62	45
s[d]	p-Cl C_6H_4	p-Cl C_6H_4	4.9	71	51

[a]**1** (8 mmol), KI (7.5 mmol), NaOMe (2.5 mmol), MeOH (40 mL), constant current: 0.3 A, rt (ca. 20 °C).
[b]Determined by GC analysis using the internal standard method.
[c]Electrolysis was carried out in the absence of any base.
[d]t-BuOH (20 mL) was used as a cosolvent. The amount of NaOMe was increased to 5.0 mmol.

with generation of gaseous nitrogen. In addition to this interesting behavior of **1** under anodic conditions in MeOH, the reaction may be applicable for the preparation of various organic compounds. Moreover, the advantages of our method include (1) very mild reaction conditions (ca. 20 °C), (2) absence of harsh toxic reagents, such as metal oxidants or special reagents, and (3) a simple one-pot reaction.

Scheme 1. Reaction pathway of indirect anodic oxidation.

EXPERIMENTAL

Ketone *N*-phenylsemicarbazones were prepared in good yields (83–95%) via typical condensation reactions between *N*-phenylsemicarbazide and a small excess of the ketone by refluxing in EtOH for 1–5 h. Preparative-scale electrooxidations were carried out in a tall 50-mL beaker equipped with a fine frit cup as the cathode compartment with a nickel coil cathode, along with a cylindrical platinum net anode (50 mesh).

A solution of acetophenone *N*-phenylsemicarbazone **1f** (8 mmol) in MeOH (40 mL) containing KI (7.5 mmol) and NaOMe (2.5 mmol) was electrooxidized under a constant current (0.3 A). During the course of the electrooxidation, the anolyte was magnetically stirred at ca. 20 °C, and the composition of the reaction mixture was monitored by GC (FFAP, 1.5 m) analysis. Passage of the electric current was continued until almost all of the substrate was dissolved. Upon electric current passage of 4.2 F mol^{-1}, the reaction mixture was concentrated *in vacuo* (ca. 10 mL) at approximately 50 °C. The resulting oily residue was treated with water (ca. 30 mL), then extracted with ethyl ether (3 × 40 mL), and dried over sodium sulfate overnight. After removal of the solvent in vacuo, the crude mixture of **2** and **3f** were purified by silica-gel column chromatography using ether/hexane (3:5) as the eluent. The electrooxidation products were identified by comparison against authentic samples using GC analysis, high-resolution mass, and/or IR spectroscopy.

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