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Original Scientific Paper

Studies in the Propiothiolactone Series.* IV. Reaction of β -Benzylmercaptopropionyl Chloride with Benzene in the Presence of Aluminum Bromide

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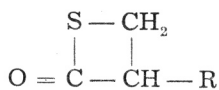
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Continuing the studies of the effect of the α -substituent upon the course of the Friedel-Crafts reaction the behaviour of α -unsubstituted β -benzylmercaptopropionyl chloride was described. When one or two moles of aluminum bromide was used, the main products were β -mercaptopropiophenone and β -benzylmercaptopropiophenone. Diphenylmethane was isolated in about 90% yield. With three moles of aluminum bromide the main product obtained from the reaction mixture was β -mercaptopropiophenone and no β -benzylmercaptopropiophenone could be isolated. The crude products from the reaction with three moles of aluminum bromide gave a high yield of 3,3'-thiodipropiophenone when treated with aqueous ammonia at room temperature.

The nature of the products obtained from the reaction of α -acylamino- β -benzylmercaptopropionyl chloride with aluminum halides in benzene was described in previous papers by D. Fleš *et al.*¹ and was found to be dependent upon the amount of aluminum halide. Thus, α -phthalimido- β -benzylmercaptopropionyl chloride treated with one mole of aluminum chloride gave a polythioester (I), while with two moles of aluminum chloride propiothiolactone (II) was obtained.



I



II



Using the same reaction conditions with two moles of aluminum chloride, α -succinimido and α -p-toluenesulfonamido- β -benzylmercaptopropionyl chloride were converted to the corresponding propiothiolactones².

In no case was the corresponding propiophenone isolated, which indicates that in these reactions debenylation is a more rapid process than acylation. The debenylation was followed by inter- or intramolecular esterification to yield either polythioester or propiothiolactone.

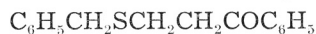
* Paper III. M. Dadić, D. Fleš, and A. Markovac-Prpić, *Croat. Chem. Acta* **33** (1961) 73.

Continuing the studies of the effect of the α -substituent upon the course of the Friedel-Crafts reaction the behaviour of α -unsubstituted β -benzylmercaptopropionyl chloride treated with variable amounts of aluminum bromide in benzene at room temperature was described. Aluminum bromide was used because of its solubility in benzene.

When one or two moles of aluminum bromide was used, the main products were β -mercaptopropiophenone (III) and β -benzylmercaptopropiophenone (IV).



III



IV

Diphenylmethane was isolated in about 90% yield.

Ketones III and IV were separated by fractional distillation and identified by conversion to propiophenone. β -Mercaptopropiophenone was converted directly to propiophenone by desulfuration with Raney nickel, while β -benzylmercaptopropiophenone was first debenzylated with aluminum bromide in benzene to yield diphenylmethane and β -mercaptopropiophenone, which was subsequently desulfurized to propiophenone.

With three moles of aluminum bromide the main product obtained from the reaction mixture was β -mercaptopropiophenone; no β -benzylmercaptopropiophenone could be isolated. It is noteworthy that a large amount of hydrogen sulfide was evolved during the hydrolysis of the aluminum bromide.

The crude reaction products gave a high yield of 3,3'-thiodipropiophenone when treated with aqueous ammonia at room temperature. The reaction mixture obtained with one or two moles of aluminum bromide gave no 3,3'-thiodipropiophenone when treated with ammonia under the same conditions.

Summarizing the experimental results, it may be concluded that in the reaction of β -benzylmercaptopropionyl chloride with benzene under conditions of a Friedel-Crafts reaction, the ketone formation is faster than the debenzylation reaction. Consequently propiophenone derivatives are formed easier than propiothiolactones or polythioesters, which resulted when propionylchloride was substituted in the α -position.

EXPERIMENTAL

All melting points are uncorrected.

β -Benzylmercaptopropionic acid

β -Benzylmercaptopropionic acid (11.0 g., 56%), m.p. 82° (recrystallized from benzene-petroleum ether) (lit. ³: m.p. 82°) was prepared from β -bromopropionic acid (15.3 g., 0.1 mole) following the method of Stoner and Hougherty⁴ for benzylmercaptoacetic acid.

Anal. C₁₀H₁₂O₂S (196.27) calc'd.: C 61.19; H 6.16%
found: C 61.01; H 6.32%

Reaction of β -benzylmercaptopropionyl chloride with benzene in the presence of two moles of aluminum bromide

To a solution of 43.1 g. (1.64 moles) of anhydrous aluminum bromide in 250 ml of dry benzene was added at once a solution of 17.5 g. (0.82 moles) of β -benzylmercaptopropionyl chloride⁵ in 50 ml. of dry benzene. The reaction mixture was

vigorously stirred for one hour at room temperature and then hydrolyzed with 200 g. of ice and 40 ml. of concentrated hydrochloric acid. The water layer was separated and extracted with three 80-ml. portions of benzene, the combined benzene layers were washed with three 50-ml. portions of diluted aqueous sodium bicarbonate and dried over sodium sulfate. Benzene was removed under reduced pressure yielding 20.0 g. of an oily residue. The crude oily product was refluxed for one hour with 16.0 g. of Girard T reagent⁶ in 184 ml. of absolute ethanol and 16 ml. of glacial acetic acid. The reaction mixture was poured into 400 g. of ice containing 25.6 g. of anhydrous sodium carbonate. The resulting mixture was extracted with three 100-ml. portions of ether, the ethereal extracts dried over sodium sulfate and evaporated *in vacuo* to give 12.2 g. (89.1%) of diphenylmethane which was purified by distillation at 95–100° and 0.2 mm.⁷

Anal. C₁₃H₁₂ (168.23) calc'd.: C 92.85; H 7.15%
found: C 92.70; H 7.10%

To the water layer from which diphenylmethane was extracted was added 24 ml. of concentrated hydrochloric acid and the reaction mixture left at room temperature for one hour. The crude ketonic material was taken into five 100-ml. portions of benzene. The benzene extract was washed with three 50-ml. portions of water and dried over sodium sulfate. Benzene was evaporated *in vacuo* to give 7.7 g. (57% calculated on basis of the conversion of β -benzylmercaptopropionyl chloride to β -mercaptopropiophenone) of an oily residue. Crude oil was distilled at 0.05 mm. and fractionated into two distinct fractions: one boiling at 215–20° (5.1 g., 37.7% based on β -benzylmercaptopropionyl chloride) and the other boiling at 235–40° (0.5 g., 3% based on acid chloride).

The first fraction was identified as β -mercaptopropiophenone (III).

Anal. C₉H₁₀OS (166.24) calc'd.: C 65.02; H 6.06%
found: C 64.90; H 5.92%

The fraction boiling at 235–40° and 0.05 mm. was proved to be β -benzylmercaptopropiophenone (IV)

Anal. C₁₆H₁₆OS (256.36) calc'd.: C 74.96; H 6.29%
found: C 74.69; H 6.15%

A sample of β -benzylmercaptopropiophenone prepared following the method of Böhme and Heller⁸ was identical with the compound IV as indicated by its boiling points and IR spectra.

Desulfuration of β -mercaptopropiophenone

β -Mercaptopropiophenone (0.5 g., 0.003 moles) was dissolved in 10 ml. of benzene and 2 g. of Raney nickel C⁹ in 50 ml. of absolute ethanol was added. The reaction mixture was heated under reflux with vigorous stirring for five hours and left overnight at room temperature. Nickel was removed by filtration, washed with two 15-ml. portions of absolute ethanol and the combined filtrate and washings were evaporated *in vacuo* to give 0.4 g. of an oily product. The crude oil was extracted with 5 ml. of hot absolute ethanol and treated with 0.5 g. of a methanolic solution of 2,4-dinitrophenylhydrazine. After standing overnight at room temperature a crystalline product precipitated. Yield 0.3 g. The analytical sample of propiophenone-2,4-dinitrophenylhydrazone was crystallized from dry benzene, m.p. 193–4°, undepressed with an authentic sample.¹⁰

Debenzylation of β -benzylmercaptopropiophenone

β -Benzylmercaptopropiophenone (0.5 g., 0.002 moles) in 10 ml. of dry benzene was stirred with a solution of 1.5 g. (0.006 moles) of aluminum bromide in 20 ml. of dry benzene at room temperature for two hours. After hydrolysis of the reaction product with 10 g. of ice in 1.5 ml. of concentrated hydrochloric acid, the water layer was extracted with three 15-ml. portions of benzene, the combined benzene

layers washed with dilute aqueous sodium bicarbonate and dried over sodium sulfate. Benzene was evaporated *in vacuo* to give 0.5 g. of an oily product. Extraction with three 20-ml. portions of petroleum ether yielded upon evaporation of solvent 0.3 g. of diphenylmethane.

The oily residue after extraction of diphenylmethane was desulfurized with Raney nickel C⁹ and the remaining oil (0.2 g.) converted with a methanolic solution of 2,4-dinitrophenylhydrazine to propiophenone-2,4-dinitrophenylhydrazone, m.p. 193—4⁰, undepressed with an authentic sample.

Reaction of β -benzylmercaptopropionyl chloride with benzene in the presence of three moles of aluminum bromide

A solution of β -benzylmercaptopropionyl chloride⁵ (5.0 g., 0.02 moles) in 20 ml. of benzene was treated with 20.0 g. of aluminum bromide (0.07 moles) in 100 ml. of dry benzene as previously described. On hydrolysis with ice and hydrochloric acid a strong evolution of hydrogen sulfide occurred. After evaporation of the benzene layer, 5.2 g. of an oily product was obtained. By extraction with petroleum ether in the previously described manner, diphenylmethane (3.4 g., 87%) was isolated.

The oily residue (1.5 g.) obtained after extraction of diphenylmethane was chromatographed on neutral aluminum oxide and eluted with dry benzene. After evaporation of benzene, 1.3 g. of an oily product was obtained. A sample was distilled for analysis at 220—5⁰ and 0.05 mm. IR absorption spectrum was identical with that of β -mercaptopropiophenone.

Anal. C₉H₁₀OS (166.24) calc'd.: C 65.02; H 6.06%
found : C 65.31; H 6.18%

β -Mercaptopropiophenone (0.5 g., 0.003 moles) was converted with a methanolic solution of 2,4-dinitrophenylhydrazine to the bis-(2,4-dinitrophenylhydrazone) of 3,3'-dithiodipropiophenone, which was purified by chromatography on a silicagel column. Recrystallization from benzene yielded red crystals melting at 159—60⁰. Sulfhydryl test was negative.

Anal. C₃₀H₂₆N₈O₈S₂ (690.70) calc'd.: N 16.22%
found : N 16.42%

3,3'-Thiodipropiophenone

To 1.0 g. of the crude oily product of the reaction of β -benzylmercaptopropionyl chloride with benzene in the presence of three moles of aluminum bromide was added 20 ml. of aqueous ammonia. After standing for 10 days at room temperature 0.7 g. of diphenylmethane was extracted with petroleum ether and the residue recrystallized from ethanol to give white crystals (0.2 g.), m.p. 104—5⁰, reported 104⁰¹¹.

Anal. C₁₈H₁₈O₂S (298.39) calc'd.: C 72.44; H 6.08%
found : C 72.30; H 5.86%

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IZVOD

Studije u redu propiotiolaktona. IV. Reakcija β -benzilmerkaptopropionil klorida s benzenom u prisutnosti aluminijskoga bromida*M. Dadić i D. Fleš*

U nastavku ispitivanja utjecaja α -supstituenta na tok Friedel-Crafts-ove reakcije izvedena je reakcija β -benzilmerkaptopropionil klorida sa različitim količinama aluminijskog bromida u benzenu na sobnoj temperaturi. Upotrebom jednog ili dva mola aluminijskoga bromida dobiveni su kao glavni reakcioni produkti β -merkaptopropiofenon i β -benzilmerkaptopropiofenon, a difenilmetan je izoliran u iskorištenju od oko 90%. Sa tri mola aluminijskog bromida nastao je kao glavni produkt reakcije β -merkaptopropiofenon, dok β -benzilmerkaptopropiofenon nije izoliran. Sirovi produkti reakcije u prisutnosti tri mola aluminijskog bromida dali su obradom sa amonijakom visoko iskorištenje 3,3'-tiodipropiofenona.

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