

Investigations in the Retene Field

V. The Structure of 4,9-Dinitro-3-hydroxyretene and of Some of its Derivatives

L. SIHLBOM

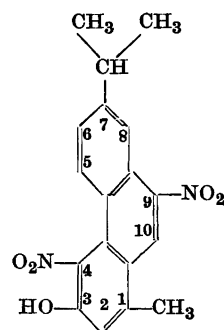
Institute of Organic Chemistry and Biochemistry, University of Stockholm, Sweden

Karrman¹ investigated the nitration of 3-hydroxyretene and some of its derivatives and prepared both mono- and dinitro-derivatives of the compounds. The structures of the nitro-derivatives were not completely elucidated although it was shown that the dinitro-derivatives could be obtained by further nitration of the mononitro-derivatives, and consequently, one nitro-group in the former series of compounds occupies the same position as in the corresponding mononitro-derivatives. Further, diazonium salts couple with mononitro-3-hydroxyretene but not with dinitro-3-hydroxyretene and this should indicate that one of the nitro-groups in the latter compound occupies the 4-position. Attempts to oxidize the nitro-derivatives to quinones were reported to fail. The formation of a quinone would have proved if a nitro-group is situated in the 9- or 10-position.

Sihlbom² proves that the mononitro-derivatives obtained by nitration of 3-acetoxyretene, 3-benzoyloxyretene, and 3-ethoxyretene were 9-nitro-derivatives. The present paper gives an account of the elucidation of the structures of the other mono- and dinitro-derivatives of 3-hydroxyretene and its derivatives described by Karrman¹.

On nitration even under vigorous conditions, 3-acetoxyretene gives solely 9-nitro-3-acetoxyretene¹. On the other hand, mild nitration of 3-hydroxyretene yields solely a dinitro-derivative¹, in which one of the nitro-groups occupies the 9-position². It may be assumed that the other nitro-group occupies the 2- or the 4-position, this also being valid for the dinitro-derivatives prepared from 3-methoxyretene and 3-ethoxyretene. Therefore, it was conceivable that amination of dinitro-3-hydroxyretene should give 2,9-dinitro-3-aminoretene or, more probably, 4,9-dinitro-3-aminoretene, a compound previously prepared (Karrman and Sihlbom³, Sihlbom⁴).

Amination experiments with urea using the procedure described by Kym⁵ gave only small yields of the dinitro-amine (about 1%) but appreciably higher yields (about 18%) were obtained when the amination was carried out by heating at 140° C for 10 hours in a solution of 35% ammonia (Merz and Ris⁶). By chromatographic purification of the crude product some unchanged starting material could be isolated. Prolongation of the reaction time or elevation of the temperature causes all the dinitro-3-hydroxyretene to react but owing to decomposition higher yields of the dinitro-amine were not obtained. The dinitro-amine was shown to be identical with 4,9-dinitro-3-aminoretene³ by a mixed m.p. determination. Similarly, the acetyl-derivative was shown to be identical with 4,9-dinitro-3-acetylaminoretene³. As 4,9-dinitro-3-aminoretene can be more easily obtained in another way³, the amination reaction was not investigated more closely, but this amination reaction indicates that 3-hydroxyretene, on nitration, yields 4,9-dinitro-3-hydroxyretene.



4,9-Dinitro-3-hydroxyretene

Karrman¹ also prepared dinitro-derivatives by nitration of 3-methoxyretene and 3-ethoxyretene. It has now been shown that these derivatives can be obtained by methylation, or ethylation, respectively, of 4,9-dinitro-3-hydroxyretene and thus their structure are proved. The methylation can be carried out with dimethyl sulphate in an alkaline ethanolic solution, but methylation with diazomethane is preferable, as the methylether is obtained directly in an almost pure state, in high yield. The ethylation was carried out with diethyl sulphate in alkaline ethanolic solution.

According to Karrman¹, nitration of 3-methoxyretene under mild conditions yields a mixture of two mononitro-3-methoxyretenes which on further nitration gives one dinitro-3-methoxyretene, shown above to be 4,9-dinitro-3-methoxyretene. It is therefore probable that the mixture contains 4-nitro-3-methoxyretene and 9-nitro-3-methoxyretene. Chromatographic separation (alumina, petroleum ether) showed that two mononitro-3-methoxyretenes were present in the ratio 4 : 5. For purposes of comparison the two anticipated compounds were prepared in the following way. 4-Nitro-3-acetoxy-9-aminoretene, prepared by partial reduction of 4,9-dinitro-3-acetoxyretene, was deaminated (diazotisation and reduction of the diazonium salt with hypophosphorous acid) and the reaction product, 4-nitro-3-acetoxyretene, was hydrolyzed. The 4-nitro-3-hydroxyretene, thus obtained, yielded 4-nitro-3-methoxyretene on methylation. 9-Nitro-3-methoxyretene was obtained by methylation of 9-nitro-3-hydroxyretene^{1,2}. Mixed m.p. determinations

showed that the above-mentioned isomers, isolated chromatographically, were identical with 4-nitro-3-methoxyretene and 9-nitro-3-methoxyretene, respectively, the latter being present in the larger amount.

It may be of interest to compare the tendency of some of the compounds investigated to form molecular compounds with acetic acid. It has been reported previously (Karrman ¹) that 4,9-dinitro-3-hydroxyretene can crystallize with acetic acid (2 moles), a property not exhibited by 4,9-dinitro-3-acetoxyretene. Obviously, the acetoxy-group reduces the tendency of the compound to form such molecular compound. After elimination of the nitro-group in the 9-position, we again have a compound, 4-nitro-3-acetoxyretene that can crystallize with acetic acid (1 mole). Nevertheless, 4-nitro-3-hydroxyretene, and 9-nitro-3-hydroxyretene crystallize without acetic acid.

The compounds discussed in this paper are listed in Table 1.

Table 1. Compounds treated in the present paper.

Name	M. p. °C *
4-Nitro-3-hydroxyretene	148—149 (decomp.)
4-Nitro-3-acetoxyretene	137—138
4-Nitro-3-methoxyretene	169—170
9-Nitro-3-methoxyretene	140—141
4,9-Dinitro-3-hydroxyretene **	166—167
4,9-Dinitro-3-methoxyretene **	173—174
4,9-Dinitro-3-ethoxyretene **	227—228
4-Nitro-3-acetoxy-9-aminoretene	ca. 190 (decomp.)
4-Nitro-3-acetoxy-9-acetylaminoretene	» 220 »

* All melting points are approximately corrected.

** Compound previously described.

EXPERIMENTAL

Amination of 4,9-dinitro-3-hydroxyretene. Finely powdered 4,9-dinitro-3-hydroxyretene (2.0 g) suspended in 35% ammonia (40 ml) in a sealed glass tube was heated at 140 °C for 10 hours. The reaction product consisting of reddish-brown crystals and friable dark pieces was filtered off and washed with warm ammonia until the washings were colourless. After drying, the reaction product was dissolved in acetone and adsorbed on a column of alumina (10 cm² × 20 cm). Development with acetone caused the separation of many zones. The yellow, most quickly moving zone, which consisted chiefly of 4,9-dinitro-3-aminoretene was eluted, and the dark crystalline residue (0.5 g), obtained after evaporation of the solvent, was dissolved in benzene and again adsorbed on a column of

alumina (10 cm² × 20 cm). On development with benzene, an orange-coloured zone appeared and from this pure 4,9-dinitro-3-aminoretene was isolated (0.35 g, 18%); m.p. 210–211 °C, undepressed on admixture with authentic material prepared via nitration of 3-acetylaminoretene³. [Calc. for C₁₈H₁₇O₄N₃ (339.3): C 63.7; H 5.05. Found: C 63.8; H 4.97].

4,9-Dinitro-3-acetylaminoretene. A sample (0.1 g) of the amine obtained above was dissolved in a mixture of benzene (2 ml) and acetic anhydride (2 ml) and the mixture was set aside overnight at 60 °C. After evaporation of the benzene, water was added to decompose the excess of acetic anhydride and precipitate the reaction product, which, after two crystallizations from glacial acetic acid, was obtained as yellow needles; m.p. 233–234 °C, undepressed on admixture with 4,9-dinitro-3-acetylaminoretene prepared by nitration of 3-acetylaminoretene³. M. p., previously reported (Karrman and Sihlbom³), 235–236 °C. [Calc. for C₂₀H₁₉O₅N₃ (381.4): C 63.0; H 5.02. Found: C 62.8; H 5.11.]

4,9-Dinitro-3-methoxyretene. An ether solution containing excess of diazomethane was added to a solution of 4,9-dinitro-3-hydroxyretene (0.1 g) in ether (10 ml) and the reaction mixture was set aside overnight at room temperature. After evaporation of the ether, the residue (m.p. 166–168 °C) was purified by two crystallizations from glacial acetic acid; m.p. 173–174 °C, undepressed on admixture with dinitro-3-methoxyretene prepared by nitration of 3-methoxyretene¹. Karrman¹ reports m.p. 172.2–172.5 °C. [Calc. for C₁₉H₁₈O₅N₂ (354.4): C 64.4; H 5.12. Found: C 64.6; H 5.20.]

4,9-Dinitro-3-ethoxyretene. Potassium hydroxide (1 g) dissolved in water (5 ml) was added to a solution of 4,9-dinitro-3-hydroxyretene (0.5 g) in ethanol (15 ml). Three portions of 1 ml of diethyl sulphate (each) were added to the stirred solution maintained at 30–40 °C during the course of 3 hours. After a further 2 hours, the yellow reaction product (0.25 g, 46 %) was filtered off, washed with ethanol, and crystallized from glacial acetic acid; m.p. 227–228 °C, undepressed on admixture with dinitro-3-ethoxyretene prepared by nitration of 3-ethoxyretene. [Calc. for C₂₀H₂₀O₅N₂ (368.4): C 65.2; H 5.47. Found: C 64.8; H 5.40.]

4-Nitro-3-acetoxy-9-aminoretene. Finely powdered 4,9-dinitro-3-acetoxyretene (5.0 g) was suspended in glacial acetic acid (50 ml) saturated with hydrogen chloride. A solution of SnCl₂ · 2H₂O (10 g) in glacial acetic acid (40 ml) saturated with hydrogen chloride was added with stirring at 20–25 °C during 2 hours. The amine formed by the reduction, precipitated as a sparingly soluble tin complex (6.6 g) which was filtered off and dried over potassium hydroxide in a vacuum. This material was dissolved in ethanol (90 ml), and pyridine (5 ml) and water (300 ml) were added. The precipitate formed on the addition of water, was filtered off, dried and extracted with boiling *n*-propanol (90 ml), in which solvent 4-nitro-3-acetoxy-9-aminoretene alone dissolved. On cooling, the amine crystallized as flat yellowish-brown prisms, m.p. ca. 190 °C (decomp.). Yield 2.6 g, 57 %. [Calc. for C₂₀H₂₀O₄N₂ (352.4): C 68.2; H 5.72. Found: C 68.4; H 5.76.]

The hydrochloride of the amine obtained above separated as colourless minute needles when hydrochloric acid (15 ml, ca. 4 *N*) was added to a solution of 4-nitro-3-acetoxy-9-aminoretene (0.1 g) in glacial acetic acid (10 ml); m.p. ca. 195 °C (decomp.). [Calc. for C₂₀H₂₁O₄N₂Cl (388.9): C 61.8; H 5.44. Found: C 61.7; H 5.52.]

The picrate separated as yellow needles on cooling a hot ethanolic solution (35 ml) containing 4-nitro-3-acetoxy-9-aminoretene (0.1 g) and picric acid (0.3 g); m.p. ca. 185 °C (decomp.). [Calc. for C₂₆H₂₃O₁₁N₅ (581.5): C 53.7; H 3.99. Found: C 53.6; H 3.99.]

4-Nitro-3-acetoxy-9-acetylaminoretene. Acetic anhydride (1 ml) was added to a solution of 4-nitro-3-acetoxy-9-aminoretene (0.2 g) in benzene (15 ml) at room temperature.

After 4 hours ligroin (75 ml) was added slowly with stirring and the 4-nitro-3-acetoxy-9-acetylamino-9-retene separated as short light-yellow needles, m.p. ca. 220 °C (decomp.). [Calc. for $C_{22}H_{22}O_5N_2$ (394.4): C 67.0; H 5.62. Found: C 66.7; H 5.71.]

4-Nitro-3-acetoxyretene. 4-Nitro-3-acetoxy-9-aminoretene (2.0 g) was dissolved in warm glacial acetic acid (70 ml). On cooling to room temperature, a colourless precipitate formed. With stirring, a mixture of glacial acetic acid (5 ml) and conc. sulphuric acid (2 ml) was added, followed by a solution of sodium nitrite (0.4 g) in water (2 ml) added dropwise at 10–15 °C. The clear, reddish-brown diazonium salt solution was mixed with 50% hypophosphorous acid (20 ml) and kept at 5 °C for 10 hours. The reaction product, 4-nitro-3-acetoxyretene, crystallized as long, yellow needles containing 1 mole of acetic acid (1.8 g, 80%). Crystallization from ethanol gave plates containing no acetic acid, m.p. 137–138 °C. [Calc. for $C_{20}H_{19}O_4N$ (337.4): C 71.2; H 5.68. Found: C 70.8; H 5.75].

Crystallization from glacial acetic acid gives needle-shaped crystals containing 1 mole of acetic acid which can be removed by heating at 110 °C. [Calc. for $C_{22}H_{23}O_6N$ (397.4): C 66.5; H 5.83. Found: C 66.7; H 5.86.]

4-Nitro-3-hydroxyretene. A sample of 4-nitro-3-acetoxyretene (1.2 g) obtained above was suspended in ethanol (8 ml) containing conc. hydrochloric acid (0.3 ml) and the mixture was refluxed for 80 minutes by which time a clear yellowish-brown solution was obtained. Evaporation of the solvent and drying of the residue at 100 °C in a vacuum yielded rather pure 4-nitro-3-hydroxyretene (1.0 g) as a yellow crystalline mass. It crystallizes from glacial acetic acid as yellow needles containing no acetic acid; m.p. 148–149 °C (decomp.). [Calc. for $C_{18}H_{17}O_3N$ (295.3): C 73.2; H 5.81. Found: C 72.6; H 5.70.]

4-Nitro-3-methoxyretene. A solution of 4-nitro-3-hydroxyretene (0.1 g) in ether (10 ml) was mixed with ether containing excess of diazomethane and kept at room temperature for 10 hours. The residue obtained by evaporation of the ether, was crystallized twice from glacial acetic acid, giving 4-nitro-3-methoxyretene as yellow needles, m.p. 169–170 °C. [Calc. for $C_{19}H_{19}O_3N$ (309.4): C 73.8; H 6.19. Found: C 73.5; H 6.29.]

9-Nitro-3-methoxyretene. 9-Nitro-3-hydroxyretene was methylated in the same way as described above for the methylation of 4-nitro-3-hydroxyretene. Yellow needles, m.p. 140–141 °C. [Calc. for $C_{19}H_{19}O_3N$ (309.4): C 73.8; H 6.19. Found: C 74.2; H 6.24.]

Chromatographic separation of 4-nitro-3-methoxyretene and 9-nitro-3-methoxyretene. A mixture of these compounds was prepared by mild nitration of 3-methoxyretene¹. A sample (0.25 g) of this mixture, dissolved in a mixture of benzene (10 ml) and petroleum ether (10 ml, b.p. 40–50 °C), was adsorbed on a column of alumina (10 cm² × 35 cm). On development with petroleum ether two light-yellow zones appeared. The lower zone yielded a yellow compound (0.10 g, m.p. 136–137 °C) which on crystallization from glacial acetic acid gave yellow needles; m.p. 140–141 °C, undepressed on admixture with 9-nitro-3-methoxyretene. [Calc. for $C_{19}H_{19}O_3N$ (309.4): C 73.8; H 6.19. Found: C 73.8; H 6.25.]

The yellow compound (0.08 g, m.p. 165–167 °C) isolated from the other zone separated as needle-shaped crystals from glacial acetic acid; m.p. 169–170 °C, undepressed on admixture with 4-nitro-3-methoxyretene. [Calc. for $C_{19}H_{19}O_3N$ (309.4): C 73.8; H 6.19. Found: C 73.8; H 6.30.]

SUMMARY

Previously prepared dinitro-derivatives of 3-hydroxyretene, 3-methoxyretene, and 3-ethoxyretene have been shown to have the nitro-groups in 4-

and 9-positions. From the mixture of mononitro-3-methoxyretenes, obtained by mild nitration of 3-methoxyretene, two components have been separated chromatographically and identified as 4-nitro-3-methoxyretene and 9-nitro-3-methoxyretene.

REFERENCES

1. Karrman, K. J. *Svensk Kem. Tid.* **57** (1945) 103.
2. Sihlbom, L. *Acta Chem. Scand.* **3** (1949) 144.
3. Karrman, K. J., and Sihlbom, L. *Svensk Kem. Tid.* **58** (1946) 189.
4. Sihlbom, L. *Acta Chem. Scand.* **2** (1948) 486.
5. Kym, O. *J. prakt. Chem.* [2] **75** (1907) 323.
6. Merz, V., and Ris, C. *Ber.* **19** (1886) 1749.

Received March 10, 1952.