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Retene Investigations

XIX. The Structure of 2-Hydroxyretene (2-Retenol)

K. J. KARRMAN

Department of Organic Chemistry, The University, Lund, Sweden

A- and B-hydroxyretene, prepared by E. Wahlforss [1] in 1924, were the first known monosubstituted retene derivatives. As a result of physico-chemical investigations, Fieser and Young [2] considered it probable that in B-hydroxyretene the hydroxyl group occupied the 3- or the 6-position and more recently Campbell and Todd [3] and Karrman [4], have by pure chemical methods decided in favour of the 3-position.

With regard to the structure of A-hydroxyretene, Fieser and Young decided that the hydroxyl group must be in the 2-position. This conclusion was based on the following two observations. A-Hydroxyretene does not couple with diazotized amines and according to Fieser and Young this indicates that the hydroxyl group occupies the 2- or the 8-position. The 8-position is ruled out on the basis of the Dimroth test for α-hydroxyquinones, as 8-hydroxyretene quinone should give a colour reaction with boroacetic anhydride and A-hydroxyretene quinone does not give this reaction.

Fieser and Young have also investigated the reduction potentials of a number of different mono- and dihydroxy derivatives of phenanthraquinone and compared these with the reduction potential of A-hydroxyretene quinone. From this comparison they again concluded that A-hydroxyretene probably had the hydroxyl group in the 2-position.

In the present communication evidence is presented to show that A-hydroxyretene is indeed 2-hydroxyretene. 9,10-Dihydroretene was nitrated to a mononitro derivative [5], known to have the nitro group in the same position as the hydroxyl group of A-hydroxyretene [5]. The nitrodihydroretene was reduced with tin and hydrochloric acid and the resulting amino compound was acetylated. The resulting acetylamino-9,10-dihydroretene was nitrated, giving a faint yellow mononitro derivative in almost quantitative yield. The acetyl

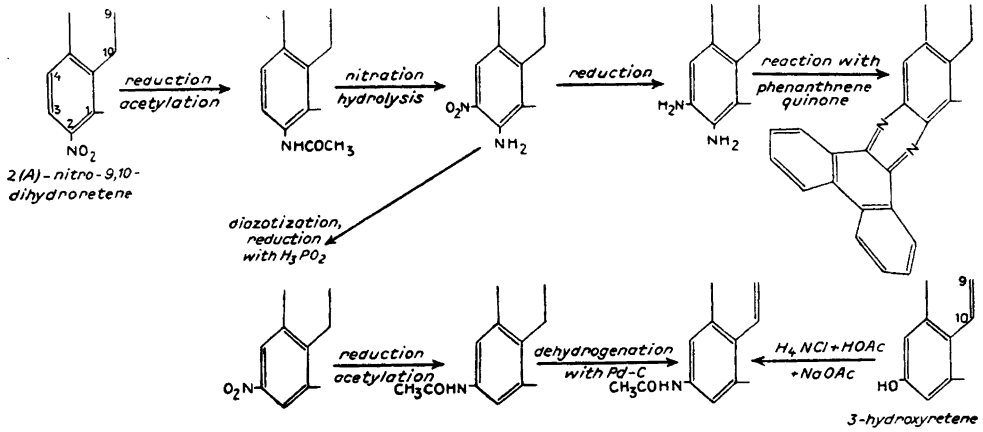

Fig. 1. Reactions showing that the A-position is adjacent to the 3-position.

group was removed and the nitro group reduced, thus producing a diamino-9,10-dihydroretene. This substance was dissolved in hot glacial acetic acid and a hot solution of phenanthraquinone in the same solvent was added. Immediatly a thick, straw-yellow precipitate of the quinoxaline was formed, thus showing that the two amino groups are situated in ortho position to one another (Fig. 1). (If retene quinone is used instead of phenanthraquinone the quinoxaline obtained is not homogeneous but a mixture of the two possible isomers, which can be separated from one another only with difficulty.)

It has thus been proved that on nitration of acet amino-9,10-dihydroretene, the nitro group enters the position ortho to the acet amino group. This nitro derivative was hydrolysed with hydrochloric acid in boiling ethanol, the corresponding ortho nitroamine being obtained as red crystals (the hydrochloride was not formed). The amine was diazotized in dilute acetic acid and the resulting diazonium salt reduced with hypophosphorous acid. A mononitro-9,10-dihydroretene was thus obtained as pale yellow crystals, which on oxidation with chromic acid in glacial acetic acid gave a nitroretene quinone. The nitrodihydroretene was reduced with tin and hydrochloric acid and the resulting amine acetylated with acetic anhydride, giving a monoacetylamino compound. Dehydrogenation by means of palladium-charcoal gave 3-acetylaminoretene m. p. 240—241° C, which was hydrolysed to 3-aminoretene, m. p. 139—140° C.

Thus it is clear that the hydroxyl group in A-hydroxyretene must be situated adjacent to the 3-position, *i. e.* in the 2- or the 4-position (Fig. 1).

The position of the methyl group in 4-methylretene is established by the syntheses of Haworth *et al.*[6] and on account of this, we have been able to decide

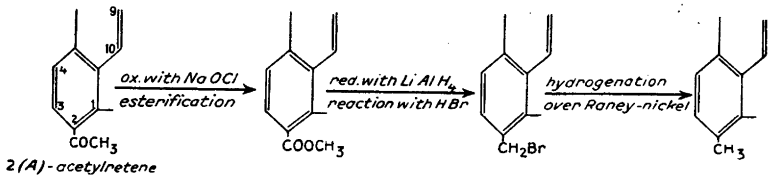

Fig. 2. Reactions leading to A-methylretene, not identical with 4-methylretene.

between 2- and 4-hydroxyretene as follows. A-Acetylretene, prepared by the method of Hakon Lund [7], has been oxidized to the corresponding carboxylic acid and the corresponding methyl ester reduced with lithium aluminum hydride in ether, giving A-hydroxymethylretene in good yield. This substance was treated with hydrobromic acid, giving A-bromomethylretene, which was hydrogenated over Raney nickel at a moderate hydrogen pressure, producing A-methylretene (Fig. 2). This substance is not identical with 4-methylretene as is shown in Table 1 and thus the hydroxyl group in A-hydroxyretene must be situated in the 2-position.

Table 1. Comparison of 2 (A)- and 4-methylretene.

Substance	M. p.	Picrate m. p.	Styphnate m. p.
2 (A)-Methylretene	122.5—123.5°	139.0—139.5°	158—159°
4-Methylretene	60.5— 61.5°	114.5—115°	142—143°

EXPERIMENTAL

2-Acetylamino-3-nitro-9,10-dihydroretene. To 0.38 g of 2-acetylaminodihydroretene, suspended in 7 ml of glacial acetic acid was added a mixture of 2 ml of concentrated nitric acid and 3 ml of glacial acetic acid. The temperature rose from 21° to 25° C and a clear, yellow solution was obtained. After 30 min. excess of water was added and the precipitate formed (0.42 g) was filtered off, dried and recrystallized from toluene, forming pale yellow crystals (0.31 g) of m. p. 228—230° C.

$C_{20}H_{22}O_3N_2$ (338.2)	Calcd.	C 71.0	H 6.56	N 8.28
	Found	» 71.3	» 6.44	» 8.22

2-Amino-3-nitro-9,10-dihydroretene was obtained by boiling a solution of 1.1 g of the above acetyl compound in 15 ml of propanol and 3 ml of concentrated hydrochloric acid for twenty four hours. On cooling, bright-red crystals of the free amine were obtai-

ned, 0.75 g, m. p. 142—143° C. The slow rate of hydrolysis of the acetyl compound is probably due to the presence of substituents in both ortho positions.

$C_{18}H_{20}O_2N_2$ (296.2)	Calcd.	C 72.9	H 6.82	N 9.45
	Found	» 72.9	» 6.63	» 9.37

2,3-Diamino-9,10-dihydroretene. 0.65 g of the 2-amino-3-nitro compound was dissolved in 20 ml of ethanol. 2 g of zinc dust and 2—3 ml of concentrated hydrochloric acid were added and the solution was boiled for 15 hours during which time the red solution gradually turned lighter and was finally almost colourless. The mixture was cooled, water was added, and the resulting colourless precipitate, collected, dried and recrystallized from 35 ml of ethanol, giving 0.41 g of white plates, m. p. 195—197° C.

$C_{18}H_{22}N_2$ (266.2)	Calcd.	C 81.1	H 8.34	N 10.5
	Found	» 81.1	» 8.28	» 10.6

Quinoxalines. To 0.02 g of the diamine in 2 ml of hot glacial acetic acid was added 0.02 g of retene quinone in 2 ml of hot glacial acetic acid. A straw-yellow precipitate (0.35 g) was formed immediately but its melting point was not sharp and the product was probably a mixture of the two possible isomers, as the analysis gave the expected result.

$C_{36}H_{34}N_2$ (494.3)	Calcd.	C 87.4	H 6.94	N 5.66
	Found	» 87.2	» 6.81	» 5.72

When the reaction was repeated with phenanthraquinone, a straw yellow precipitate was obtained.

This was extremely insoluble, but had a sharp melting point, 258—259° C. On account of the symmetry of phenanthraquinone only one isomer can be formed.

$C_{32}H_{26}N_2$ (438.2)	Calcd.	C 87.6	H 5.98	N 6.39
	Found	» 88.0	» 5.77	» 6.31

3-Nitro-9,10-dihydroretene. 2-Amino-3-nitrodihydroretene (0.4 g) was suspended in 30 ml of glacial acetic acid and 9 ml of dilute sulfuric acid (1 : 3) was added. The mixture was cooled to 4° C and 0.4 g of sodium nitrite in 5 ml of water was added with stirring. A clear solution was formed. One hour later 15 ml of 30 % hypophosphorous acid was added and the solution was left in an ice-box for two days, then neutralised with sodium hydroxide and extracted with ether. The ether solution was dried with anhydrous sodium sulphate and evaporated, giving a dark oil which was diluted with hexane and filtered through aluminium oxide (Brockmann). The hexane solution was evaporated giving 0.15 g of pale yellow crystals. Recrystallisation from 5 ml of ethanol gave the pure compound, melting at 88—89° C.

$C_{18}H_{19}O_2N$ (281.1)	Calcd.	C 76.8	H 6.81	N 4.98
	Found	» 76.4	» 6.66	» 5.02

3-Nitroretene quinone. 0.3 g of chromic acid was added to 0.1 g of 3-nitro-dihydroretene in 2 ml of glacial acetic acid and the mixture was heated at 90° C for half an hour,

then cooled and diluted with water. The yellow solid precipitated (0.06 g) was recrystallized from 4 ml of acetic acid, giving orange needles (0.038 g), which did not melt below 280° C.

$C_{18}H_{15}O_4N$ (309.1)	Calcd.	C 69.9	H 4.89
	Found	» 70.1	» 4.76

3-Amino-9,10-dihydroretene. To 0.19 g of 3-nitrodihydroretene in 25 ml of ethanol was added 2 ml of concentrated hydrochloric acid and ca 2 g of granulated tin. The mixture was boiled for half an hour by which time it was almost colourless, then water was added and the precipitate (0.17 g) filtered off and dried. This hydrochloride was treated with sodium hydroxide and extracted with ether. The ether was evaporated, and the residue 0.14 g, taken up in 30 ml of benzene. The solution was treated with charcoal, concentrated to 10 ml, and left in an ice-box overnight, giving 0.046 g of transparent plates, m. p. 111—112° C.

$C_{18}H_{21}N$ (251.2)	Calcd.	N 5.57
	Found	» 5.54

3-Acetylamino-9,10-dihydroretene, was obtained by acetylation of the above amine with acetic anhydride. Recrystallization from ethanol gave colourless crystals, melting at 228—229° C.

$C_{20}H_{23}ON$ (293.2)	Calcd.	C 81.9	H 7.91
	Found	» 81.6	» 7.82

This acetylamino compound (0.020 g) was heated with palladiumcharcoal at 225—235° C for one hour during which time 1.2 ml of hydrogen was evolved. The reaction mixture was extracted with 5 ml of hot toluene, which on cooling deposited 0.011 g of a white substance melting at 240—241° C either alone or mixed with an authentic sample of 3-acetylaminoretene (m. p. 240—241° C). Hydrolysis of the acetyl compound gave the free amine, m. p. 139—140° C.

Methyl ester of retene-2-carboxylic acid. 7.0 g of retene-2-carboxylic acid, prepared as described by H. Lund [7] was boiled in 150 ml of methanol containing 10.5 g of concentrated sulfuric acid for 24 hours. After cooling and filtration, 6.6 g of the methyl ester was obtained, m. p. 174—175° C. Further recrystallization from ethanol raised the m. p. to 175—176° C.

$C_{20}H_{20}O_2$ (292.2)	Calcd.	C 82.2	H 6.90
	Found	» 82.4	» 6.82

The picrate, prepared from the components in ethanol formed yellow needles, m. p. 114—115° C. It is stable in solution only in the presence of an excess of picric acid.

$C_{26}H_{23}O_9N_3$ (521.2)	Calcd.	C 59.9	H 4.45
	Found	» 59.4	» 4.31

2-Hydroxymethylretene. 5.0 g of the methyl ester of retene-2-carboxylic acid was dissolved in 350 ml of dry ether, a solution of 1.0 g of lithium aluminum hydride in 600 ml of dry ether added, the mixture boiled gently for 30 min. Then cooled and treated with 600 ml of water added in small amounts. The ether solution was separated, dried with anhydrous sodium sulfate and evaporated to dryness, giving 3.9 g of product m. p. 166.5—168° C. This was recrystallized from 50 ml of ethanol and gave 2.8 g of pure material as transparent plates, m. p. 168.5—169.5° C.

$C_{19}H_{20}O$ (264.2)	Calcd.	C 86.3	H 7.63
	Found	» 86.7	» 7.79

The picrate, was obtained from the components in ethanol solution as yellow needles, m. p. 138—139° C.

$C_{25}H_{23}O_8N_3$ (493.2)	Calcd.	C 60.8	H 4.70
	Found	» 60.4	» 4.54

2-Acetoxymethylretene, was prepared from the corresponding hydroxymethyl compound and acetic anhydride. It formed white plates, m. p. 136.5—137.5° C.

$C_{21}H_{22}O_2$ (306.2)	Calcd.	C 82.3	H 7.24
	Found	» 82.0	» 7.11

2-Bromomethylretene. 1.5 g of 2-hydroxymethylretene was dissolved in 120 ml of glacial acetic acid and gaseous hydrobromic acid was passed into the solution for twenty minutes. The reaction mixture was then allowed to stand for six hours at 15° C. After filtration, washing and drying, the pure product obtained (1.52 g) melted at 175—176° C.

$C_{19}H_{19}Br$ (327.1)	Calcd.	C 69.7	H 5.85	Br 24.4
	Found	» 70.1	» 5.92	» 24.5

This product has also been obtained by passing gaseous hydrobromic acid into a solution of the carbinol in benzene, or by treating a boiling solution of the carbinol in carbon tetrachloride with phosphorous tribromide.

2-Ethoxymethylretene, was obtained by boiling the bromomethyl compound with ethanol for twenty minutes. It formed transparent plates, m. p. 89—90° C.

$C_{21}H_{24}O$ (292.2)	Calcd.	C 86.2	H 8.28
	Found	» 85.5	» 8.11

2-Methoxymethylretene, was prepared similarly by boiling the bromomethyl compound with methanol. M. p. 112.5—113.5° C.

$C_{20}H_{22}O$ (278.2)	Calcd.	C 86.2	H 7.98
	Found	» 85.8	» 8.05

2-Phenylaminomethylretene. 2-Bromomethylretene (0.1 g) was heated with 0.5 g of aniline at 150° C for some minutes. After cooling, dilute hydrochloric acid was added and the precipitate filtered off, washed and dried. Recrystallization from ethanol gave 0.065 g of white plates, m. p. 192—193° C.

$C_{25}H_{25}N$ (339.2)	Calcd.	C 88.4	H 7.43	N 4.13
	Found	» 87.5	» 7.28	» 4.08

2-Methylretene. 1.00 g of the 2-bromomethyl compound was dissolved in 15 ml of dioxan. Raney nickel (0.5 g) was added to the solution and hydrogenation was carried out for one hour at 70 atmos. and 80° C. After cooling, filtration, and evaporation to dryness 0.71 g (94 %) of crude methylretene was obtained, m. p. 119—121° C. Recrystallization from 40 ml of ethanol gave 0.37 g of white plates, melting at 123—124° C. From the mother liquor a further 0.17 g of the pure compound was obtained.

$C_{19}H_{20}$ (248.2)	Calcd.	C 91.9	H 8.12
	Found	» 91.1	» 8.07

The picrate, was obtained from 0.1 g of 2-methylretene and 0.1 g of picric acid in 5 ml of ethanol, as orange plates, m. p. 139—139.5° C.

$C_{25}H_{23}O_7N_3$ (477.2)	Calcd.	C 62.9	H 4.86	N 8.80
	Found	» 62.6	» 4.76	» 8.85

The styphnate, prepared from the components in ethanol solution formed orange needles, m. p. 158—159° C.

$C_{25}H_{23}O_8N_3$ (493.2)	Calcd.	C 60.8	H 4.70
	Found	» 60.8	» 4.63

SUMMARY

A chemical proof of the position of the hydroxyl group in A-hydroxyretene has been given as follows. Nitration of 9,10-dihydroretene gave a mononitro derivative with the nitro group in the A-position; this compound was reduced to the amine and acetylated. Nitration of this acetylamino compound gave a mononitro derivative, which by hydrolysis and reduction was converted into a diamino dihydroretene. This compound reacted with phenanthraquinone to form a quinoxaline. Thus the two amino groups are situated in adjacent positions. The above acetylamino nitro compound was hydrolysed and the amino group replaced by hydrogen via the diazonium salt. The nitrodihydroretene thus obtained was reduced to the amine, acetylated and dehydrogenated to the corresponding retene derivative. This was identical with 3-acetyl aminoretene and the A-position is thus the 2- or the 4-position.

A-acetylretene was oxidized to the corresponding acid, and the methyl ester reduced with lithium aluminum hydride to the carbinol. This was treated with hydrobromic acid, giving A-bromomethylretene, which, on hydrogenation at moderate pressure over Raney nickel, gave A-methylretene. This product was not identical with 4-methylretene, the structure of which has been fully established by the synthesis of Haworth *et al.*[6]. Thus it has been shown that the A-position is the 2-position.

LITERATURE

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