

New Synthesis of 4-Nitrobenzamide

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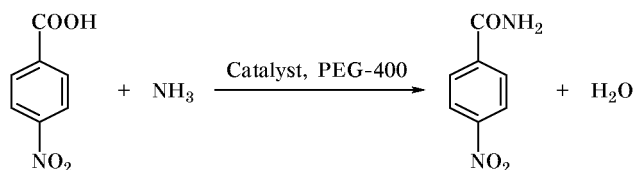
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Abstract—The reaction of 4-nitrobenzoic acid with ammonia in the presence of various catalysts was studied. Tetrabutoxytitanium and boric acid with addition of PEG-400 favor formation of 4-nitrobenzamide in a high yield. The amidation occurs in the temperature range from 160 to 185°C in trichlorobenzene and in a mixture of trichlorobenzene with *o*-xylene. Neither PEG-400 nor the above catalysts in the absence of PEG-400 do not catalyze the reaction.

We previously showed that titanium, phosphorus, and tin compounds catalyze acylation of aromatic amines with aromatic carboxylic acids. Conditions were found for the preparation of *N*-arylbenzamides, 2,3-hydroxynaphthanilide, 1-benzoylaminoanthraquinone, and 2-arylbenzimidazoles in high yields [1–4]. In the present work we examined catalytic reaction of 4-nitrobenzoic acid with ammonia.

Taking into account that ammonium salts of substituted benzoic acids are poorly soluble in weakly polar solvents which are usually used in the catalytic acylation of substituted anilines [1–3], as reaction medium we selected more polar *o*-dichlorobenzene and trichlorobenzene. In some experiments, toluene or *o*-xylene was added to facilitate removal of the liberated water.

The reaction of 4-nitrobenzoic acid with ammonia was studied in the temperature range from 160 to 185°C in the presence of various catalysts. Ammonia was taken in a stoichiometric amount (as ammonium 4-nitrobenzoate) or was bubbled through the reaction mixture (in excess) throughout the process (5–10 h). Under the above conditions, none of the catalysts listed below turned out to be effective: $\text{Ti}(\text{OBu})_4$, SnCl_4 , H_3BO_3 , H_3PO_3 , H_3PO_4 , $(\text{CH}_3\text{O})_2\text{P}(\text{O})\text{H}$, $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$. Almost no 4-nitrobenzamide was obtained.



We have found that addition of PEG-400 as co-catalyst considerably enhances the catalytic activity. By bubbling gaseous ammonia through a solution of 4-nitrobenzoic acid in the presence of a catalyst and PEG-400, 4-nitrobenzamide was formed in high yield (see table).

When PEG-400 was added to the reaction mixture containing ammonium 4-nitrobenzoate without bubbling ammonia, 4-nitrobenzamide was not formed. By special experiments, using the catalytic system boric acid–PEG-400, we showed that trichlorobenzene does not react with ammonia and that 4-nitrobenzamide is not converted into 4-aminobenzamide or *N*-(4-nitrobenzoyl)-4-nitrobenzamide.

As follows from the data in table, in the presence of PEG-400, effective catalysts are tetrabutoxytitanium (run nos. 1, 2), boric acid (run nos. 3, 4), and dimethyl hydrogen phosphite (run no. 5). Iron(II) sulfate and tin(IV) chloride showed no catalytic activity (run nos. 6, 7). The latter catalysts promoted formation in a low yield of compounds other than 4-nitrobenzamide. PEG-400 did not exhibit catalytic activity in the absence of other catalyst (run no. 8).

It should be emphasized that 4-nitrobenzamide is formed in a high yield in the presence of various amounts of a catalyst and PEG-400 (cf. run nos. 1–4); therefore, there exists the possibility for further optimization of the reaction conditions.

According to the results of run nos. 1 and 2, vigorous boiling of the mixture and removal of water as azeotrope are not necessary for the reaction to be successful, in contrast to the data of [2]. Presumably, the liberated water can also leave the reaction mixture

Synthesis of 4-nitrobenzamide

| Run no. | Reaction conditions | | | | | Yield of 4-nitrobenzamide, % |
|---------|---|-----------------------------|------------------------------------|-----------------|------------------|------------------------------|
| | catalyst, mol % ^a | PEG-400, mol % ^a | solvent | temperature, °C | reaction time, h | |
| 1 | Ti(OBu) ₄ , 2.0 | 0.9 | Trichlorobenzene | 170–175 | 6 | 60 |
| | | | | | 10 | 90 |
| 2 | Ti(OBu) ₄ , 0.9 | 22.0 | Trichlorobenzene | 180–185 | 5 | 74 |
| 3 | H ₃ BO ₃ , 7.0 | 16.0 | Trichlorobenzene- <i>o</i> -xylene | 160–165 | 5 | 59 |
| | | | | | 10 | 92 |
| 4 | H ₃ BO ₃ , 34.0 | 54.0 | Trichlorobenzene- <i>o</i> -xylene | 160–165 | 4 | 64 |
| 5 | (CH ₃ O) ₂ P(O)H, 3.0 | 18.0 | Trichlorobenzene- <i>o</i> -xylene | 180–183 | 9 | 35 |
| 6 | FeSO ₄ ·7H ₂ O, 3.0 | 15.0 | <i>o</i> -Dichlorobenzene-toluene | 160–165 | 6 | 2 |
| 7 | SnCl ₄ , 7.0 | 35.0 | <i>o</i> -Dichlorobenzene-toluene | 160–165 | 6 | 3 |
| 8 | – | 10.0 | Trichlorobenzene- <i>o</i> -xylene | 160–165 | 6 | 4 |
| 9 | H ₃ PO ₄ , 2.0 | 0.9 | Trichlorobenzene | 170–175 | 7 | 16 |
| 10 | H ₃ PO ₃ , 2.0 | 0.9 | Trichlorobenzene | 170–175 | 7 | 17 |

with a stream of ammonia. It is also probable that, even without removal of water, a large excess of ammonia bubbled through the mixture shifts the equilibrium toward formation of 4-nitrobenzamide which is thus obtained in high yield.

The role of PEG-400 in the process under study remains unclear, though this compound is known as an efficient phase-transfer catalyst [5]. It may be seen that PEG-400 favors dissolution of boric acid and hence homogenization of the reaction mixture. On the other hand, the other efficient catalyst, tetrabutoxytitanium, is readily soluble in trichlorobenzene in the absence of PEG-400.

Thus, catalytic systems have been proposed (tetrabutoxytitanium-PEG-400 and boric acid-PEG-400) which ensure direct synthesis of 4-nitrobenzamide. The procedure is advantageous, for it does not involve carbonyl chloride or thionyl chloride (for preliminary conversion of 4-nitrobenzoic acid into 4-nitrobenzoyl chloride).

EXPERIMENTAL

4-Nitrobenzoic acid, Ti(OBu)₄, SnCl₄, H₃BO₃, H₃PO₃, H₃PO₄, (CH₃O)₂P(O)H, *o*-xylene, toluene, and trichlorobenzene were purified as described in [2, 3, 6]. Iron(II) sulfate heptahydrate FeSO₄·7H₂O of pure grade was used without preliminary purification, and *o*-dichlorobenzene was purified by vacuum distillation.

The reaction mixtures and products were analyzed by thin-layer chromatography on Silufol UV-254

plates using binary mixtures acetone-hexane and acetone-chloroform as eluent; spots were visualized with UV light.

Synthesis of 4-nitrobenzamide. A mixture of 2.5 g (14.9 mmol) of 4-nitrobenzoic acid, 45 ml of appropriate solvent, catalyst, and PEG-400 was heated for 0.5 h at 160–185°C in a flask equipped with a thermometer, stirrer, gas-inlet tube, Dean-Stark trap, and reflux condenser while bubbling ammonia at a flow rate of 500 ml/h. When *o*-dichlorobenzene or trichlorobenzene was used as solvent, the Dean-Stark trap was initially empty. When the reaction was carried out in binary mixtures containing toluene or *o*-xylene (5 ml) as the second component, the Dean-Stark trap was filled with that solvent.

When the reaction was complete, the mixture was cooled to room temperature, and the precipitate was filtered off, washed with 20 ml of a 10–15% aqueous solution of ammonia and with 20 ml of water, and dried. The product had mp 196–197°C [7]. The results of experiments are summarized in table.

4-Nitrobenzamide was synthesized from ammonium 4-nitrobenzoate following the same procedure, but no ammonia was bubbled through the mixture. The solvent was a mixture of trichlorobenzene and *o*-xylene, ammonium 4-nitrobenzoate-H₃BO₃-PEG-400 molar ratio 1:0.07:0.16, reaction time 10 h, temperature 160–165°C.

Ammonium 4-nitrobenzoate. 4-Nitrobenzoic acid, 4.0 g (20.5 mmol), was dispersed in 20 ml of 25% aqueous ammonia. The mixture was stirred and dried

at 60–80°C until a colorless solid, ammonium 4-nitrobenzoate, precipitated.

The reactions of 4-nitrobenzoic acid with 4-nitrobenzamide and of 4-nitrobenzamide with ammonia were carried out in trichlorobenzene at 180–185°C (reaction time 6 h); 4-nitrobenzoic acid–4-nitrobenzamide–H₃BO₃–PEG-400 molar ratios 1:1:0.07:0.16 and 0:1:0.07:0.16, respectively.

REFERENCES

1. Kondratov, S.A., Shteinberg, L.Ya., Boiko, V.D., and Shein, S.M., *Zh. Org. Khim.*, 1986, vol. 22, p. 2466.
2. Shteinberg, L.Ya., Kondratov, S.A., and Shein, S.M., *Zh. Org. Khim.*, 1988, vol. 22, p. 1968.
3. Shteinberg, L.Ya., Kondratov, S.A., and Shein, S.M., *Zh. Org. Khim.*, 1989, vol. 25, p. 1945.
4. Kondratov, S.A., Shteinberg, L.Ya., Shein, S.M., Udovichenko, L.V., and Boiko, V.D., *Zh. Org. Khim.*, 1994, vol. 30, p. 284.
5. Gol'dberg, Yu.Sh., *Izbrannye glavy mezhfaznogo kataliza* (Selected Topics in Phase-Transfer Catalysis), Riga: Zinatne, 1989, p. 554.
6. Shteinberg, L.Ya., Boiko, V.D., Kondratov, S.A., Shein, S.M., and Shteinberg, Ya.B., *Zh. Org. Khim.*, 1992, vol. 28, p. 1034.
7. Laptev, N.G. and Vysokosova, A.I., USSR Inventor's Certificate no. 127657, 1960; *Byull. Izobret.*, 1960, no. 8.