

Effect of Dicarboxylic Acids on the Rate of Oxidation and Bromination of Cyclododecane under GoAgg^{II} Conditions

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The development of new procedures for the selective functionalization of saturated hydrocarbons under mild conditions has been intensively studied during the last two decades.¹ Classical methods usually require drastic conditions, affording mixtures of products derived from overoxidation.² Therefore, the selective functionalization of alkanes that are the most abundant and cheapest class of organic compounds is an intellectually stimulating and industrially important task of current relevance.

It has been attractive to chemists that various enzymatic processes have emerged their promising ability for the selective functionalization of saturated hydrocarbons.³ Among them, non-heme iron catalyzed oxygenation systems are quite interesting for enzyme-mimetic chemical processes. Barton and co-workers have developed a family of chemical models that are one of promising candidates for non-heme chemical models attempting to mimic biological systems. These models are recognized as Gif systems.⁴ These systems can oxidize saturated hydrocarbons to mainly ketones under mild conditions. All use a pyridine-acetic acid solution of the hydrocarbon being oxidized and iron-based catalysts. Among Gif family, the most practical ones are GoAgg^{II} (pyridine-acetic acid with a catalytic amount of FeCl₃·6H₂O and H₂O₂ as an oxidant).

It has recently been reported that the ligands coordinated to iron are very crucial for elaborating a potential catalyst in the oxidation of saturated hydrocarbons.⁵ Those studies clearly demonstrated that the electronic environment around iron is very important in Gif-type oxidation. In this paper, we present our work on the influence of dicarboxylic acids as ligating agents on the rate of the oxidation and bromination of saturated hydrocarbons under GoAgg^{II} conditions.

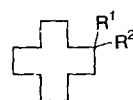
We have examined various dicarboxylic acids for the oxidation of cyclododecane (**1**) under GoAgg^{II} conditions (Table 1). Compared with the normal oxidation conditions (without dicarboxylic acids), almost every dicarboxylic acid had no significant effect in terms of rate-enhancement or the amount of the oxidized products, cyclododecanone (**2**) and cyclododecanol (**3**). However, oxalic acid (**5**) and malonic acid (**6**) revealed remarkable effects on the GoAgg^{II} oxidation reaction. Whereas the former completely inhibited the oxidation reaction, the latter promoted the activation process of alkane oxidation.

The ability of **6** to promote the GoAgg^{II} reaction was re-investigated. Although it did not provide a profound rate enhancement for the conversion of **1** to **2** compared with that obtained from the GoAgg^{III} system (GoAgg^{II} + picolinic acid

Table 1. Effect of Dicarboxylic Acids in the GoAgg^{II} Oxidation Reaction of **1**^a

Dicarboxylic Acid ^b	Yield (%) ^c					
	2 h			24 h		
	1	2	Σ	1	2	Σ
none	97.9	-	97.9	72.9	24.5	97.4
5	99.9	-	99.9	99.3	-	99.3
6	85.6	11.6	97.2	68.0	29.3	97.3
7	99.8	-	99.8	71.9	23.5	95.4
8	99.2	-	99.2	73.2	26.2	99.4
9	95.0	-	95.0	72.9	25.3	98.2
10	97.8	-	97.8	71.5	25.3	96.4
11	99.1	-	99.1	71.3	24.0	95.3
12	97.5	-	97.5	69.2	26.3	95.5
13	99.6	-	99.6	73.2	25.0	98.2

^aThe amount of **3** is negligible. See experimental for the reaction conditions in detail. ^bRatio of Fe^{III} to acid, 1 : 3. ^cBased on the substrate.



1 R¹ = H, R² = H

2 R¹, R² = O

3 R¹ = OH, R² = H

4 R¹ = Br, R² = H

HOOC(CH₂)_nCOOH

5 n = 0

6 n = 1

7 n = 2

8 n = 4

9 n = 5

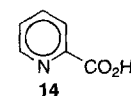
10 n = 6

11 n = 7

12 n = 8

HOOCCH₂C(CH₃)₂CH₂COOH

13



14

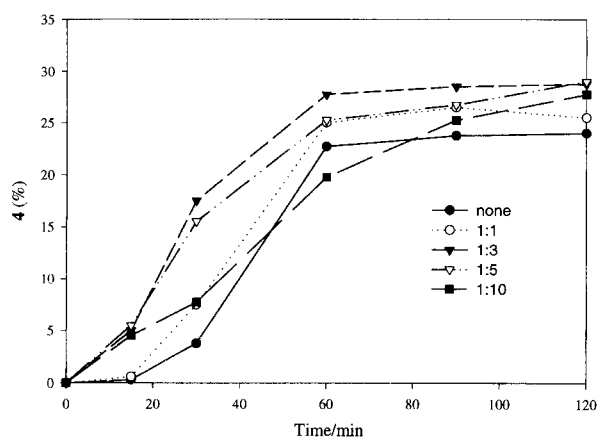
(**14**)), the rate of the oxidation reaction in the presence of **6** was found to be twice as fast as that observed in the normal GoAgg^{II} reaction. In contrast, both the yield and the rate for the GoAgg^{II} bromination reaction utilizing BrCCl₃ in the presence of **6** were remarkably found to be superior to those derived from GoAgg^{II} and GoAgg^{III} systems. The comparative results are displayed in Table 2.

The effect of the ratio variation of Fe^{III} to **6** on the bromination reaction was examined as presented in Figure 1. The rate of the bromination was increased on adding **6** up to a ratio of 1 to 3. The ratio of Fe^{III} to **6** of 1 : 3 provided the optimal conditions with regards to the yield of the desired product, cyclododecyl bromide (**4**), and the rate of the reaction. When more **6** (up to 10) was applied to the GoAgg^{II} bromination reaction, a slower rate of reaction with lower

Table 2. Comparative Results from the Oxidation and Bromination of **1** in the GoAgg^{II} and Modified Systems Consisting of **14** and **6**^a

System	Yield (%) ^c							
	Oxidation				Bromination			
	1	2	Σ	Half-life (min)	1	4	Σ	Half-life (min)
GoAgg ^{II}	72.4	25.0	97.4	300	70.3	25.3	95.6	45
GoAgg ^{II} + 14	68.3	26.7	95.0	10	72.4	26.4	98.8	20
GoAgg ^{II} + 6	69.8	27.5	97.3	150	70.1	29.6	99.7	25

^aSee experimental for the reaction conditions in detail. ^bRatio of Fe^{III} to acid, 1 : 3. ^cBased on the substrate.

**Figure 1.** Effect of the Ratio of Fe^{III} to **6** on the Bromination of **1**.

yields of **4** was observed.

In summary, this research demonstrated that the ligands around iron are very crucial for Gif-type chemistry. Various dicarboxylic acids have no significant effect on the rate of the reaction and the yields of the oxidized products with exception of **5** and **6**. Both of them were found to have activation and deactivation effect on the activation process of alkane oxidation. Especially, **6** revealed its enhancement ability on the rate of bromination of alkane comparable to **14**.

Experimental Section

General Procedures and Starting Materials. Melting points were determined with a Kofler hot stage melting point apparatus and were uncorrected. Gas chromatography analysis was carried out on a Hewlett Packard 5890 series II instrument, on Chrompack Model 439 or 437S instrument equipped with flame ionization detector with nitrogen as a carrier gas. The columns used for chromatography were DB-WAX (30 m) or DB-5 (15 or 30 m) capillary columns for J&W Scientific (0.32 mm, i.d. 25 μm film thickness). Gas chromatography-mass spectrometry (GC-MS) analysis was conducted on a Hewlett-Packard gas chromatograph Model 5790A coupled to a Hewlett-Packard 5970 mass selective detector (40 eV, electron impact). Solvents were used either as purchased or dried and purified by standard methodology under argon. Chemicals were purchased from Aldrich Chemical Co., except for Zn powder from Baker. H₂O₂ was used as

a 30% solution in water.

Effect of Dicarboxylic Acids on GoAgg^{II} Reactions. To a stirred solution of FeCl₃·6H₂O (54 mg, 0.2 mmol), cyclododecane (840 mg, 5.0 mmol) and an appropriate ratio of the ligating agent in pyridine (28 mL)-acetic acid (2.3 mL) was added 30% aqueous H₂O₂ (1.5 mL) in one portion. The resulting solution was stirred at room temperature in a closed flask for 16 h. An aliquot (1.0 mL) was taken from the reaction mixture, acidified with 25% H₂SO₄, extracted twice with diethyl ether, and then analyzed by GLC.

Effect of Picolinic Acid on GoAgg^{II} Reactions. A GoAgg^{II} reaction on cyclododecane was carried out as above, using a ratio picolinic acid /Fe of 3.

Bromination of Cyclododecane under GoAgg^{II} with Malonic Acid or Picolinic Acid. To a stirred solution of FeCl₃·6H₂O (54 mg, 0.2 mmol), cyclododecane (840 mg, 5.0 mmol), BrCCl₃ (198 mg, 5.0 mmol) and malonic acid or picolinic acid (0.6 mmol) in pyridine (28 mL)-acetic acid (2.3 mL) was added 30% aqueous H₂O₂ (1.5 mL) in one portion. The resulting solution was stirred at room temperature in a closed flask for 16 h. An aliquot (1.0 mL) was taken from the reaction mixture, acidified with 25% H₂SO₄, extracted twice with diethyl ether, and then analyzed by GLC.

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