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Facile Synthesis of α-Keto Carbonyl Compounds by Indirect Anodic Oxidation

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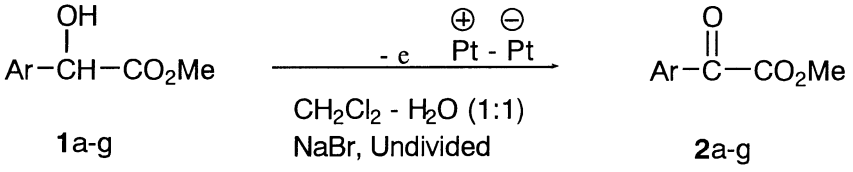
Secondary alcohols having a carbonyl group at the neighboring carbon atom were electrochemically oxidized to the corresponding α-keto carbonyl compounds in good yields. Thus, aromatic α-hydroxyl esters were easily transformed to arylglyoxylates in excellent yields using an undivided cell while efficient anodic oxidation of α-hydroxyl ketones and aliphatic α-hydroxyl esters successfully proceeded in a divided cell to give the corresponding α-keto carbonyl compounds.

Extensive studies have been focused on preparation of α-keto carbonyl compounds which are of much use as synthetic potent precursors of important substances such as optically active α-amino acids,[1] cyanoacrylate type of adhesives, and some heterocyclic compounds,[2] and as an excellent solvent for photoresist in optoelectronics processing.[3] Synthetic utility of hitherto known methods[4] for those compounds, however, has been considerably limited because of troublesome procedure, low selectivity and use of pollutive and/or expensive reagents. On the other hand, electrochemical indirect oxidation of secondary alcohols are known to give the corresponding ketones in good yields,[5,6] although only few anodic oxidation of alcohols having an electron-withdrawing group at the neighboring position was achieved using specific substances as mediators.[7]

In this study, we wish to report indirect anodic oxidation of α-hydroxyl carbonyl compounds using a readily available bromonium ion as a mediator to give the corresponding α-keto carbonyl compounds in good to excellent yields.

Indirect anodic oxidation was in general carried out in a double layer solvent system of water and dichloromethane (volume ratio 1:1) using sodium bromide as a supporting electrolyte at room temperature under the constant current conditions. Thus, a variety of aromatic α-hydroxyl esters (**1**a-g) were electrochemically oxidized to the corresponding arylglyoxylates (**2**a-g) in excellent yields using an undivided cell, as shown in Table 1.



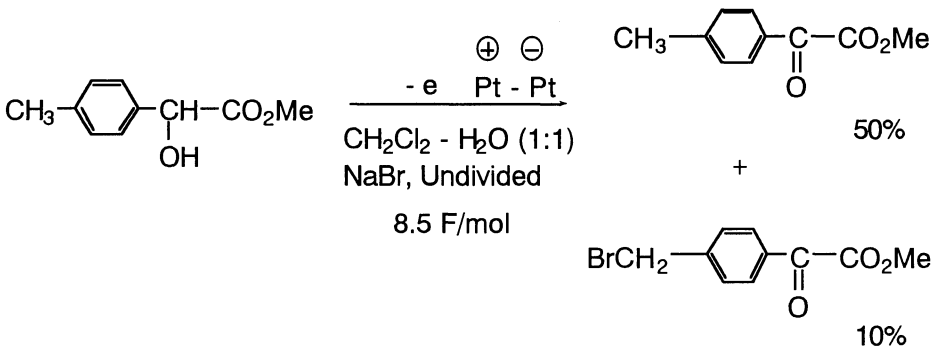
It may be noteworthy that efficient transformation of **1**a-g to **2**a-g required use of sodium bromide as a supporting electrolyte,[8] and the present anodic oxidation could smoothly proceed even for a solution containing relatively high concentration[9] of the starting compound **1**a-g, which is evidently favorite for large-scale preparation of **2**a-g.

Table 1. Indirect Anodic Oxidation of Aromatic α-Hydroxyl Esters (**1**)

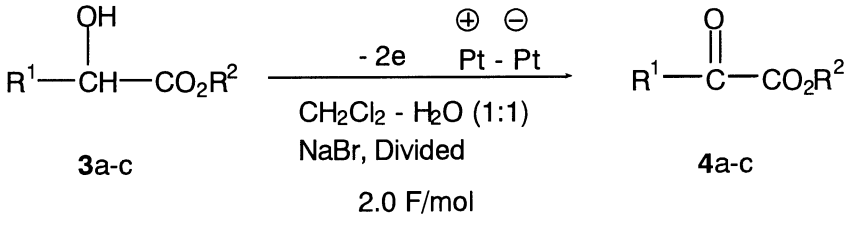
	Starting Substrate (**1**) Ar :	Supplied Electricity / F mol^{-1}	Isolated Yield of **2** / %
a	C_6H_5	6.0	87
b	4-ClC_6H_4	8.0	88
c	3-ClC_6H_4	8.5	92
d	2-ClC_6H_4	7.0	70
e	4-BrC_6H_4	6.0	95
f	4-FC_6H_4	6.0	80
g	4-$CF_3C_6H_4$	8.0	80

Reaction Conditions : Solvent [CH_2Cl_2-H_2O (1:1)], Current Density [0.1 A cm^{-2}], Concentration of **1** [0.5 M in CH_2Cl_2,1 M =1 mol dm^{-3}], Anode and Cathode [Pt], Concentration of NaBr [1.0 M in H_2O]

It is also interesting that even mandelates (**1**f,g) having a strong electron-withdrawing substituent such as a fluorine or a trifluoromethyl group on the phenyl ring of **1** could be easily transformed to the corresponding α-keto esters (**2**f,g) in good yields. The existence of a hydrogen atom at the benzylic position , however, was found to lead partial benzylic bromination under the similar conditions.

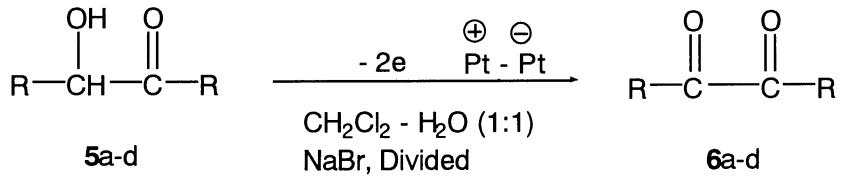


On the other hand, the indirect anodic oxidation of aliphatic α-hydroxyl esters (**3**a-c) required use of a divided cell because of their inefficient reaction with an undivided cell. Thus, some aliphatic α-hydroxyl esters (**3**a-c) were efficiently oxidized to the corresponding α-keto esters (**4**a-c) in good yields using a divided cell equipped with a ceramic cylinder as diaphragm and platinum plates as anode and cathode.



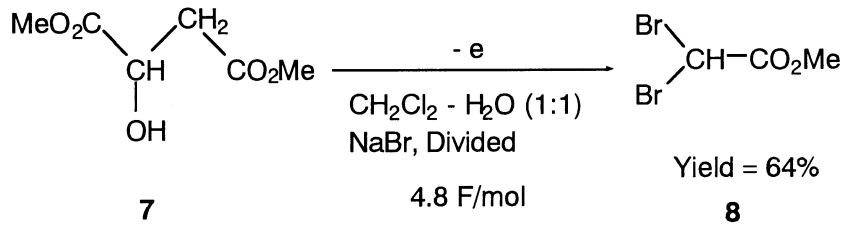
a : $R^1 = CH_3$, $R^2 = C_2H_5$ Yield = 60%
b : R^1 = iso-C_4H_9, R^2 = iso-C_3H_7 Yield = 65%
c : R^1 = n-C_4H_9, $R^2 = C_2H_5$ Yield = 80%

Furthermore, a variety of 1,2-diketones (**6**a-d) were successfully prepared in satisfactory yield by the indirect anodic oxidation of the corresponding α-hydroxyl ketones (**5**a-d) under the similar conditions using a divided cell, as shown below.



a : R = C_6H_5	3.5 F/mol	Yield = 95%
b : R = CH_3	2.0 F/mol	Yield = 54%
c : R = C_2H_5	2.0 F/mol	Yield = 86%
d : R = n-C_4H_9	2.0 F/mol	Yield = 96%

It is of some surprise that similar anodic oxidation of dimethyl malate (**7**), a kind of α-hydroxyl esters, under the same conditions brought about exclusive formation of methyl dibromoacetate (**8**) as a single product.[10]



It may be proposed that a bromonium ion or the related species generated by electron transfer from a bromide anion to anode played an important role as a potent oxidizing mediator in the present reaction.

Because of good yield and usefulness of the products, simple and convenient procedure , and non-pollutive reaction, the present method may possess high potentiality as a tool for synthesis of α-keto carbonyl compounds in both of laboratory and industrial scales.

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References

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7) It was reported that benzoin and dodecane-6,7-diol were transformed to the corresponding 1,2-diketones by indirect anodic oxidation using 2,2,6,6-tetramethylpiperidine N-oxide/NaBr as a mediator.[6b)]

8) Use of sodium chloride or iodide as a supporting electrolyte instead of sodium bromide resulted in no formation of phenylglyoxylate **2**a accompanying almost quantitative recovery of the starting methyl mandelate **1**a.

9) Increase in concentration of **1**a in CH_2Cl_2 from 0.5 M to 1.0 M did not lead to decrease in yield of **2**a (80%).

10) B. A. Shainyan and Z. Rappoport, *J. Org. Chem.*, **58**, 3421 (1993).

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