Investigations in the Retene Field

VI.* The Composition of the Mixture of Mononitroretenes Obtained by Nitration of Retene in the Presence of Boron Trifluoride

L. SIHLBOM

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

In a previous work it was shown that nitration of retene and subsequently chromatographic purification of the crude nitration product gave a mixture of mononitroretenes in a yield of 83 %. In the present investigation, the composition of the mixture has been determined by reducing the mononitroretenes and separating the mixed aminoretenes so obtained. By acetylation, 9-acetamidoretene (38 %) and 10-acetamidoretene (12 %) were isolated. The remaining part of the acetylation product was chromatographed and yielded 3- (4 %), 4- (16 %), 6- (2 %), 9- (4 %), and 10-acetamidoretene (4 %). Thus the mixture of nitroretenes contained 3- (4 %), 4- (16 %), 6- (2 %), 9- (42 %), and 10-nitroretene (16 %).

A simple method for the preparation of 9-acetamidoretene has been described. It includes only three operations, namely, nitration of retene, reduction of the crude nitration product, and acetylation of the mixture of aminoretenes so obtained, and gives the pure compound in a yield of 24 %.

In a previous investigation of this series [1] it was found that retene, when treated with slightly more than the theoretically required amount of nitric acid at 80—90° in a glacial acetic acid solution containing boron trifluoride, gave, after chromatographic purification of the crude product, a mixture of mononitroretenes in a yield of *ca.* 83 % (85 % if the amount of retene recovered is taken into account). In the present work attempts were made to determine the composition of the mixture.

Karrman and Bergkvist [2] nitrated retene in a mixture of glacial acetic and propionic acids at 7—10° with excess of concentrated nitric acid and obtained mixed mononitroretenes in a yield of *ca.* 60 %. By chromatography (Al_2O_3, light petroleum-benzene) they were able to separate 3-nitroretene (*ca.* 30 % of the mixture), and a mononitroretene of unknown structure ** (*ca.* 0.5 %), but

---

* Part V. *Acta Chem. Scand.* **6** (1952) 1528.
** Proved to be 8-nitroretene. K. J. Karrman *Private communication.*

not the other components of the mixture. However, by fractional crystallization carried out in light petroleum, the process being followed using a microscope, they succeeded in separating this part of the mixture into 4-nitroretene (*ca.* 20 %) and 9-nitroretene (*ca.* 50 %).

In view of these results, it was to be expected that the mixture of mono-nitroretenes obtained in the boron trifluoride nitration should also contain 3-, 4- and 9-nitroretene. Before the mixture was more closely investigated, some experiments were carried out in order to find a more convenient method for the separation of the two last mentioned isomers. These experiments showed that they could indeed be separated by chromatography (Al$_2$O$_3$, light petroleum) if a big column was used. However, the mixture of mono-nitroretenes obtained in the nitration could not be successfully chromatographed under these conditions. Only 9-nitroretene could be separated in a pure state (*ca.* 27 %); 3- and 4-nitroretene were also obtained but were contaminated with considerable amounts of isomers. As 3-, 4- and 9-nitroretene can be separated under these conditions, the above result indicates the presence of compounds other than these three isomers.

Apparently, it is rather difficult to achieve a clear separation of the mixed mononitroretenes obtained in the boron trifluoride nitration. Attempts were made, therefore, to determine the composition of the mixture by reducing the mononitroretenes and separating the corresponding amines. By catalytic reduction with Raney nickel, 4- and 9-nitroretene can easily be converted to aminoretenes in almost quantitative yields, and this method could also be successfully used for the reduction of the mixture of mononitroretenes. The theoretically required amount of hydrogen was taken up and the mixed amino-retenes were obtained as a straw-coloured, viscous product which gradually crystallized.

Two of the amines could be separated as their N-acetyl-derivatives by taking advantage of their different rates of acetylation. Acetic anhydride was added to an ether solution of the mixed aminoretenes and in about half an hour 9-acetamidoretene (*ca.* 38 %) had separated. It was removed, and after fifteen hours another acetamidoretene (*ca.* 12 %), hitherto unknown, could be collected. When oxidized with chromic acid it yielded retenequinone and its structure must, therefore, be 10-acetamidoretene.

The rest of the acetylation product did not separate from the solution. After removal of the solvents it was obtained as a light-brown material which was found to consist chiefly of acetamidoretenes. These were successfully chromatographed on alumina using a mixture of light petroleum and ethyl-acetate. For a satisfactory separation alumina with relatively weak adsorptive power must be used. It should be pointed out that the acetamidoretenes show blue fluorescence and most zones could be located, therefore, by inspection of the column in ultraviolet light (glass tube with a thickness of 1 mm was used). The result of the chromatographic investigation is displayed in Table 2 (p. 380). As can be seen, fractions of relatively pure 3-, 4-, 9- and 10-acetamido-retene were obtained. Fractions 24—26 were found to be a mixture of 3- and 6-acetamidoretene which, however, could be separated on alumina using a mixture of benzene and ethylacetate — the result appears in Table 3 (p. 381). In connexion with these separations, it was observed that an inversion of the

Table 1. Compounds isolated by the acetylation of the mixture of aminoretenes and by the chromatographic separation of the products soluble in the acetylation solution.

Compound	Yield % *		
	A. Precipitated by acetylation of the mixture of aminoretenes	B. Isolated by chromatography from the soluble part of the acetylation product (cf. Table 2—3)	Total (A + B)
3- Acetamidoretene	—	3.7	4
4-　　»	—	16.6	16
6-　　»	—	1.7	2
9-　　»	38	4.0	42
10-　　»	12	4.5	16
Mixtures	—	16.8	17
Material lost during the operations	—	3.2	3

* Calculated on the mixture of aminoretenes.

chromatographic sequence on alumina for 3- and 9-acetamidoretene can be effected by changing the developer. Separations have been carried out with ethylacetate (8—16 % by volume) in light petroleum and with ethylacetate (0—6 %) in benzene. In the former cases 3-acetamidoretene was located above the 9-isomer while in the latter cases the inverse order was obtained.

The result of the investigation is summarized in Table 1. The yields of the acetamidoretenes obtained and thus also the composition of the mixture of mononitroretenes appear from the last column of the Table. The yields are, of course, rather approximate. This can already be seen from the fact that some of the fractions, from which the yields are calculated, were not quite pure whilst others consisted of mixtures of the separated compounds. As appears from the Table, the nitration of retene gave a mixture of mononitroretenes containing 9-, 10-, 4-, 3- and 6-nitroretene, approximately in the ratio 20 : 8 : 8 : 2 : 1. The nitration carried out by Karrman and Bergkvist [2] yielded 9-, 4- and 3-nitroretene in the ratio 20 : 12 : 8. As in the case of phenanthrene which gives 9-, 4-, 2- and 3-nitrophenanthrene [3-4] (ratio 20 : 11 : 11 : 7), 9 and 4 are the most reactive positions. From the nitration of phenanthrene, and from the theoretical calculations by Buu-Hoi, Royer, Daudel and Martin [5] according to which 2 is the most reactive position, it was to be expected that 2-nitroretene should also be formed. However, this isomer has not been detected in the nitration products of retene.

The 10-acetamidoretene isolated above was not more closely investigated but the following observations of interest may be mentioned:

1. In the acetylation experiment 10-acetamidoretene was formed much more slowly than the 9-isomer.

2. When refluxed in a mixture of ethanol and concentrated hydrochloric acid, 10-acetamidoretene was only slowly attacked and gave 10-ethoxyretene instead of the expected amine. For comparison, when treated in the same way,

the 9-isomer was hydrolysed to 9-aminoretene and 9-retenol was converted to its ethyl ether (similar etherifications are reported in the literature [6]).

These observations indicate an influence of the methyl-group of retene on a substituent in the 10-position, similar to that found by Fieser and Young [7] when retenequinone was condensed with p-nitrophenylhydrazine or reduced with zinc dust and acetic acid. In the former case, a reaction at the ketonic group closest to the methyl-group is retarded and only 10-hydroxy-9-(p-nitrophenylazo)retene is formed. In the latter case, the retenehydroquinone first formed easily splits off the hydroxy-group in the 10-position to give 9-retenol. From the fact that 1-methylphenanthrenequinone reacts in the same way, but phenanthrenequinone is reduced only to the hydroquinone under similar conditions, they concluded that it is the methyl-group which activates the bond holding the hydroxy-group.

As seen in the foregoing, 90 % of the 9-acetamidoretene separated on the acetylation of the mixed aminoretenes—the yield corresponds to 32 % calculated on retene. This method for the preparation of 9-acetamidoretene may be preferred to those reported in the literature [8-9] which include more operations and give lower yields. The mixture of mononitroretenes used as starting material in the catalytic reduction was isolated from the crude nitration product by chromatography (cf. Part IV [1]), this being a disadvantage of the method especially if large amounts of the 9-derivative should be prepared. The method can, however, be simplified by excluding the chromatographic purification. Certainly, a lower yield (24 % calculated on retene) is then obtained, but on the other hand only three operations are required, namely nitration of retene in the presence of boron trifluoride, catalytic reduction of the crude nitration product with Raney nickel, and acetylation with acetic anhydride of the reduction product dissolved in ether.

EXPERIMENTAL *

Separation of 4- and 9-nitroretene. A solution of 4- and 9- nitroretene (45 mg of each) in light petroleum (b.p. 40—60°) was introduced in a column of alumina (10 cm² × 30 cm). On passing light petroleum through the column, two faintly yellow zones were developed and successively eluted. Three fractions were collected, the first containing 9-nitroretene (38 mg, m.p. 126—27°), the second a mixture of 4- and 9-nitroretene (15 mg, m.p. 118—23°), and the third 4-nitroretene (31 mg, m.p. 135—36°).

Attempt to separate the mixed mononitroretenes obtained by the nitration of retene. The mixture (160 mg) was chromatographed on a column of alumina (10 cm² × 31 cm). The column was first washed with light petroleum (3.2 l) and then fifteen fractions, accounting for ca. 90 % of the amount adsorbed, were collected. Light petroleum was used for the elution of the first thirteen fractions but fractions 14—15 were eluted with a mixture of light petroleum (9 vol.) and benzene (1 vol.). Fractions 5—9 contained 9-nitroretene (44 mg, m.p. 122—24° to 126—27°) but all the other fractions were mixtures melting over wide ranges. However, after recrystallizations from ethanol and from

---

* All melting points are corrected.

light petroleum, fraction 12 (12 mg, m.p. 105—15°) gave 4-nitroretene, m.p. 136—37°, and fraction 14 (13 mg, m.p. 110—25°) 3-nitroretene, m.p. 152—53°. The isolated nitroretenes were identified by mixed melting point determinations.

4-Aminoretene was prepared by catalytic reduction of 4-nitroretene (0.28 g) in absolute ethanol (50 ml) over Raney nickel. The theoretically required amount of hydrogen was taken up, and, from the reaction solution, 4-amino-retene (0.21 g, m.p. 79—82°) was obtained. After one recrystallization from ligroin (b.p. 60—90°) it was obtained as colourless needles, m.p. 88—89°. (Found: C 87.1; H 7.59. Calc. for $C_{18}H_{19}N$ (249.3): C 86.9; H 7.69).

4-Acetamidoretene separated in a pure state when acetic anhydride was added to an ethereal solution of 4-aminoretene. It was collected after 4 hours and obtained as colourless flat needles, m.p. 201—02°. (Found: C 82.0; H 7.35. Calc. for $C_{20}H_{21}ON$ (291.4): C 82.4; H 7.26).

9-Aminoretene was prepared by reduction of 9-nitroretene (0.28 g) as described above for the 4-isomer. The crude product (0.22 g) melted at 124—25° undepressed on admixture with an authentic sample.

Reduction of the mixture of mononitroretenes. The mixture (5.6 g) was dissolved in absolute ethanol (250 ml) and reduced over Raney nickel (ca. 4.5 g). In 5 hours 1 370 ml (N.T.P.) of hydrogen were taken up. From the reaction solution the mixed aminoretenes were obtained as a straw-coloured viscous product (4.9 g, 99 %) which gradually crystallized. (Found: C 86.9; H 7.72. Calc. for $C_{18}H_{19}N$ (249.3): C 86.9; H 7.69).

Acetylation of the mixture of aminoretenes. The mixture (3.20 g) was dissolved in ether (100 ml) and the solution mixed with acetic anhydride (6.5 ml). Within 5 minutes crystals began to separate. After 35 minutes these were collected and washed with ether (yield: 1.42 g, 38 %, m.p. 205—06.5°). The product was recrystallized twice from toluene and melted then at 210—11°, undepressed on admixture with 9-acetamidoretene. After 15 hours another acetamidoretene which gradually separated from the acetylation solution was collected and washed with ether (yield: 0.45 g, 12 %, m.p. 216—17°). It was recrystallized from benzene and from *n*-propanol and obtained as colourless needles, m.p. 219—20°. (Found: C 82.6; H 7.42; N 4.72. Calc. for $C_{20}H_{21}ON$ (291.4): C 82.4; H 7.26; N 4.81). Its oxidation to retenequinone indicates its structure to be 10-acetamidoretene (see below).

The filtrate from the acetylation was shaken with a dilute sodium carbonate solution to remove acetic acid and acetic anhydride, washed with water and dried over sodium sulphate. After removal of the ether a light-brown friable product (1.86 g) was obtained. (Found: C 82.0; H 7.32. Calc. for acetamido-retene $C_{20}H_{21}ON$ (291.4): C 82.4; H 7.26).

In another experiment, a product (0.50 g), prepared by catalytic reduction of the crude material obtained by the nitration of retene, was dissolved in ether (10 ml) and treated with acetic anhydride (2 ml). After 1 hour the 9-acetamidoretene which had separated (0.15 g, ca. 24 % calculated on retene, m.p. 210—11°) could be collected. No other pure compounds separated from the reaction solution.

Separation of acetamidoretenes from the product obtained from the filtrate in the acetylation. The product (780 mg) was dissolved in a mixture of light petroleum (20 ml) and ethylacetate (10 ml) and the solution was introduced in

Table 2. Fractions collected by the chromatographic separation of the compounds which remained dissolved in the acetylation solution. Amount adsorbed = 780 mg.

Fraction No.	Mg	M. p. °C	Compound	M.p. of the pure compound °C	Yield % *
1—18	93.1	not cryst.	Mixtures	—	6.0
19—20	49.8	211—12	9-Acetamidoretene[6-9]	212—13	4.0
21	13.5	208—09			
22	8.8	165—80	Mixtures	—	1.2
23	10.3	partly cryst.			
24	18.6	165—85	Mixtures of 3- and		
25	27.2	184—92	6-acetamidoretene	—	4.4
26	23.2	200—18	(cf. Table 3)		
27	20.3	241—42	3-Acetamidoretene[10]	241—42	2.3
28	16.1	239—40			
29	10.7	204—17			
30	7.4	165—95	Mixtures	—	1.7
31	8.8	partly cryst.			
32	31.1	186—89			
33—35	175.6	199—200	4-Acetamidoretene	201—02	16.6
36	30.0	194—95			
37	21.5	182—86			
38	15.9	162—71	Mixtures	—	2.0
39	15.0	148—64			
40	21.2	210—13			
41	23.6	215—17	10-Acetamidoretene	219—20	4.5
42	25.9	204—08			
43	15.0	163—75	Crystalline prod.		
44—54	56.3	—	melting over	—	5.0
55—65	7.3	—	wide ranges		
1—65	746.2				

* Calculated on the mixture of aminoretenes.

a column of alumina (12 cm² × 30 cm). The alumina used was the commercial "Aluminium oxide, standardized for chromatographic adsorbtion analysis according to Brockmann, Merck" which had been deactivated by the addition of water (2 g/100 g of alumina). A mixture of light petroleum (7 vol.) and ethylacetate (1 vol.) was passed through the column and the filtrate collected in 150-ml portions. The results is given in Table 2. Some of the fractions from which the yields of the acetamidoretenes were calculated were somewhat impure but could be purified by recrystallizations from either toluene or

Table 3. Chromatographic separation of 3- and 6-acetamidoretene (Fractions 24—26, Table 2). Amount adsorbed = 60 mg.

Fraction No.	Mg	M.p. °C	Compound	M.p. of the pure compound °C	Yield % *
1—9	1.4	—	—	—	0.1
10	2.5	238—39			
11—12	10.2	241—42	3-Acetamidoretene	241—42	1.4
13	3.7	239—40			
14	2.3	233—35			
15	1.8	220—26			
16	1.4	203—10	Mixtures	—	0.3
17	1.5	174—85			
18	3.9	217—19			
19—22	17.0	221—22	6-Acetamidoretene [11]	225—26	1.7
23	2.2	214—16			
24	1.8	206—10			
25	1.4	198—205	Mixtures	—	0.5
26—30	3.2	—			
1—30	54.3				

* Calculated on the mixture of aminoretenes.

ethanol. The acetamidoretenes were identified by mixed melting point determinations with authentic samples.

Most (60 mg) of the material from fractions 24—26 was rechromatographed on alumina (the above mentioned commercial product). The column was washed with a mixture of benzene (19 vol.) and ethylacetate (1 vol.) and 100-ml fractions were collected. The result is given in Table 3.

Oxidation of the acetamidoretene (m.p. 219—20°) isolated from the acetylation. The compound (0.15 g) was oxidized with CrO_3 (0.35 g) in hot glacial acetic acid (3 ml). After cooling to room temperature the crystals which separated were collected, washed with 50 % acetic acid and recrystallized from glacial acetic acid giving retenequinone, m.p. 196—97°, undepressed on admixture with an authentic sample.

10-Ethoxyretene was obtained when 10-acetamidoretene (0.25 g) was refluxed for 9 hours in a mixture of ethanol (15 ml) and conc. hydrochloric acid (4 ml). On cooling colourless needles separated (0.18 g, m.p. 100—01°). These were collected and recrystallized from ethanol to give needles melting at 101 —02°. (Found: C 86.3; H 8.03; C_2H_5O 16.0. Calc. for $C_{20}H_{22}O$ (278.4): C 86.4; H 7.96; C_2H_5O 16.2). When oxidized with chromic acid, as described above for 10-acetamidoretene, it yielded retenequinone.

A hydrolysis of 9-acetamidoretene was carried out under the above conditions. After 3 hours the reaction solution was cooled, diluted with water and neutraliz-

ed. The product which separated was collected, washed with water and dried. It melted at 122—24°, undepressed on admixture with 9-aminoretene.

9-Ethoxyretene. 9-Retenol (0.10 g) was refluxed for 5 hours in a mixture of ethanol (8 ml) and conc. hydrochloric acid (2 ml). The reaction solution was worked up as described for 10-ethoxyretene. The crude product (0.11 g) melted at 95—97° and the colourless needles obtained from ethanol at 98—99°. On admixture with 10-ethoxyretene it melted at 88—90°. (Found: C 86.4; H 8.00. Calc. for $C_{20}H_{22}O$ (278.4): C 86.4; H 7.96).

REFERENCES

1. Sihlbom, L. *Acta Chem. Scand.* **5** (1951) 1210.
2. Karrman, K. J. and Bergkvist, R. *Svensk Kem. Tidskr.* **65** (1953) 103.
3. Schmidt, J. and Heinle, E. *Ber.* **44** (1911) 1488.
4. Bavin, P. M. G. and Dewar, M. J. S. *Chemistry & Industry* **1953** 543.
5. Buu-Hoï, Royer, R., Daudel, R. and Martin, M. *Bull. soc. chim. France* **1948** 329.
6. Liebermann, C. and Hagen, A. *Ber.* **15** (1882) 1427. *Cf.* Houben, J. *Die Methoden der organischen Chemie III*, Verlag Georg Thieme, Leipzig 1930, p. 137.
7. Fieser, L. F. and Young, M. N. *J. Am. Chem. Soc.* **53** (1931) 4120.
8. Karrman, K. J. and Sihlbom, L. *Svensk Kem. Tidskr.* **58** (1946) 189.
9. Elderfield, R. C., Dodd jr, T. N. and Gensler, W. J. *J. Org. Chem.* **12** (1947) 393.
10. Adelson, D. E. and Bogert, M. T. *J. Am. Chem. Soc.* **58** (1936) 653.
11. Karrman, K. J. and Persson, K. *Svensk Kem. Tidskr.* **65** (1953) 135.