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Deuterated Organic Compounds XXV Synthesis of 1,4,5,8-Tetradeuterionaphthalene *

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SUMMARY

1,4,5,8-Tetradeuterionaphthalene was synthesized from 1,4-dibromonaphthalene by two methods. In the first method naphthalene was repeatedly brominated in chloroform and then debrominated with zinc dust in alkaline deuterium oxide. In the second, 1,4-dibromonaphthalene was nitrated to produce 1,4-dibromo-5-nitronaphthalene which underwent reductive debromination with zinc in alkaline deuterium oxide to 1-amino-5,8-dideuterionaphthalene. The latter was converted into 1-bromo-5,8-dideuterionaphthalene by a modified Sandmeyer reaction which was brominated to 1,4-dibromo-5,8-dideuterionaphthalene and then debrominated to 1,4,5,8-tetradeuterionaphthalene.

In connection with some spectroscopic studies by MITRA and BERNSTEIN which have now been published [1] a number of deuterionaphthalenes were synthesized. Monodeuteriated naphthalene, methyl naphthalene and ethylnaphthalene had previously been prepared from the bromo derivatives through the Grignard synthesis by GOUBEAU, LUTHER, FELDMANN and BRANDES [2]. Octadeuterionaphthalene is also reported in this paper. While our work was in progress SHATENSHTEIN, PEREGUDOV, ISRAILEVICH and KALINACHENKO [3] reported the preparation of 1,4,5,8-tetradeuterionaphthalene by exchanging naphthalene with liquid deuterium bromide at room temperature. Although their extensive studies of the kinetics of aromatic hydrocarbon exchange in liquid deuterium halides constitute an important contribution in this field, serious experimental problems arise in using liquid deuterium halides for preparative exchange reactions.

In the present work, we were particularly interested in obtaining 1,4,5,8-tetradeuterionaphthalene. Our first attempts to prepare this compound were

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based on the observation that mono- and dibromonaphthalenes could be converted in good yield into the corresponding deuterionaphthalenes with zinc dust in alkaline deuterium oxide. 1-Monodeuterio-, 2-deuterio- and 1,4-dideuterionaphthalenes were prepared in this manner. The corresponding chloro derivatives did not undergo reductive dechlorination under these conditions. According to ZECHMEISTER and ROM [4] chloronaphthalenes are dechlorinated with magnesium in methyl alcohol but for synthesizing the deuteriated compounds this method obviously requires the use of expensive deuteriomethanol as solvent.

On the basis of our results with the dibromonaphthalenes, 1,4,5,8-tetrabromo- or 1,5-dibromo-4,8-diodonaphthalene would be expected to give the desired tetradeuterionaphthalene. However, the work of WHITEHURST [5], of BAYER and O'REILLY [6] and our own results indicated the tetrahalonaphthalenes could not be prepared in the quantity needed because of very low yields. Since our objective was to prepare twenty to twenty-five grams of 1,4,5,8-tetradeuterionaphthalene this method was therefore abandoned.

Another route explored for the synthesis of the tetradeuterionaphthalene was repeated bromination of naphthalene and debromination with zinc dust in alkaline deuterium oxide. According to the literature [6] bromination of naphthalene in chloroform gives mainly 1,4-dibromonaphthalene and a little of the 1,5-isomer. A recent study of the reaction with radioactive bromine by BERLINER, OCHS and ZIMMERMAN [7] indicates that bromination occurs in the 2, 3, 6 or 7 positions to the extent of less than 1 %. Reductive debromination of the product in basic deuterium oxide produces, of course, 1,4-dideuterionaphthalene. Bromination of the latter results in a mixture of normal dibromonaphthalene and 1,4-dibromo-5,8-dideuterionaphthalene. Reductive debromination of this mixture as before leads to 1,4-dideuterionaphthalene and 1,4,5,8-tetradeuterionaphthalene. After having repeated this cycle six times 1,4,5,8-tetradeuterionaphthalene which analyzed 76.5 mol % $C_{10}H_4D_4$ was obtained. It also contained 11.0 mol % $C_{10}H_3D_5$ and 7.2 mol % $C_{10}H_5D_3$.

A second synthesis of the deuterionaphthalene was developed from 1,4-dibromonaphthalene. Nitration of the latter with concentrated nitricacid as described by CAMPBELL and MCLEISH [8] produced a 50-55 % yield of the 5-nitro derivative. Having established that 2,4-dibromo-1-naphthylamine is readily converted into 2,4-dideuterio-1-naphthylamine by the reductive debromination already described it was felt that 1,4-dibromo-5-nitronaphthalene might likewise be converted into 5,8-dideuterio-1-naphthylamine in one step. This was found to be the case provided that a large excess of zinc dust is present and that the reaction mixture is well stirred. When these conditions were met nearly quantitative yields of deuteriated naphthylamine were regularly obtained. The modification of the Sandmeyer reaction described by NEWMAN and WISE [9] was used to convert the amine without loss of deuterium into 5,8-dideuterio-1-bromonaphthalene in 60 % yield.

The deuteriated bromonaphthalene resisted further bromination in chloroform. This interesting observation shows that 1-bromonaphthalene is not an intermediate in the formation of 1,4-dibromonaphthalene from naphthalene in chloroform. However, bromination of the mono-bromonaphthalene took place in acetic acid to give a moderately good yield of 1,4-dibromo-5,8-dideuterionaphthalene. Debromination of the compound with zinc dust in alkaline deuterium oxide gave 1,4,5,8-tetradeuterionaphthalene which however contained up to 25 % pentadeuterionaphthalene besides small amounts of less deuteriated species.

The presence of so much pentadeuterionaphthalene was somewhat puzzling at first. It seemed that this deuterium could only be introduced during the conversion of the nitrobromonaphthalene to the amine. When ordinary 1-naphthylamine was stirred with the same reactants used in the reduction under the same conditions the naphthylamine recovered contained less than 5 % deuterium. Slight exchange obviously occurred between the amine and the deuterium oxide. It was then decided to reduce 1-nitronaphthalene under the same conditions and convert the amine obtained into naphthalene. Although the yield was extremely low in the reduction sufficient amine was obtained to convert it into naphthalene. This naphthalene was now found to contain 10% monodeuterionaphthalene. It appears that deuterium is introduced to some extent into the naphthalene molecule by exchange before, during and after reduction to the amine takes place. Fortunately, however, the deuterium was introduced in a labile position because it could be re-exchanged for hydrogen by heating the solution of hydrobromide for several hours before diazotization. When this precaution was followed the amount of pentadeuterionaphthalene in the product was less than 4 %. However, if the period of refluxing is prolonged, further, loss of deuterium occurs and the final product then contains more trideuterionaphthalene.

EXPERIMENTAL

1-Deuterionaphthalene.

A suspension of 1-bromonaphthalene (2.5 g; 0.08 mole), zinc dust (5.0 g) and calcium oxide (1.5 g) in 10.0 ml deuterium oxide (99.7 % D) was stirred under reflux for 24 hrs. with a magnetic bar. The naphthalene which had sublimed into the condenser was dissolved in pentane and the solution was evaporated on the steambath. The naphthalene was purified by recrystallization from ethyl alcohol or sublimation. Yield : 1.2 g (70 %). Mass analysis 98.5 mol % $C_{10}H_7D$. 2-Deuterionaphthalene was similarly prepared from 2-bromonaphthalene.

1,4-Dideuterionaphthalene.

1,4-Dibromonaphthalene was similarly converted into the dideuterio derivative in 90 % yield. Mass analysis : 94.4 mol % $C_{10}H_6D_2$, 5.6 mol % $C_{10}H_7D$.

Bromination of Naphthalene.

To a stirred solution of naphthalene (128 g; 1 mole) in chloroform (500 ml) in a 1 l-round-bottomed three-necked flask equipped with a separatory funnel and a condenser connected to a gas-absorption tube there was added at room temperature bromine (330 g; 4.03 moles) at the rate of 1 drop per second. When it had all been added the solution was heated to 40° for two hours, then washed in succession with water, 10 % sodium carbonate and again water. Evaporation of the chloroform on the steambath left a nearly white solid (286 g), m.p. 55-65°. The low melting point was due to the presence of 1,5-dibromonaphthalene which is obviously of no importance in the preparation of 1,4,5,8-tetradeuterionaphthalene.

1,4,5,8-Tetradeuterionaphthalene.

The following description of the debromination of 1,4-dibromonaphthalene gave an optimum yield of deuterionaphthalene. A *very efficiently stirred* suspension of dibromonaphthalene (61 g; 0.21 mole) zinc dust (150 g) and calcium deuteroxide (20.0 g; 0.27 mole) in deuterium oxide (150 ml) was heated under reflux for 36 hours. During this period some naphthalene sublimed into the condenser. The reaction mixture was stirred as it cooled and absolute ether (150 ml) was added through the condenser just before the reaction mixture began to solidify. The ether solution was decanted and the residue was washed by decantation with five 50 ml portions of ether. The deuterionaphthalene was recovered by distilling off most of the ether on the steambath and the last portion under vacuum. The naphthalene was distilled on the vacuum line from a waterbath at 50° into a Stock trap cooled in dry ice. The yield of deuterionaphthalene was 25.6 g (92 %). A small amount of residual non-volatile monobromonaphthalene which remained in the distilling flask was added to a second run. Debromination on a larger scale was avoided because of difficulty in keeping the reaction mixture well stirred. If the stirring is interrupted for any reason the zinc dust collects on the bottom of the flask and forms a hard cake which inhibits further reaction even if stirring is resumed.

The cycle of bromination and debromination was repeated six times. The final yield of tetradeuterionaphthalene which analyzed 76.5 mol % $C_{10}H_4D_4$, 11 % $C_{10}H_3D_5$, and 7.2 mol % $C_{10}H_5D_3$ was 45.0 g (35 %). Considering the numerous operations the yield is not unreasonably low.

2,4-Dibromo-1-naphthalamine.

The bromination of 1-naphthylamine about to be described was found to give a better product than the method of VAN ALPHEN [10]. To a solution of 7.1 g (0.05 mole) of 1-naphthylamine in glacial acetic acid (300 ml) was added dropwise with stirring a solution of bromine (5.3 ml) in glacial acetic acid (300 ml). A thick creamy precipitate which began to form at once was filtered off after 2 hours' standing, sucked as dry as possible and washed with 50 % acetic acid-water. The slightly purplish solid was recrystallized from 50 % acetic acid-water (400 ml). The hot solution was decanted from a slight amount of gum and cooled. The yield of purplish needles, m.p. 115-6° was 12.0 g (85 %). The m.p. of the product indicates it is the free base rather than the hydrobromide.

2,4-Dideuterio-1-Naphthylamine.

A suspension of 2,3-dibromo-1-naphthylamine, m.p., 115-6° (3.5 g; 0.01 mole), zinc dust (10.0 g) and calcium oxide (4.0 g) in deuterium oxide (15 ml) was stirred under gentle reflux overnight and then for six hours longer after having added one more gram of zinc dust. The cold reaction mixture was diluted somewhat with water and filtered with suction. The solid was washed several times with water and then with ether. The filtrate was poured into a separatory funnel and the aqueous layer was drawn off. It was acidified with dilute nitric acid and treated with excess aqueous silver nitrate. The copious precipitate of silver bromide was filtered off, washed with water, methanol, dried and weighed. Yield; 3.5 g (90 % of the theoretical amount).

The ether solution was dried over a few pellets of potassium hydroxide, filtered and concentrated to a small volume on the steambath. The residue was treated with acetic anhydryde (5.0 ml), heated on the steambath for a few minutes and then diluted with water. The precipitated acetyldeuterionaphthylamine was recrystallized from dilute acetic acid and then from water. M. P., alone or admixed with acetylnaphthylamine, 159-60°. Yield : 1.5 g. (80 %).

In later experiments naphthylamine was isolated rather than the acetyl derivative by transferring the residue from the ether into a Späth bulb and distilling the naphthylamine in an air bath at 90° under 0.1 mm. It distilled as a pale yellow liquid which solidified on standing to a nearly white solid, m.p. 49-50°.

1,4-Dibromo-5-nitronaphthalene.

A suspension of 1,4-dibromonaphthalene (51.0 g; 0.17 mol) in concentrated nitric acid (400 ml) was stirred for 24 hrs. in a basin of water at room temperature. Oxides of nitrogen were evolved and the white crystalline solid gave place to a fine yellow amorphous powder. It was filtered off on a fritted glass funnel and washed first with a little concentrated nitric acid (10 ml) then with cold glacial acetic acid (25 ml) and finally with methyl alcohol (25 ml). The crude product was recrystallized from glacial acetic acid (350 ml), heated to 85-90° on the steam bath. The 1,4-dibromo-5-nitronaphthalene separated in tufts of pale yellow needles, m.p. 114-5° C. Yield : 30-2 g (50-54 %).

1-Naphthylamine.

1,4-Dibromo-5-nitronaphthalene (3.3 g; 0.01 mole) was heated under reflux with *very efficient* stirring with zinc dust (15.0 g) and calcium hydroxide (5.0 g) in water (15 ml) for 24 hours. The amine was extracted from the reaction mixture by repeated stirring with ether (25 ml) and decantation of the ether extract. The solution was dried over alkali pellets, filtered and evaporated. The residue was transferred to a Späth bulb and distilled under reduced pressure (.01 mm) in an air bath heated to 90°. The yield of pale yellow distillate which solidified on standing was 1.3 g (92 %). The acetyl derivative prepared from acetic anhydride melted at 159° as reported in the literature for 1-acetylnaphthalene. The Beilstein test performed on the amine was negative.

The aqueous suspension of zinc and calcium hydroxides was filtered off and the precipitate was washed several times with small amounts of hot water. The filtrate was acidified with dilute nitric acid and treated with aqueous silver nitrate. The copious precipitate of silver bromide was filtered off and washed with water and then with methanol. Yield : 4.0 g (nearly the theoretical amount).

5,8-Dideuterio-1-naphthylamine

This compound was prepared by conducting the reductive debromination of 5-nitro-1,4-dibromonaphthalene in deuterium oxide. The reaction mixture was slowly heated to 90° while stirring continuously with a magnetized teflon-enclosed bar. The deuterium oxide was recovered by distilling the reaction mixture under reduced pressure on a vacuum line. The residue was extracted several times with ether (150 ml) and the solution was dried over pellets of alkali before removing the solvent. The residue was distilled in a Späth bulb as described for the normal compound. From 10.0 g of the bromonitronaphthalene 3.5 to 4.0 g of 5,8-dideuterio-1-naphthylamine were regularly obtained.

1-Bromo-5,8-dideuterionaphthalene.

5,8-Dideuterio-1-naphthylamine (3.5 g; 0.024 mole) was dissolved in 48 % hydrobromic acid (15.0 ml) diluted with water (85 ml). The stirred solution was cooled to +5° in an ice bath and diazotized with sodium nitrite (1.0 g) added in small portions. After 5 minutes stirring a solution of mercuric bromide (15 g) in 48 % hydrobromic acid (20 ml) was added. The yellowish green diazonium complex was filtered off after one hour and washed with water and methyl alcohol. Yield : 11.0 g.

The dry mercuric complex was intimately mixed with sodium bromide (25 g) in a mortar and the mixture was transferred to one liter flask connected to an apparatus for steam distillation. After having heated the complex for a few minutes on the steambath it suddenly decomposed filling the apparatus with grey smoke. The bromonaphthalene formed was then distilled over in a current of steam. The distillate was extracted with pentane or petroleum ether. The deuteriated bromonaphthalene recovered after distilling off the solvent was purified by distillation in a Späth bulb under 0.6 mm the yield of pale yellowish oil was 2.8 g (60 %), n_D^{23} 1.6554. For normal 1-bromonaphthalene n_D^{23} is 1.6563.

1,4-Dibromo-5,8-dideuterionaphthalene.

1-Bromo-5,8-dideuterionaphthalene (8.0 g; 0.39 mole) was dissolved in acetic acid (30 ml) and bromine (2.0 ml) was added. Shortly after the solution had been stirred it began to deposit crystals of the dibromo derivative. After standing overnight the crystals were filtered off and washed with methanol. Yield : 4.0 g, m.p. 78-9° sintering at 72°. More crystals separated from the filtrate after a day. A total of 7.7 g (68 % of product) was collected.

1,4,5,8-Tetradeuterionaphthalene.

The dibromonaphthalene prepared above was debrominated byt the method earlier described. The deuteriated naphthalene analyzed 3.2 mol % $C_{10}H_2D_6$, 26.8 mol % $C_{10}H_3D_5$, 49.5 mol % $C_{10}H_4D_4$, 17.2 mol %$C_{10}H_5D_3$ and 3.2 mol % $C_{10}H_6D_2$ by mass spectrometry. Some deuterium had evidently been introduced by exchange in an earlier stage of the synthesis.

Exchange Between 1-Naphthylamine and Alkaline Deuterium Oxide.

In order to determine whether deuterium had been introduced into the molecule after reductive debromination to naphthylamine, normal 1-naphthylamine (4.0 g) was stirred for 24 hrs. under reflux in deuterium oxide (60 ml) with zinc dust (40 g) and calcium oxide (10.0 g). The deuterium oxide was recovered by distillation under reduced pressure on a vacuum line. The naphthylamine in the residue was taken up in ether and recovered by evaporation of the solvent. It was converted into bromonaphthalene by the Sandmeyer reaction described above and a portion of the bromo-derivative was converted into naphthalene which analyzed 1.6 mol % $C_{10}H_6D_2$, 4.1 mol % $C_{10}H_7D$ and 93.5 mol % $C_{10}H_8$. Slight exchange had evidently occurred but not extensive enough to explain the 29 mol % content of D_5 in the tetradeuterionaphthalene.

Exchange in 1-Nitronaphthalene During Reduction to 1-Naphthylamine.

Reduction of nitronaphthalene (5.3 g) to naphthylamine with zinc dust in alkaline deuterium oxide as described above for the dibromonitronaphthalene gave only 0.2 g of 1-naphthylamine but this was still sufficient to prepare naphthalene through the bromo derivative for analysis. The naphthalene contained 10.37 mol % $C_{10}H_7D$ and 89.10 mol % $C_{10}H_8$. Apparently a slight amount of deuterium was introduced before or during reduction of the nitro compound.

The deuterium introduced by exchange is probably in the 2- or the 4-position. It should therefore be possible to remove it by heating the solution of 1-amino-5,8-dideuterio-naphthalene hydrobromide under reflux for a short time before diazotization. This experiment was carried out with 2.6 g of the deuterated naphthylamine. The solution of the hydrobromide was heated under reflux for 24 hours. It was then converted into 1-bromo-5,8-dideuterio-naphthalene and an aliquot of the latter was debrominated to naphthalene which analyzed 2.88 mol % $C_{10}H_5D_3$, 79.62 mol % $C_{10}H_6D_2$, 15.59 mol % $C_{10}H_7D$ and 1.91 mol % $C_{10}H_8$. The deuterium introduced during reductive debromination of the nitro compound had therefore been nearly all removed. At the same time some deuterium in the other ring may also have been removed by the long period of refluxing.

In another experiment the solution of deuteriated 1-naphthylamine hydrobromide was heated on the steambath for three hours before diazotization. The synthesis was then carried through to 1,4,5,8-tetradeuterionaphthalene which analyzed 85.74 mol % $C_{10}H_4D_4$. It contained only 1.9 mol % $C_{10}H_3D_5$ and 10.1 mol % $C_{10}H_5D_3$.

By starting with octadeuterionaphthalene and employing ordinary water in the reductive debromination 2,3,6,7-tetradeuterionaphthalene can be prepared.

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