SYNTHESIS OF METHOXY-HYDROXY-N-METHYL-3·4-DIHYDROISOQUINOLINIUM SALTS.

By Shirō AKABORI.

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6-Methoxy-7-hydroxy-2-methyl-3·4-dihydroisoquinolinium Salts (VIII). 1 gram of 6-methoxy-7-benzyloxy-2-methyl-3·4-dihydroisoquinolinium chloride and 3 c.c. of concentrated hydrochloric acid were slightly warmed on a water-bath. The solution became gradually opaque and finally deposited oily drops of benzyl chloride. When the solution was separated from benzyl chloride and evaporated in a vacuum over potassium hydroxide, 6-methoxy-7-hydroxy-2-methyl-3.4-dihydroisoquinolinium chloride (VIII) remained as a crystalline mass. This was recrystallized from a mixture of methyl alcohol and acetone, from which it was deposited in the form of yellow glistening plates. It melts and decomposes at 187°, after sintering at 155°. Sometimes it crystallized in needles which frothed at 150–153°, after sintering at 140°.

0.1254 gr. subst. became 0.1161 gr. after being dried in a vacuum at 80°, and gave 0.0715 gr. AgCl. 8.74 mg. subst. gave 0.425 c.c. nitrogen (12,° 755.4 mm.) (Found: $H_2O=7.42$, $Cl=14.11$, $N=5.83$. $C_{11}H_{14}O_2NCl.H_2O$ requires $H_2O=7.34$, $Cl=14.44$, $N=5.70$ %).

The iodide is readily obtained by the action of potassium iodide on the aqueous solution of the chloride; decomp. p. 213° (corr. 218°).(1)

0.1127 gr. subst. gave 0.0820 gr. AgI. 5.85 mg. subst. gave 4.28 mg. AgI (methoxyl). (Found: $I=39.33$, $CH_3O-=9.67$. $(CH_3O)-C_{10}H_{11}ONI$ requires $I=39.78$, $CH_3O-=9.72$ %).

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(1) Compare F. L. Pyman, *J. Chem. Soc.*, **97** (1910), 278.

The perchlorate crystallizes in white needles, which melt at 196–197°.

6-Methoxy-7-hydroxy-2-methyl-3·4-dihydroisoquinolinium salts dissolve in dilute alkali to deep yellow solutions, which on a further addition of a concentrated solution of caustic alkali become colourless, and, on dilution with water, regain their colour. The picrate of this base shows peculiar phenomena ; the aqueous solution of the chloride, when mixed with aqueous picric acid first deposits yellow needles, which on being gently heated, or on standing for several hours, are converted into orange-red prisms, and these when left standing for many days, or on being boiled with water,—but in not sufficient quantity to dissolve them all—, once more turn to yellow granular crystals. The orange-red modification contains one molecule of the water of the crystallization ; m. p. 92°.

0.1522 gr. subst. became 0.1465 gr. after being dried in a vacuum at 56°. (Found : $H_2O=4.19$. $C_{17}H_{16}O_9N_4 \cdot H_2O$ requires $H_2O=4.11$ %).

The yellow granular modification is the most stable and anhydrous ; m. p. 159–160°.

0.0787 gr. subst, gave 0.1396 gr. CO_2 and 0.0296 gr. H_2O. (Found : $C=48.38$, $H=4.21$. $C_{17}H_{16}O_9N_4$ requires $C=48.55$, $H=3.84$ %).

6·7-Dihydroxy-2-methyl-3.4-dihydroisoquinolinium Chloride (IX). 2 grams of hydrostinine and 5 grams of phosphorus pentachloride were heated in a sealed tube at 145–150° for five hours. After being cooled to room temperature, the tube was opened and 10 c.c. of alcohol was poured in, when a copious evolution of gas took place and 6·7-dihydroxy-2-methyl-3·4-dihydroisoquinolinium chloride separated as a yellow crystalline powder. This was purified by recrystallization from glacial acetic acid, from which it was deposited in anhydrous prisms, decomp. p. 268° (corr. 276°). All its properties are in agreement with the description given by Pyman.(1)

0.1467 gr. subst. gave 0.0993 gr. AgCl. (Found : $Cl=16.75$. $C_{10}H_{12}O_2NCl$ requires $Cl=16.60$ %).

On addition of sodium carbonate to a concentrated solution of chloride IX, the phenolbetaine of 6·7-dihydroxy-2-methyl-3·4-dihydroisoquinolinium hydroxide separates in deep yellow glistening leaflets. The same compound is also obtained from compound VIII in the same way as was done by Pyman from 6·7-dimethoxy-2-methyl-3·4-dihydroisoquinolinium chloride.

Action of Methyl Iodide on the Phenolbetaine of 6·7-Dihydroxy-2-methyl-3·4-dihydroisoquinolinium-hydroxide. 1 gram of finely powdered anhydrous phenolbetaine and 3 grams of methyl iodide were heated together in a sealed tube for 3 hours at 100°. The product was dissolved in water, treated with a concentrated solution of potassium iodide, when 6-

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(1) Pyman, loc. cit., p. 275.

methoxy-7-hydroxy-2-methyl-3·4-dihydroisoquinolinium iodide separated as yellow crystals (0.6 gram). It was easily purified by recrystallization from alcohol; decomp. p. 213° (corr. 218°).

8.79 mg. subst. gave 6.45 mg. AgI. 6.92 mg. subst. gave 4.95 mg. AgI (methoxyl). (Found: $I=39.66$, $CH_3O-=9.45$. $(CH_3O)-C_{10}H_{11}ONI$ requires $I=39.78$, $CH_3O-=9.72$ %).

The chloride was prepared by digesting the alcoholic solution of the iodide with freshly precipitated silver chloride; decomp. p. 187°. When the picrate (m. p. 159–160°) was mixed with the picrate of synthesized 6-methoxy-7-hydroxy-2-methyl-3·4-dihydroisoquinolinium base, no depression of the melting point occurred.

6-Benzyloxy-7-hydroxy-2-methyl-3·4-dihydroisoquinolinium iodide (XI). 1.6 grams of phenolbetaine and 3 grams of benzyl iodide were heated together for half an hour on a bath of boiling water. The excess of benzyl iodide was removed by trituration with absolute ether. After fractional crystallization from hot water, two compounds were isolated from the product; the one is readily soluble in hot water, while the other is only slightly soluble. The former is soluble in dilute alkali to a deep yellow solution, a behaviour exactly similar to that of 6-methoxy-7-hydroxy-2-methyl-3·4-dihydroisoquinolinium salt. The result of analysis agreed with 6-benzyloxy-7-hydroxy-2-methyl-3·4-dihydroisoquinolinium iodide; m. p. 189–190°. Yield 1.5 grams.

16.15 mg. subst. gave 9.53 mg. AgI. (Found: $I=31.90$. $C_{17}H_{18}O_2NI$ requires $I=32.11$ %).

The latter is insoluble in alkali, and is nothing but 6·7-dibenzyloxy-2-methyl-3·4-dihydroisoquinolinium iodide; m.p. 194–195°. Yield 0.5 gram.

13.85 mg. subst. gave 6.68 mg. AgI. (Found: $I=26.07$. $C_{24}H_{24}O_2NI$ requires $I=26.18$ %).

6-Benzyloxy-7-(6-benzyloxy-7-hydroxy-2-methyl-3·4-dihydroisoquinoliniumoxy)-2-methyl-3·4-dihydroisoquinolinium Iodie (XII). When a concentrated solution of compound XI was treated with potassium carbonate, orange coloured oily drops were deposited, which on standing for many days, were converted into orange prisms. After recrystallization from alcohol it melted at 196–198°. This still contains iodine, and is assumed to have the constitution of XII.

11.26 mg. subst. gave 4,02 mg. AgI. (Found: $I=19.30$. $C_{17}H_{18}O_2N$-O-$C_{17}H_{17}ONI$ requires $I=19.16$ %).

6-Benzyloxy-7-hydroxy-2-methyl-3·4-dihydroisoquinolinium Salts (XIII.) The mixture of 1 gram of the above mentioned compound (XII) and 0.5 gram of methyl iodide was left at room temperature for one day. At the end of the reaction the orange colour changed to a pale yellow. The product was dissolved in water, treated with a concentrated solution of sodium hydroxide, and extracted with ether. The ethereal solution was shaken with water containing a little hydrochloric acid, whereby the aqueous layer exhibited a green fluorescence. On addition of picric acid to this aqueous solution, precipitation of yellow crystalline picrate took place. After repeated crystallization from alcohol this picrate formed yellow leaflets, which melted at 176–177°. On mixing with 6-methoxy-7-benzyloxy-2-methyl-3•4-dihydroisoquinolinium picrate, it melted at 150–160°.

6.11 mg. subst. gave 0.554 c. c. nitrogen (22°, 761 mm.) (Found : N= 10.74. $C_{24}H_{22}O_9N_4$ requires N=10.98 %).

The perchlorate crystallizes in beautiful needles exhibiting a green fluorescence. This is almost insoluble in water but moderately soluble in alcohol ; m. p. 222–225°.

ClO_4 in perchlorates was estimated as nitron perchlorate, according to the method of Fichter and Schmidt.(1) In filtering and weighing the precipitate, Pregl's microfiltering tube was employed with good results. The accuracy of this method was confirmed in the case of several known substances.

12.78 mg. subst. gave 14.01 mg. $C_{20}H_{16}O_4 \cdot HClO_4$. (Found : ClO_4=26.42. $C_{18}H_{20}O_2NClO_4$ requires ClO_4=26.06%);

6-Hydroxy-7-methoxy-2-methyl-3•4-dihydroisoquinolinium Salt (XIV). 15 milligrams of 6-benzyloxy-7-methoxy-2-methyl-3•4-dihydroisoquinolinium perchlorate were treated with 2 c. c. of concentrated hydrochloric acid. After the crystals had all dissolved, the solution was evaporated in a vacuum, and the residue was crystallized from alcohol, from which it separated in the form of slightly brownish coloured, spear-head-like crystals, m. p. 178–179.5°. Yield 10 milligrams. This is easily soluble in alcohol or water to light yellow greenish fluorescent solutions. With ferric chloride the solutions give no colouration.

7.12 mg. subst. gave 10.19 mg. $C_{20}H_{16}N_4 \cdot HClO_4$. (Eound : ClO_4=34.50. $C_{11}H_{14}O_2NClO_4$ requires ClO_4 =34.11%).

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Chemical Institute, Tohoku Imperial University, Sendai.

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(1) *Z. anorg. Chem.*, **98** (1916), 142.