Arbeitsvorschriften und Meßwerte · Procedures and Data

Synthesis of Phenylacetic Acid by Oxidation of Phenyl Acetaldehyde with Molecular Oxygen

Wilhelm Pritzkow, Volkmar Voerckel and Heike Weber

Merseburg, Institut für Technische Chemie der Technischen Hochschule

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Dedicated to Prof. Dr. Werner Schroth on the occasion of his 65th birthday

Phenylacetic acid is an intermediate for the synthesis of phenyl acetone; moreover, it is needed as a component of the culture medium of the microbiological synthesis of penicillin in order to favour the formation of penicillin G which can be especially

chain initiation

Ph-CH₂-CH=O + O₂ --- Ph-CH₂-C=O + •O-OH

Ph-CH2-CO-O-OH ---- Ph-CH2-CO-O++OH

chain propagation

Ph-CH2-C=O + O2 --- Ph-CH2-CO-O-O-

Ph-CH₂-CH=O + Ph-CH₂-CO-O-O-—— Ph-CH₂-Ċ=O + Ph-CH₂-CO-O-OH

chain termination

Ph-CH2-C=O --- Ph-CH2 + CO

 $\begin{array}{rrrr} 2 \mbox{ Ph-CH}_2\mbox{-CO-O-O} & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & &$

Ph-CH₂· + O₂ ---- Ph-CH₂-O-O-

2 Ph-CH₂-O-O· --- Ph-CH₂-O-O-O-CH₂-Ph --- Ph-CH=O + O₂ + Ph-CH₂OH

radical consecutive reaction

 $\begin{array}{rl} \mbox{Ph-CH}_2 & + \mbox{Ph-CH}_2 \mbox{CH=O} \\ & & ---- \mbox{Ph-CH}_3 & + \mbox{Ph-CH}_2 \mbox{\dot{C}=O} \end{array}$

nonradical consecutive reaction

Formula Scheme 1. Mechanism of the free-radical chain oxidation of phenyl acetaldehyde and of the side reactions taking place.

easily isolated [1]. One possibility for the synthesis of phenylacetic acid is the oxidation of phenyl acetaldehyde which can be obtained by the acid-catalyzed rearrangement of styrene oxide [2]. Styrene oxide is formed from styrene either by oxidation with organic hydroperoxides in the presence of molybdenum catalysts [3] or by direct oxidation with oxygen [4].

Considering the oxidation of phenyl acetaldehyde as an interesting pathway for the industrial synthesis of phenylacetic acid one must have regard to the fact that the intermediate phenylacetyl radical decarbonylates very easily [5].

Acyl radicals are intermediates of the oxidation of aldehydes with molecular oxygen [5] (Formula Scheme 1). The more stable the alkyl radical formed, the more easily the decarbonylation of the corresponding acyl radical proceeds [5, 6]. The decarbonylation of acyl radicals is competitive to their reaction with molecular oxygen.

The decarbonylation has a remarkable activation energy (in the case of the phenylacetyl radical 25 to 30 kJ mol⁻¹ [6, 7]) whereas the oxidation as a reaction between two radicals (triplet oxygen must be regarded as a diradical in this case) needs no activation energy. This means that the desired reaction is favoured by decreasing temperature. Moreover the oxygen concentration should always be high enough to make the wanted reaction possible. This can be secured by using a suitable solvent and by working at a low temperature.

The oxidation of phenyl acetaldehyde acid is described in a patent of the firm Rhone-Poulenc [8]. In this patent acetic acid is recommended as the solvent, cobalt acetate as the catalyst and 20 °C as the reaction temperature. The yield of phenylacetic acid is described as 83 %; as by-products benzoic acid, benzal-dehyde and benzyl formiate (consecutive products of the benzyl radical formed by decarbonylation of the intermediate phenylacetyl radical) were found.

More recently, a group of Czechoslovakian authors published results concerning the oxidation of phenyl acetaldehyde with molecular oxygen [9]. They used n-heptane as the solvent and cobalt acetate as the catalyst; the reaction temperature was 35 °C. Phenylacetic acid was obtained with a yield of 56%, benzyl alcohol (19%) and benzoic acid (19%) were found as side products.

| reaction product | temperature | yield in | mmol per 1 | 00 mmol of | the starting | phenyl aceta | aldehyde aft | er a reaction | time (h) of |
|---------------------------------|-------------|----------|------------|------------|--------------|--------------|--------------|---------------|-------------|
| | °C | 1.0 | 1.5 | 2.0 | 2.5 | 3.0 | 4.0 | 5.0 | 6.0 |
| Benzaldehyde | 30 | 10.5 | 12.0 | 10.0 | 8.6 | 3.7 | 1.8 | ········ | |
| | 20 | | | 9.3 | | 4.0 | 3.2 | 1.7 | 2.7 |
| | 10 | | | 6.0 | | 4.7 | 3.3 | 2.4 | 1.4 |
| | 5 | | | 5.3 | | 5.2 | 3.9 | 2.2 | 3.1 |
| benzoic acid ^{a)} | 30 | 4.1 | 11.2 | 23.2 | 35.4 | 29.6 | 47.3 | | |
| | 20 | | | 16.3 | | 23.4 | 26.5 | 29.1 | 34.7 |
| | 10 | | | 5.9 | | 12.3 | 16.0 | 16.2 | 20.3 |
| | 5 | | | 2.6 | | 5.7 | 11.6 | 11.1 | 13.6 |
| phenyl acetaldehyde | 30 | 23.5 | 3.2 | 1.8 | 1.2 | 1.7 | 0.2 | | |
| | 20 | | | 4.1 | | - | _ | | _ |
| | 10 | | | 4.5 | | _ | _ | | _ |
| | 5 | | | 8.1 | | 3.9 | - | | - |
| benzyl formiate | 30 | 3.8 | 2.5 | 7.5 | 2.4 | 2.0 | 3.3 | | |
| | 20 | | | 3.0 | | 3.0 | 4.0 | 3.1 | 4.2 |
| | 10 | | | 2.8 | | 2.7 | 3.6 | 3.5 | 2.8 |
| | 5 | | | 2.7 | | 3.6 | 2.6 | 3.4 | 3.3 |
| phenylacetic acid ^{a)} | 30 | 20.1 | 34.3 | 30.2 | 39.6 | 38.7 | 37.7 | | |
| | 20 | | | 46.4 | | 56.4 | 62.8 | 58.9 | 52.0 |
| | 10 | | | 62.3 | | 66.7 | 73.2 | 75.3 | 65.9 |
| | 5 | | | 59.7 | | 73.7 | 72.4 | 83.5 | 75.9 |
| benzył alcohol | 30 | 3.8 | 5.8 | 3.6 | 3.3 | 1.6 | 0.4 | | |
| | 20 | | | 1.6 | | _ | _ | | _ |
| | 10 | | | 1.2 | | 0.1 | _ | _ | |
| | 5 | | | 0.9 | | 0.4 | _ | - | _ |

 Table 1.
 Oxidation of phenyl acetaldehyde in the presence of cobalt acetate as the catalyst; acetic acid as the solvent

^{a)}analyzed as the corresponding methyl ester (after reaction with diazomethane)

We have oxidized solutions of phenyl actealdehyde in acetic acid at 5 to 30 °C with pure oxygen. In most cases cobalt acetate was used as the catalyst. Some experiments at 5 °C were accomplished with manganese acetate as the catalyst. After a definite time the mixture was analyzed by gaschromatogra-

Table 2. Oxidation of phenyl acetaldehyde at 5 °C in the presence of manganese acetate as the catalyst; acetic acid as the solvent

| reaction product | yield in mmol per 100 mmol of the starting phenyl acetaldehyde after a reaction time (h) of | | | | | | |
|---------------------------------|---|------|------|------|------|--|--|
| | 3.0 | 4.0 | 5.0 | 6.0 | 7.0 | | |
| benzaldehyde | 5.6 | 5.1 | 3.5 | 4.3 | 4.0 | | |
| benzoic acid ^{a)} | 1.0 | 3.0 | 5.2 | 4.7 | 6.9 | | |
| phenyl acetaldehyde | 11.9 | 4.6 | 4.3 | 3.4 | - | | |
| benzyl formiate | 1.7 | 1.2 | 1.6 | 1.6 | 0.9 | | |
| phenylacetic acid ^{a)} | 48.0 | 71.0 | 81.4 | 84.1 | 85.7 | | |
| benzyl alcohol | _ | _ | _ | _ | | | |

^{a)}analyzed as the corresponding methyl ester (after reaction with diazomethane)

phy. The results obtained in the presence of cobalt acetate are collated in Table 1. The yield of phenylacetic acid is insufficient at 30 °C, but increases with decreasing temperature and amounts to about 80 % at 5 °C. A further decrease of temperature was impossible with acetic acid as the solvent because of the crystallization that took place below 5 °C. When we tried to work-up a greater amount of the reaction mixture obtained at 5 °C in the presence of cobalt acetate a vigorous decomposition took place. Thereafter we followed the concentration of peroxidic compounds (peroxy acids, addition products of peroxy acids with aldehydes, benzyl hydroperoxide) during the oxidation at 5 °C. This concentration showed a maximum of about 13 mmol peroxy groups per 100 mmol of the initial phenyl acetaldehyde (Table 3) although the concentration of catalyst was unusual high. Therefore we accomplished, also at 5 °C, some oxidations in the presence of manganese acetate as the catalyst and, surprisingly, the maximum peroxide concentration diminished to only 1-2 mmol peroxy groups per 100 mmol of the inital phenyl acetaldehyde (Table 3). Evidently, manganese acetate is a far better catalyst than cobalt acetate for the decomposition of the peroxidic intermediates of the oxidation. The yields of phenyl acetic acid in the presence of manganese acetate (Table 2) lie in the same order of magnitude (85%) as in the presence of cobalt acetate.

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Experimental

Oxidations

30 g (0.22 mol) phenyl acetaldehyde, 70 g acetic acid and 1 g (4.01 mmol) $Co(OAc)_2$.4H₂O were given into an 150 ml oxidation vessel equipped with heating/cooling jacket, oxygen inlet tube and reflux condenser. The mixture was thermostated to the wanted temperature (5 to 30 °C). Then an oxygen stream of 5 l h⁻¹ was introduced for the wanted reaction time (1 to 7 h). To a 5 g sample of the oxidation mixture 10 g of ethyl benzene were added, then the ethyl benzene/acetic acid azeotrope [10] was distilled off from a water bath at 35–40 °C/4 kPa. For this distillation a 30 cm-Vigreux column was used. The residue was dissolved in diethyl ether, the organic acids present were esterified by diazomethane. The main part of the diethyl ether was distilled off from a water bath, a weighed amount (0.3 to 0.5 g) of bromobenzene (internal standard) was added to the residue, and the resulting mixture was analyzed by gaschromatography

Table 3. Peroxide contents during the oxidation of phenyl acetaldehyde at $5 \,^{\circ}$ C in acetic acid as the solvent

| Reaction time (h) | peroxide content in mmol per 100 mmol of the starting phenyl acetaldehyde in the presence of | | | | | | |
|-------------------|--|---------|-------------------------|--|--|--|--|
| | Co(OAc) ₂ . | $4H_2O$ | $Mn(OAc)_2 \cdot 4H_2O$ | | | | |
| | 1.0% | 0.1 % | 0.1 % | | | | |
| 0 | 0.43 | 0.19 | 0.19 | | | | |
| 0.5 | 3.45 | 1.84 | 0.10 | | | | |
| 1.0 | 6.13 | 4.05 | 0.30 | | | | |
| 1.5 | 10.07 | 5.54 | 0.48 | | | | |
| 2.0 | 11.60 | 6.19 | 0.39 | | | | |
| 2.5 | 12.66 | 9.18 | 0.68 | | | | |
| 3.0 | 13.54 | 11.16 | 0.79 | | | | |
| 3.5 | 12.84 | 11.86 | 1.05 | | | | |
| 4.0 | 11.67 | 11.76 | 1.13 | | | | |
| 4.5 | 10.08 | 11.29 | 1.31 | | | | |
| 5.0 | 9.36 | 11.23 | 1.40 | | | | |

(5 m-column with 15% diethyleneglycol adipate on silanized chromatone; 120-210 °C (2 K min⁻¹); $3 \ l h^{-1}$ Ar; FID). Table 1 shows the results of the experiments at various temperatures and various reaction times. The results obtained at 5 °C using 0,1 g (0.41 mmol) Mn(OAc)₂.4H₂O instead of 1 g (4.01 mmol) Co(OAc)₂.4H₂O as the catalyst are collated in Table 2.

The amount of peroxidic compounds present after various reaction times was determinated by iodometric titration of samples of 0.1 to 0.3 g taken during the oxidation at 5 °C in the presence of cobalt or manganese acetate. The results are collated in Table 3.

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Address for Correspondence:

Prof. Dr. W. Pritzkow

Martin-Luther-Universität Halle-Wittenberg

Institut für Technische und Makromolekulare Chemie Geusaer Straße

D-06127 Merseburg