

Production of Phenylacetic Acid by the Liquid Phase Oxidation of Acetophenone with Sulphur in the Presence of Aqueous Ammonia

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The liquid phase oxidation of acetophenone by aqueous ammonia and sulphur to phenylacetamide and/or phenylacetic acid was investigated in a stainless steel autoclave maintained under autogenous pressure. The effects of type and amount of solvent, amount of sulphur, concentration of acetophenone and ammonia, temperature and period of reaction, and the presence of impurities in commercial grade acetophenone, on the conversion and yield of phenylacetamide and/or phenylacetic acid were studied with a view to obtain the most suitable conditions for the production of phenylacetic acid. Since the product was a mixture of phenylacetamide and phenylacetic acid, hydrolysis of phenylacetamide was studied with a view to obtaining phenylacetic acid. Also, the solubility of phenylacetamide in water was determined.

1. Introduction

Phenylacetic acid is an important chemical used in the manufacture of penicillin. Addition of phenylacetic acid, or one of its derivatives, to the fermentation liquor increases the yield of benzylpenicillin.⁷ Phenylacetic acid is one of the most important perfumery acids, and it is widely used, although in minute proportions in fragrances and flavours.¹ Phenylacetic acid is manufactured commercially by the hydrolysis of benzylcyanide which is obtained from benzylchloride.⁷

An interesting possibility would be the use of a modified Willgerodt's reaction,⁹ where acetophenone is oxidised with sulphur and aqueous ammonia to phenylacetamide, which could be converted by hydrolysis to phenylacetic acid.⁵



Acetophenone can be readily obtained by the liquid phase oxidation of ethylbenzene with air.⁸ The information available on the oxidation of acetophenone, however, is very limited. A few investigators²⁻⁶ have dealt with the chemistry of the process. These investigators have employed relatively costly and hazardous solvents like pyridine and dioxane. Work was, therefore, undertaken to investigate the reaction under conditions suitable for an industrial process.

2. Experimental

The reactor consisted of a high pressure stainless steel horizontal rotating autoclave of 1 l capacity. The speed of rotation of the autoclave was 18 rev/min. It was electrically heated and the temperature was controlled by a 'variac'.

2.1. Analytical

The reaction mixture consisted of unreacted acetophenone, ammonium polysulphide, phenylacetamide, phenylacetic acid and some tarry material. In order to analyse the unreacted acetophenone, the reaction mixture was refluxed to decompose the ammonium polysulphide present. Ammonia and hydrogen sulphide escaped to atmosphere and sulphur precipitated from the solution. Sulphur was filtered off and the filtrate was treated for the determination of acetophenone by the gravimetric method using 2,4-dinitrophenyl hydrazine.¹⁰ The precipitate of 2,4-dinitrophenyl hydrazone was washed with hot water to remove all phenylacetamide and phenylacetic acid from the precipitate.

A mixture of phenylacetamide and phenylacetic acid was recovered from the reaction mixture by the procedure discussed elsewhere.⁴ The product so obtained was analysed for phenylacetamide and phenylacetic acid together by saponification with an alkali. Phenylacetic acid alone in the product mixture was determined by titrating it against a standard alkali.

3. Results and discussion

The oxidation of acetophenone using sulphur and aqueous ammonia was essentially a heterogeneous reaction. When only water was used as solvent, four phases were present, (i) molten sulphur, (ii) aqueous phase of ammonium polysulphide, (iii) acetophenone dispersed in the aqueous phase, and (iv) gaseous phase. When alcohol was added to the solvent, only three phases were present; (i) molten sulphur, (ii) aqueous phase of ammonium polysulphide containing alcohol and dissolved acetophenone, and (iii) gaseous phase.

When ammonia was used as the base, the product mixture consisted mainly of phenylacetamide along with small amount of phenylacetic acid. When caustic soda was used as a base instead of ammonia in an attempt to get phenylacetic acid directly, no phenylacetic acid was detected, the product being mainly benzoic acid. This is in agreement with the work of Toland.¹¹

In the following discussion of results, the yield of the product refers to the combined yield of phenylacetamide and phenylacetic acid. Since most of the reaction takes place in the solvent phase, concentrations are based on the volume of the solvent phase. The total volume of the solvent phase includes the volume of the solvent and acetophenone. The material balance accounts for as much as 95.5% acetophenone (Table 1). Therefore, other by-products may be neglected.

3.1. Effects of reactant concentrations

The beneficial effect of adding ethanol is shown in Tables 2 and 3, where yields up to 96% (69% using water alone) are obtained. This yield was obtained using 1.4 g mol/l

TABLE 1. Product distribution and material balance with respect to acetophenone

	g mol	Mol (%) acetophenone accounted for
Unreacted acetophenone	0.00375	1.5
Phenylacetamide	0.20075	80.4
Phenylacetic acid	0.00600	2.4
Tarry materials*	0.02800	11.2
Total	0.23850	95.5

Concentration of acetophenone = 0.8 g mol/l of solvent phase; concentration of ammonia = 2.4 g mol/l of solvent phase; amount of sulphur = 4.8 g mol/l of solvent phase; reaction temperature = 165 °C; reaction period = 1.0 h; pressure = 18 atm; acetophenone taken = 0.25 g mol.

* Assumption is made that the equal weight of tarry material is formed from acetophenone.

TABLE 2. Effect of type and amount of solvent

Run no.	Amount of sulphur g mol/l of solvent phase	Alcohol % in the solvent	Combined yield of phenylacetamide and phenylacetic acid (%)
1	16.90	0	69.0
2	8.45	0	55.6
3	16.90	55	96.0
4	8.45	55	69.5

Acetophenone, 0.25 mol; concentration of acetophenone, 1.4 g mol/l of solvent phase; concentration of ammonia, 5.65 g mol/l of solvent phase; temperature, 165 °C; preheating period, 1.25 h; heating period, 4 h; conversion of acetophenone, 100%.

TABLE 3. Effect of dilution

Run no.	(G mol/l of solvent phase) Amount concentration of			Alcohol % in the solvent	Combined yield of phenylacetamide and phenylacetic acid (%)
	C ₆ H ₅ COCH ₃	S	NH ₃		
1	1.4	8.45	5.65	55	69.5
2	0.8	4.80	3.20	75	92.8
3	0.8	3.20	3.20	75	84.0

Acetophenone, 0.25 mol; temperature, 165 °C; preheating period, 1.25 h; heating period, 4 h; conversion of acetophenone, 100%.

of solvent phase acetophenone which resulted in a thick unworkable slurry. Consequently, the acetophenone concentration was reduced to 0.8 g mol/l of solvent phase.

An increase in the amount of sulphur increased the yield as shown in Figure 1. This was so despite a molar ratio of sulphur to acetophenone of 6 or more and this also applied in the system with reduced acetophenone (Table 3). An increase in ammonia concentration up to 2.4 g mol/l solvent phase also increased the yield

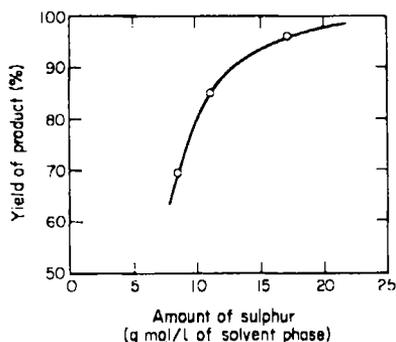


Figure 1. Effect of amount of sulphur. Acetophenone, 0.25 mol; concentration of acetophenone, 1.4 g mol/l of solvent phase; concentration of ammonia 5.65 g mol/l of solvent phase; temperature, 165 °C; preheating period, 1.25 h; reaction period 4 h, conversion of acetophenone, 100%.

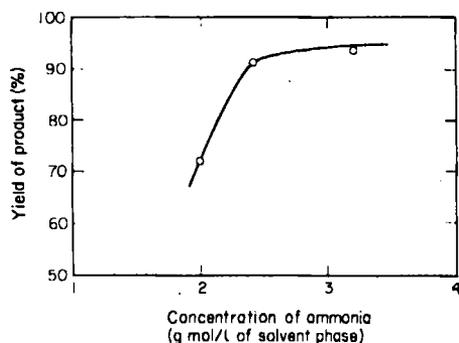


Figure 2. Effect of concentration of ammonia. Acetophenone, 0.25 mol; concentration of acetophenone; 0.8 g mol/l of solvent phase; amount of sulphur, 4.8 g mol/l of solvent phase; temperature, 165 °C; preheating period, 1.25 h; reaction period, 4 h; conversion of acetophenone, 100%.

(Figure 2). It appears that all the factors which tend to increase the relative concentrations of acetophenone, sulphur and ammonia in the solvent phase have a beneficial effect on the yield. This indicates that the rate of the desired reaction is, presumably, more sensitive to increased concentrations than are the rates of the reactions producing tars.

3.2. Effects of process conditions

Although heating (1.25 h) and quenching (10 min) times for the autoclave coupled with a threshold temperature for reaction of approximately 125 to 130 °C made an accurate assessment of the period of reaction difficult, it was observed that an increase in the reaction time from 1 to 4 h had a small but significant effect on the yield (Figure 3).

Table 4 shows the effect of temperature (the reaction time at 150 °C was extended to attain a comparable conversion) and indicates that temperatures below 165 °C are inefficient.

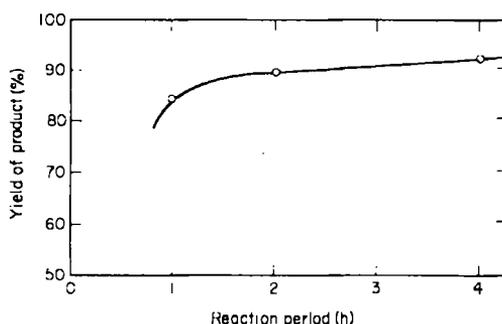


Figure 3. Effect of period of reaction. Acetophenone, 0.25 mol; concentration of acetophenone, 0.8 g mol/l of solvent phase; concentration of ammonia, 2.4 g mol/l of solvent phase; amount of sulphur, 4.8 g mol/l of solvent phase; temperature, 165 °C; preheating period, 1.25 h; conversion of acetophenone, 100%.

TABLE 4. Effect of reaction temperature

Run no.	Reaction temperature (°C)	Preheating period (h)	Reaction period (h)	Combined yield of phenylacetamide and phenylacetic acid (%)
1	150	1.25	2.0	77.4
2	165	1.25	1.0	84.0
3	180	1.25	1.0	8.57

Acetophenone taken, 0.25 mol; concentration of acetophenone, 0.8 g mol/l of solvent phase; concentration of ammonia, 2.4 g mol/l of solvent phase; amount of sulphur, 4.8 g mol/l of solvent phase; conversion of acetophenone, > 98%.

3.3. The effect of impurities

The commercial acetophenone derived from ethylbenzene contains about 4% phenylmethyl carbinol, but in a run with commercial acetophenone no effect on the yield was observed.

3.4. Work-up and purification

The reaction mixture discharged from the autoclave is a thin slurry of sulphur in an alcoholic solution containing dissolved phenylacetamide, phenylacetic acid, ammonium polysulphide and some tarry material. This slurry may be evaporated to decompose the ammonium polysulphide. Alcohol, ammonia, hydrogen sulphide and water will go in vapours while a solid residue consisting of sulphur, phenylacetamide, phenylacetic acid and tarry material will remain behind. The ammoniacal alcoholic solution containing dissolved hydrogen sulphide, obtained after condensing vapours, may be reused after making it up with sulphur and ammonia. The solid residue may be leached with hot water to extract all the phenylacetamide and phenylacetic acid. Sulphur with tarry materials which are insoluble in hot water, will remain behind. This may be washed with hot alcohol to remove all tarry material and the purified sulphur may be reused.

The hot water extract obtained is slightly yellowish in colour. When it is evaporated, a solid mass containing mainly phenylacetamide along with about 3 to 5% phenylacetic acid is obtained. The mass is slightly brown in colour.

For the recovery of phenylacetic acid, the hot water extract was refluxed with activated carbon to decolourise and then hydrolysed by adding the required amount of mineral acid. The precipitate was filtered, washed with water and finally dried to give pure phenylacetic acid having melting point 76 to 77 °C (reported 77 °C), and equivalent weight 137 (calculated 136).

3.5. Solubility of phenylacetamide in water

Since the product mixture mainly consisted of phenylacetamide (about 95%), which was leached with hot water, solubility data of phenylacetamide in water were collected. The plot of $\ln S$ vs. $1/T$ was a straight line (Figure 4).

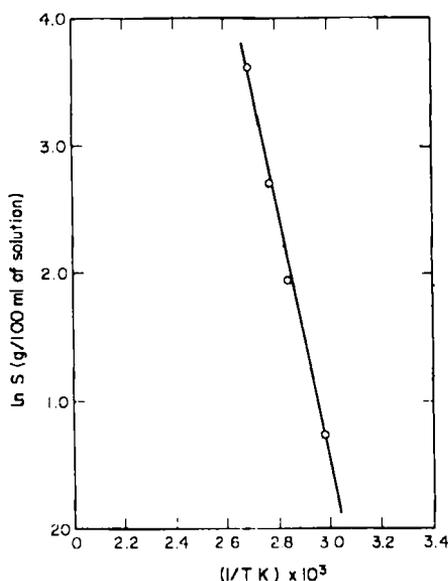


Figure 4. Solubility of phenylacetamide in water.

3.6. Hydrolysis of phenylacetamide

The hydrolysis of phenylacetamide was studied with different concentrations of hydrochloric acid for a given reaction period at 87 and 100 °C. The desirable concentration of hydrochloric acid found was 3 g mol/l. Above this concentration the conversion to phenylacetic acid did not increase significantly (Figure 5).

In the kinetic study of the hydrolysis, 3 N-hydrochloric acid was taken in excess, about four times of the stoichiometric amount, in order to study the reaction order w.r.t. phenylacetamide. Hydrolysis of phenylacetamide was found to be first order w.r.t. phenylacetamide (Figures 6 and 7). The pseudo rate constants calculated were $0.783 \times 10^{-3} \text{ s}^{-1}$ and $2.16 \times 10^{-3} \text{ s}^{-1}$ at the temperature of 87 and 100 °C respectively.

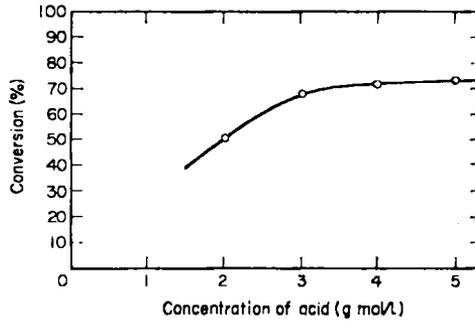


Figure 5. Hydrolysis of phenylacetamide at different concentration of HCl.

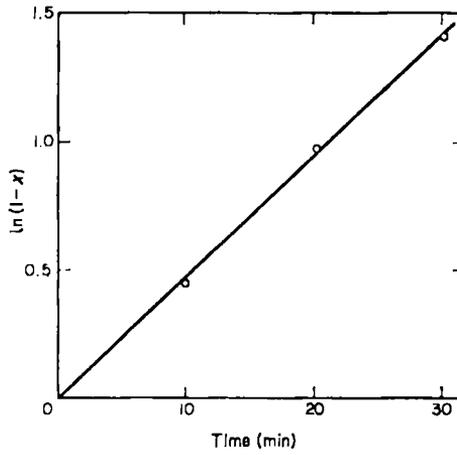


Figure 6. Hydrolysis of phenylacetamide at 87 °C with 3 N-HCl. Pseudo rate constant at 87 °C = $0.783 \times 10^{-3} \text{ s}^{-1}$.

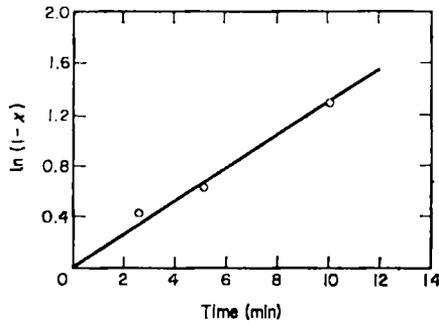


Figure 7. Hydrolysis of phenylacetamide 100 °C with 3 N-HCl. Pseudo rate constant at 100 °C = $2.16 \times 10^{-3} \text{ s}^{-1}$.

4. Conclusions

Acetophenone can be oxidised, in the temperature range of 150 to 180 °C with sulphur and ammonia, using 75% alcohol, to phenylacetamide and phenylacetic acid in good yields with only small amount of tarry materials. The amount of phenylacetic acid in the acid-amide mixture is about 3 to 5%. Under the most suitable reaction condition viz., concentration of acetophenone, ammonia and amount of sulphur, 0.8, 2.4 and 4.8 g mol/l of solvent phase respectively; solvent 75% aqueous alcohol; reaction temperature, 165 °C; reaction period, 4 h; and pressure, 18 atm; the percentage conversion to phenylacetamide and phenylacetic acid is about 92% with 100% conversion of acetophenone.

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