3-HYDROXYPHENYL DERIVATIVES OF PYRAZOLINES AND TETRAHYDROPYRIDAZINES IN A CATALYTIC DECOMPOSITION REACTION

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UDC 547.772.2'852:542.924.2

The isomeric 3-(hydroxyphenyl)-1,4,5,6-tetrahydropyridazines differ from their five-membered-ring analogs, the 3-(hydroxyphenyl)-Δ^2-pyrazolines, in their behavior in catalytic decomposition reactions. The catalytic conversion of 3-(hydroxyphenyl)-1,4,5,6-tetrahydropyridazines takes place at 120-200°C, dehydrogenation being the main reaction. The hydroxyphenylpyrazolines, under the same conditions, undergo decomposition with liberation of nitrogen and formation of the corresponding cyclopropanes.

We have previously shown that 3-aryl-1,4,5,6-tetrahydropyridazines under conditions of catalytic decomposition (heating at 250-300° C in the presence of KOH and platinum) behave in a manner similar to pyrazolines, decomposing with liberation of nitrogen and formation of the corresponding arylcyclobutane [1-5].

It was found, in investigating this reaction, that 3-(p-hydroxyphenyl)-1,4,5,6-tetrahydropyridazine behaves anomalously, undergoing dehydrogenation only, to give the corresponding pyridazine [6].

In order to determine how general this anomalous behavior of 3-(hydroxyphenyl)-1,4,5,6-tetrahydropyridazines was, and whether five-membered cyclic hydrazones , 3-(hydroxyphenyl-Δ^2-pyrazolines), behave in a similar manner, we investigated the catalytic decomposition of 3-(hydroxyphenyl)-1,4,5,6-tetrahydropyridazines (I) and 3-(hydroxyphenyl)pyrazolines (II) containing a hydroxyl group in various positions in the benzene ring (relative to the heterocyclic radical).

The isomeric 3-(hydroxyphenyl)-1,4,5,6-tetrahydropyridazines (I) were synthesized by the method used previously [6].

The meta and para isomers of 3-(hydroxyphenyl)-Δ^2-pyrazoline (II) were synthesized from Mannich bases by the general method used previously for the preparation of pyrazolines with other substituents in the aromatic ring [7].

In order to determine whether the mode of decomposition of the cyclic hydrazones is dependent on the relative position of the hydroxyphenyl group and the multiple bond in the heterocyclic radical, we examined the catalytic decomposition of 3-methyl-5-o-hydroxyphenyl-Δ^2-pyrazoline (III).

A detailed examination of the previously described catalytic decomposition of 3-p-hydroxyphenyl-1,4,5,6-tetrahydropyridazine (I-p) using gas chromatography showed that the decomposition begins at temperatures as low as 120° C, i.e., at a much lower temperature than that previously given [6].

Analysis of the gases evolved during the decomposition revealed the presence of both hydrogen (80%) and nitrogen (20%). The presence of nitrogen in the gases indicated that the catalytic decomposition of I-p was not simple, as we had previously assumed [6]. In addition to dehydrogenation of the tetrahy-

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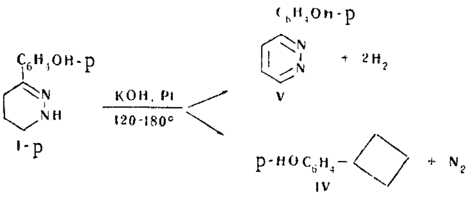
Moscow State University. Translated from Khimiya Geterotsiklicheskikh Soedinenii, Vol. 6, No. 5, pp. 657-659, May, 1970. Original article submitted February 23, 1968.

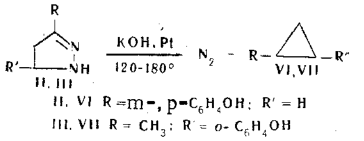
dropyridazine, partial (20%) decomposition occurred with the formation of the corresponding cyclobutane (IV).



The catalytic decomposition of 3-(hydroxyphenyl)-1,4,5,6-tetrahydropyridazines with the hydroxyl groups in the ortho (I-o) and meta (I-m) positions led to similar results. The gaseous reaction products contained nitrogen (10%) and hydrogen (90%).

It is apparent that the decomposition route does not depend on the position of the hydroxyl group in the aromatic ring.

Experiments on the catalytic decomposition of the isomeric 3-(hydroxyphenyl)-Δ^2-pyrazolines (II) and of 3-methyl-5-o-hydroxyphenyl-Δ^2-pyrazoline (III) showed that in these cases no dehydrogenation occurred. Only the hydroxyphenylcyclopropanes (VI and VII) were formed, with the liberation of nitrogen.



The reaction, therefore, proceeds by the usual route for the synthesis of cyclopropanes, and the position of the aryl radical in the pyrazoline ring does not affect its course.

EXPERIMENTAL

Synthesis of Hydroxyphenyltetrahydropyridazines

o-, m-, and p-Nitrophenyl-1,3-butadienes were obtained as in [9], mp's (from octane), 68, 53, and 79° C.

1,2-Bisethoxycarbonyl-3-p-, -m-, and -o-nitrophenyl-1,2,3,6-tetrahydropyridazines (adducts from the diene synthesis of nitrophenylbutadienes with azodicarboxylic esters): yields, respectively, 95, 30, and 90%; mp's (from hexane) 85 [5], 86, and 71-74° C. m-Isomer. Found, %: C 55.12, 55.02; H 5.74, 5.54; N 11.91, 11.84. o-Isomer. Found, %: C 55.37; 55.21; H 5.52; 5.53; N 12.01; 11.93. Calculated for $C_{16}H_{19}N_3O_6$, %: C 55.01; H 5.48; N 12.03.

1,2-Bisethoxycarbonyl-3-p-,-m-, and -o-aminophenyl-1,2,3,6-tetrahydropyridazines were obtained by the reduction of the nitro compounds [5], the yields being, respectively, 60, 73, and 63%; mp's (from ligroin) 85-86 [6], 53-54, and 73.5-74.5° C. m-Isomer. Found, %: C 60.10; 60.05; H 6.64; 6.73. o-Isomer. Found, %: C 60.50; 59.97; H 6.60; 6.65. Calculated for $C_{16}H_{21}N_3O_4$, %: C 60.17; H 6.63.

1,2-Bisethoxycarbonyl-3-p-, -m-,and -o-Hydroxyphenyl-1,2,3,6-tetrahydropyridazines. A solution of 9 g (0.027 mole) of the amino compound, 30 ml of conc H_2SO_4, and 45 ml of water was cooled, and 2.1 g (0.03 mole) of sodium nitrite in 6 ml of water added at -5 to -2° C. The mixture was heated on a water bath until evolution of nitrogen ceased, then cooled, and the solid mass which was formed was dissolved in caustic alkali, neutralized with acetic acid, and the precipitate recrystallized from a mixture of ether and heptane (1: 3). p-Isomer: yield 50%; mp 109-110° C. Found, %: C 60.10; 59.67; H 6.27; 6.64. m-Isomer: yield 50%, mp 93-94° C. Found, %: C 60.46; 60.32; H 6.75; 6.61. o-Isomer: yield 47%, mp 55-56° C. Found, %: C 60.39; 60.48; H 6.53; 6.60. Calculated for $C_{16}H_{20}N_2O_5$, %: C 60.01; H 6.24.

3-p-, -m-, and -o-Hydroxyphenyl-1,4,5,6-tetrahydropyridazines (I) obtained by hydrolysis of the corresponding 1,2-bisethoxycarbonyl-3-(hydroxyphenyl)-1,2,3,6-tetrahydropyridazines by heating with alcoholic KOH for 7-8 hr on a water bath. The potassium carbonate which separated was filtered off, most of the alcohol was distilled off, and the residue was treated with HCl. The mixture was then neutralized with aqueous ammonia, and the precipitate isolated. The yields were, respectively, 52, 54, and 50%; mp's (from a 1 : 3 mixture of ether and hexane) 225° C [6], 136-137° C, and 178-180° C.

m-Isomer. Found, %: C 68.51; 68.64; H 6.64; 6.65. o-Isomer. Found, %: C 68.55; 68.62; H 6.52; 6.37. Calculated for $C_{10}H_{12}N_2O$, %: C 68.16; H 6.86.

Synthesis of 3-(Hydroxyphenyl)-Δ^2-pyrazolines

p- and m-Hydroxy-β-dimethylaminopropiophenone hydrochlorides were obtained from p-hydroxyacetophenone [10] and m-hydroxyacetophenone [11, 12] by the Mannich reaction [7]. p-Isomer: yield 62%; mp 198° C. Found, %: C 57.43; 57.37; H 7.03; 7.21. m-Isomer: yield 50%, mp 170-172° C. Found, %: C 57.77; 57.42; H 7.36; 7.03. Calculated for $C_{11}H_{16}NO_2Cl$, %: C 57.54; H 6.96.

3-(Hydroxyphenyl)-Δ^2-pyrazolines (II) were obtained from p- and m-hydroxy-β-dimethylaminopropiohenones by the method described in [7]. p-Isomer: yield 58%; mp 154-155° C. Found, %: C 67.04, 67.14; H 6.33, 6.24. m-Isomer: yield 30%; mp 146-148° C. Found, %: C 66.80, 66.37; H 6.34, 6.46. Calculated for $C_9H_{10}N_2O$, %: C 66.67; H 6.16.

3-Methyl-5-o-hydroxyphenyl-Δ^2-pyrazoline (III) was obtained from salicylideneacetone [13,14], yield 45%, mp 104° C [8].

Catalytic Decomposition of the Isomeric 3-(Hydroxyphenyl)-1,4,5,6-tetrahydropyridazines and Hydroxyphenylpyrazolines

The decomposition of I-p was carried out by the previously described method [6], but at 120-180° C.

The gas which was liberated consisted of nitrogen (20%) and hydrogen (80%). The catalysate was dissolved in 2-N alkali, acidified with HCl, and neutralized with ammonia. The 3-p-hydroxyphenylpyridazine (V) which separated was filtered off and sublimed in vacuo to give 55%, mp 226° C [15].

The filtrate was extracted with ether, the ether extract was dried over $MgSO_4$, and the ether was removed. The residue was chromatographed on an alumina column using an alcohol–hexane mixture (1 : 3), giving p-hydroxyphenylcyclobutane (IV) in 10% yield, mp 86° C [16].

Decomposition of I-m and I-o by the same method gave a gas consisting of hydrogen (90%) and nitrogen (10 %). The catalysate from I-m gave 3-m-hydroxyphenylpyridazine (V-m) in 60% yield, mp 148-149° C. Found, %: C 68.28, 68.04; H 6.48, 6.56. Calculated for $C_{10}H_{12}N_2O$, %: C 68.22; H 6.82.

Decomposition of pyrazolines II (para and meta) gave only nitrogen. The catalysate was dissolved in alcohol, neutralized with HCl and extracted with ether. The ether extract was dried over $MgSO_4$, the ether was distilled off, and the residue was distilled in vacuo to give p-hydroxyphenylcyclopropane (IV-p) in 70% yield, bp 112° C (8 mm), mp 66° C [17]. m-Hydroxyphenylcyclopropane (VI-m), yield 55%, mp 57-58° C. Found, %: C 80.48, 80.52; H 7.40, 7.37. Calculated for $C_9H_{10}O$, %: C 80.59; H 7.46. Benzoyl derivative mp 115-117° C. Found, %: C 80.33, 80.49; H 6.25, 6.37. Calculated for $C_{16}H_{15}O_2$, %: C 80.75; H 5.90.

1-Methyl-2-o-hydroxyphenylcyclopropane (VII) was obtained by decomposition of III, in 43% yield, bp 98-99° C (13 mm), n_D^{20} 1.5315, d_4^{20} 1.0471. Found, %: C 81.12, 80.98; H 8.10, 8.13. MR_D 43.84. Calculated for $C_{10}H_{12}OF_3$, %: C 81.05; H 8.16. MR_D 44.10.

Analysis of the gaseous reaction products was carried out on a chromatograph (designed in these laboratories) with a thermal conductivity detector on two glass chromatographic columns. One of them used silica gel as the stationary phase (length of column 0.9 m, diameter 5 mm, temp 40° C), and the other used molecular sieve 5 A (column length 0.4 m, diameter 5 mm, room temperature). The carrier gas was helium, velocity 30 ml/min. The zeolite column was used to determine nitrogen, oxygen, hydrogen, and methane, and the silica gel column to determine saturated and unsaturated hydrocarbons. The amount of the separated components was determined from the peak areas by the absolute calibration method.

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