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The Monoreduction of 2,5-Dinitrofluorene

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The reduction of 2,5-dinitrofluorene by hydrogen sulfide in basic medium or by stannous chloride in acid medium gave both of the possible isomers, 2-amino-5-nitrofluorene and 2-nitro-5-aminofluorene. A small amount of 2,5-diaminofluorene was also obtained.

In a recent paper[1] the unambiguous preparation of 2-nitro-5-aminofluorene by a Schmidt reaction on 2-nitrofluorene-5-carboxylic acid was described. The melting point of this compound was 163°, that of the acetyl derivative 283°. However, the same melting points were reported earlier[2] for the isomeric 2-amino-5-nitrofluorene, obtained by hydrogen sulfide reduction of 2,5-dinitrofluorene, and the corresponding acetyl derivative. We also found that the ultraviolet and infrared spectra of the two samples of aminonitrofluorene, and separately of the acetyl derivatives, were identical. A mixture melting point of the authentic compound and of that produced by reduction, and a similar experiment with the acetyl derivatives, showed no depression. It thus appeared that the compound reported as 2-amino-5-nitrofluorene was the other isomer; this was confirmed by deamination when 2-nitrofluorene rather than the expected 4-nitrofluorene was obtained.

A re-examination of the products of the reported monoreduction of 2,5-dinitrofluorene was thus in order. The compound isolated in relatively poor yield by recrystallization from benzene of the crude reaction mixture was 2-nitro-5-aminofluorene, m.p. 163°. On the other hand, deamination of the reduction product recrystallized from acetic acid as the sulfate led to 4-nitrofluorene. The structure of this compound was established without doubt by oxidation to 4-nitrofluorenone, by reduction to 4-aminofluorene, and by the difference of the ultraviolet spectra of 2-acetylaminofluorene and of the 4-isomer. The melting point of the latter compound has been confirmed recently in two independent syntheses.[3,4] Thus, the reduction of 2,5-dinitrofluorene by hydrogen sulfide yielded both possible isomers, 2-nitro-5-aminofluorene, and 2-amino-5-nitrofluorene.

By guiding the purification procedures with infrared spectroscopy we have now separated a crude reduction mixture into a major component, 2-amino-5-nitrofluorene, m.p. 104–105° (acetyl derivative, m.p. 235–237°) and a minor component, 2-nitro-5-aminofluorene, m.p. 164–166° (acetyl derivative, m.p. 282–284°). In addition, a small amount of 2,5-diaminofluorene, m.p. 177–178.5°, was isolated. Similarly, the reduction with stannous chloride in acid medium produced both isomers. The reactions are therefore not specific with respect to one of the nitro groups. This may be a more general occurrence than has hitherto been suspected.[5-8]

EXPERIMENTAL

The melting points were taken on a Kofler hot stage. Ultraviolet spectra were determined in 0.05 *mmolar* ethanol solution on a Cary instrument. Infrared spectra were recorded by Mr. P. H. Grantham on a Perkin-Elmer spectrophotometer, model 21, using the solid potassium bromide disk method.

Hydrogen sulfide reduction. A finely ground suspension of 17 g. (66.2 mmoles) of 2,5-dinitrofluorene in 435 ml. of ethanol and 63 ml. of 15 *N* ammonium hydroxide was kept near the boiling point while hydrogen sulfide was introduced for 3 hours. After 1 and 2 hours another 12 ml. of 15 *N* ammonium hydroxide was added. At the end of a total of 3.5 hours the mixture was diluted with 12.5 g. of sodium chloride in 500 ml. of ice-water. Upon cooling the precipitate was filtered off and extracted two times with 1000 ml. of 0.25 *N* and 800 ml. of 0.15 *N* hydrochloric acid, respectively. The insoluble residue (8 g.) was mostly sulfur. The combined extracts were refluxed gently for 45 minutes with 0.7 g. of Norit, filtered, and cooled in ice. The crystalline hydrochloride was filtered off and the filtrate (A) was reserved for the isolation of 2,5-diaminofluorene. The solid was suspended in 100 ml. of ethanol and 10 ml. of 15 *N* ammonium hydroxide was added with swirling. After 0.5 hour the dark red mixture was diluted with 500 g. of ice. The initially colloidal precipitate (9.5 g.) crystallized after six hours at 5°. It was recrystallized from a mixture of 190 ml. of acetic acid and 25.5 ml. of 5.4 *N* sulfuric acid. The sulfate was filtered (filtrate B), washed with ethanol, and converted to the free aminonitrofluorene (8.2 g., m.p. 88–101°) by the method used above. The product was recrystallized again from 210 ml. of acetic acid and 26.5 ml. of 5.4 *N* sulfuric acid (filtrate C), and the sulfate was converted to 6.3 g. of aminonitrofluorene, m.p. 100–102°. Recrystallization from 205 ml. of 55% ethanol afforded 6.0 g. (26.5 mmoles) of long dark red needles m.p. 103–104.5°. One further recrystallization of 3.8 g. from 950 ml. of cyclohexane gave

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[1] Weisburger and Weisburger, *J. Org. Chem.*, **20**, 1396 (1955).

[2] Weisburger, Weisburger, and Morris, *J. Am. Chem. Soc.*, **74**, 4540 (1952).

[3] Neish, *Rec. trav. chim.*, **72**, 899 (1953).

[4] Schinz, Fritz-Niggli, Campbell, and Schmid, *Oncologia*, **8**, 233 (1955).

[5] Blanksma, *Rec. trav. chim.*, **65**, 203 (1946).

[6] Verkade and Meerburg, *Rec. trav. chim.*, **65**, 768 (1946).

[7] Hodgson, *J. Soc. Dyers Colourists*, **62**, 114 (1946).

[8] Hodgson, *J. Soc. Dyers Colourists*, **59**, 246 (1943).

3.2 g. of *2-amino-5-nitrofluorene,* m.p. 104.5–105°. Ultraviolet absorption maxima were at 280 (ϵ = 14,800) and 406 mμ (ϵ = 5,400) and minima at 244 (ϵ = 6,610) and 343 mμ (ϵ = 2,900).

Anal. Calc'd for $C_{13}H_{10}N_2O_2$: C, 69.01; H, 4.46; N, 12.39. Found: C, 68.98; H, 4.53; N, 12.39.

Filtrate A was made basic with 50 ml. of 15 *N* ammonium hydroxide and cooled in ice. A tan precipitate (700 mg.) was filtered off, dissolved in 40 ml. of benzene, and chromatographed on a column (2 cm. in diameter, 6.6 cm. high) of *Woelm* basic alumina using benzene as eluant. The movement of colored bands on the column guided the fractionation. Preliminary identifications were made by the infrared spectra of the cuts. Fraction 1 contained 32 mg. of impure 2-nitro-5-aminofluorene, m.p. 144–155°. Fractions 2 to 5 were oily. On crystallization from ethanolic hydrochloric acid 190 mg. of a mixture of amino nitrofluorenes, m.p. 75–95° was obtained; the filtrate, concentrated and adjusted to *p*H 7 with sodium bicarbonate, deposited 112 mg. of impure *2,5-diaminofluorene* which, when crystallized twice from ligroin (b.p. 90–120°) and once from water, consisted of white needles weighing 68 mg., m.p. 177–178.5°. The infrared spectrum was identical to that of the authentic 2,5-diaminofluorene.[1] Fraction 6 from the column was almost pure 2,5-diaminofluorene (87 mg., m.p. 170–173°). Fractions 7–9 were mixtures of 2-amino-5-nitrofluorene and 2,5-diaminofluorene which yielded 66 mg. of the former by appropriate crystallizations.

Filtrate B was added to 500 g. of ice and neutralized with 15 *N* ammonium hydroxide. The oily dark precipitate was dissolved in 50 ml. of benzene and chromatographed as described for filtrate A. Fraction 1 gave 290 mg. of 2-nitro-5-aminofluorene, m.p. 161–163°, which was combined with fraction 1 from filtrate A above, and recrystallized from 11 ml. of benzene. Pure *2-nitro-5-aminofluorene,* m.p. 164.5–166°, weighing 255 mg., with the spectra of the authentic compound and undepressed mixture melting point was obtained. Further fractions consisted of minor amounts of mixtures of this compound and 2-acetylamino-5-nitrofluorene, produced during the crystallization from acetic acid.

Filtrate C was neutralized with ammonium hydroxide and the resulting precipitate crystallized from 20 ml. of benzene. Red needles (500 mg.), m.p. 159–163°, of *2-nitro-5-aminofluorene* were obtained. Further fractionation of the filtrate produced 230 mg. of impure 2-acetylamino-5-nitrofluorene and a small amount of 2-amino-5-nitrofluorene.

It may be noted that crystallization of mixtures of the isomeric aminonitrofluorenes from benzene deposits only the 2-nitro-5-amino derivative. The other isomer is soluble under those conditions, explaining why it could not be isolated by the procedure used earlier.[2]

Thus, the reaction produced a total of 26.5 mmoles (40%) of 2-amino-5-nitrofluorene, 3.6 mmoles (5.5%) of 2-nitro-5-aminofluorene, and 1 mmole (1.5%) of 2,5-diaminofluorene.

Deamination of 2-amino-5-nitrofluorene. The pure compound, m.p. 104–105°, (2.3 mmoles) was deaminated by the method described earlier.[1] After chromatography 1.95 mmoles of *4-nitrofluorene,* m.p. 64–68°, were obtained. Crystallization from 10 ml. of cyclohexane (this solvent is more suitable than the methanol used earlier) left 1.4 mmoles of yellow needles, m.p. 74.5-76°,[2] with the correct ultraviolet and infrared spectra, thus definitely proving the structure of the aminonitro derivative.

2-Acetylamino-5-nitrofluorene. Acetic anhydride (1 ml.) was added to a refluxing solution of 2.3 mmoles of 2-amino-5-nitrofluorene in 20 ml. of benzene. The acetyl derivative (2.2 mmoles, m.p. 228–234°) crystallized after 0.5 hour. Successive recrystallization from 75 ml. of ethanol and 8 ml. of acetic acid left 1.74 mmoles of *2-acetylamino-5-nitrofluorene,* m.p. 235–237°. The crystals of this compound are characteristically gelatinous when moist with solvent and shrink considerably to a hard cake on drying. The ultraviolet spectrum showed maxima at 272.5 (ϵ = 22,100) and 360 mμ (ϵ = 7,490) and minima at 241.5 (ϵ = 7,660) and 317.5 mμ (ϵ = 4,090). Among numerous other distinguishing features the infrared spectrum of this compound, and also of 2-amino-5-nitrofluorene, exhibited two important fairly symmetrical peaks at 13.30 and 13.70 μ, while the 2-nitro-5-amino- and -5-acetylamino derivatives showed a single asymmetrical peak in that region at 13.65 to 13.70 μ.

Anal. Calc'd for $C_{15}H_{12}N_2O_3$: C, 67.15; H, 4.51; N, 10.44. Found: C, 67.12; H, 4.42; N, 10.49.

Stannous chloride reduction. The reaction was carried out exactly as described previously[2] with 10.2 mmoles of 2,5-dinitrofluorene. One millimole of unchanged compound and 5.75 mmoles of crude acid-soluble aminonitro compounds were obtained. The latter in 125 ml. of benzene was treated with Norit then percolated through an alumina column. Evaporation of the solvent in a stream of air left a dark red oil which was fractionated as described above for the crude mixture obtained in the hydrogen sulfide reduction. 2-Amino-5-nitrofluorene, 2-nitro-5-aminofluorene, and 2,5-diaminofluorene accounted for 1.84, 2.20, and 0.22 mmoles or 18, 22, and 2% yield, respectively.

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