SOME DERIVATIVES OF HYDROXYPHENYLGLYCINE. II.

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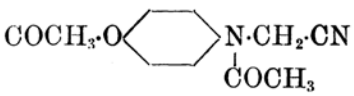
Acetyl or Benzoyl Derivatives of Hydroxyphenylglycine Nitriles.

1. Diacetyl-p-hydroxyanilidoacetonitrile.



7.4 Gr. of the nitrile were treated with 11.5 c.c. of acetic anhydride, in an alkaline solution, 8 gr. of diacetyl-p-hydroxyanilidoacetonitrile was obtained, which was recrystallised several times from 50% alcohol, in small white platy crystals melting at 94–95° (uncorr.). Galatis(2) described 75° for its

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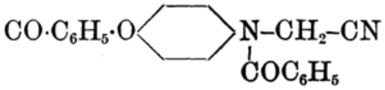
(2) See this journal 1 (1926), 202.

melting point. The analytical results and chemical properties of this substance agree with those described by Galatis.

0.1763 gr. subst. gave 0.4028 gr. CO_2 and 0.0807 gr. H_2O. 0.1888 gr. subst. gave 18.8 c.c. N_2 (9°, 765 mm.). (Found: C=62.31; H=5.09; N=12.47. $C_{12}H_{12}O_3N_2$ requires C=62.07; H=5.17; N=12.07%).

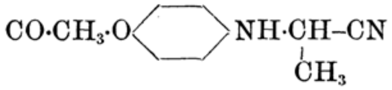
2. Dibenzoyl-p-hydroxyanilidoacetonitrile.



It was prepared by the action of benzoyl chloride on p-hydroxyanilidoacetonitrile in alkaline solution, and found to melt at 129–130° (uncorr.).

0.1092 gr. subst. gave 0.2980 gr. CO_2 and 0.0462 gr. H_2O. 0.0921 gr. subst. gave 6.3 c.c. N_2 (10.5°, 749.4 mm.). (Found: C=74.40; H=4.70; N=8.16. $C_{11}H_{12}O_3N_2$ requires C=74.16; H=4.49; N=7.87%).

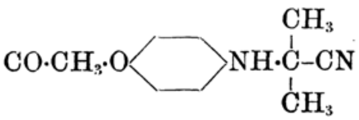
3. Acetyl-p-hydroxyanilidomethylacetonitrile.



The acetyl compound was obtained by acetylation of the nitrile by means of acetic anhydride and sodium acetate at room temperature. The pure substance was obtained as small platy crystals melting at 129–131° (uncorr.).

0.1136 gr. subst. gave 0.2683 gr. CO_2 and 0.0617 gr. H_2O. 0.1031 gr. subst. gave 12.2 c.c. N_2 (13°, 757.5 mm.). (Found: C=64.41; H=6.31; N=14.14. $C_{11}H_{12}O_2N_2$ requires C=64.71; H=5.88; N=13.73%).

4. Acetyl-p-hydroxyanilidodimethylacetonitrile.



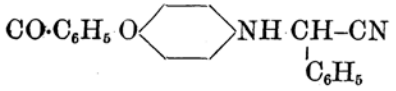
The nitrile was acetylated with acetic anhydride in alkaline solution and the crude product was purified from alcohol solution. The pure substance is beautiful long needles and melts at 77–78° (uncorr.).

0.1195 gr. subst. gave 0.2875 gr. CO_2 and 0.0712 gr. H_2O. 0.1059 gr. subst. gave 11.3 c.c. N_2 (9.5°, 764 mm.). (Found: C=65.61; H=6.67; N=13.02. $C_{12}H_{14}O_2N_2$ requires C=66.05; H=6.42; N=12.85%.)

The nitrile, however, on benzoylation by means of Schotten-Bauman's method instead of the expected benzoyl derivative, dibenzoyl-p-aminophenol, melting at 233–234° (uncorr.) was the result.

0.1121 gr. subst. gave 4.25 c.c. N_2 (11.5°, 761.5 mm.). (Found: N=4.58. $C_{20}H_{15}O_3N$ requires N=4.42%).

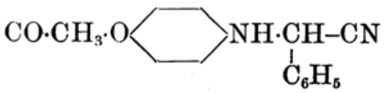
5. Benzoyl-p-hydroxyanilidophenylacetonitrile.



The nitrile was benzoylated by means of Schotten-Bauman's method and the benzoyl derivative which was recrystallised from alcohol, began to sinter at 160° and melted clear at about 200°.

0.1209 gr. subst. gave 0.3389 gr. CO_2 and 0.0537 gr. H_2O. 0.1336 gr. subst. gave 8.1 c.c. N_2 (13.5°, 762.6 mm.). (Found: C=76.63; H=4.97; N=8.95. $C_{21}H_{16}O_2N_2$ requires C=76.83; H=4.89; N=8.54%).

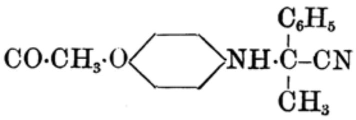
6. Acetyl-p-hydroxyanilidophenylacetonitrile.



The nitrile was acetylated by means of acetic anhydride, in alkaline solution, and the pure acetyl derivative melting at 119–120° was obtained as small hexagonal crystals.

0.1262 gr. subst. gave 0.3330 gr. CO_2 and 0.0601 gr. H_2O. 0.1067 gr. subst. gave 9.8 c.c. N_2 (9°, 758 mm.). (Found: C=71.97; H=5.29; N=11.14. $C_{16}H_{14}O_2N_2$ requires C=72.18; H=5.26; N=10.53%).

7. Acetyl-p-hydroxyanilidophenylmethylacetonitrile.



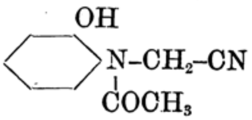
The acetyl compound was obtained by acetylation of the nitrile either by acetic anhydride in alkaline solution or by acetic anhydride and sodium acetate. It was purified by dilute alcohol and the pure substance melts at 142–143° (uncorr.).

0.1137 gr. subst. gave 0.3042 gr. CO_2 and 0.0587 gr. H_2O. 0.1059 gr. subst. gave 9.0 c.c. N_2 (8°, 759.4 mm.). (Found: C=72.97; H=5.78; N=10.36. $C_{17}H_{16}O_2N_2$ requires C=72.86; H=5.71; N=10.00%).

By the action of benzoyl chloride and alkali on the nitrile, dibenzoyl-p-aminophenol melting at 233–234° (uncorr.) was obtained.

0.1025 gr. subst. gave 0.2851 gr. CO_2 and 0.0452 gr. H_2O. (Found: C=75,86; H=4.90. $C_{20}H_{15}O_3N$ requires C=75.71; H=4.73%).

8. Acetyl-o-hydroxyanilidoacetonitrile.



When the crude nitrile which was extracted with ether from the reaction mixture, above mentioned,(1) was acetylated immediately by acetic anhydride, in alkaline solution, monoacetyl derivative was obtained. The pure sub-

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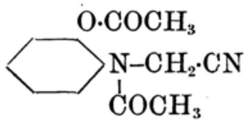
(1) This journal 1 (1926), 206.

stance which was purified from alcohol solution is fine colorless cubic crystals melting at 167–168° (uncorr.). It shows a pale reddish violet coloration with ferric chloride, yellowish red coloration with conc. nitric acid and red coloration with Millon's reagent.

0.1249 gr. subst. gave 0.2893 gr. CO_2 and 0.0606 gr. H_2O. 0.1064 gr. subst. gave 13.25 c.c. N_2 (10°, 757 mm.). (Found: C=63.17; H=5.39; N=15.03. $C_{10}H_{10}N_2O_2$ requires C=63.30; H=5.26; N=14.74%).

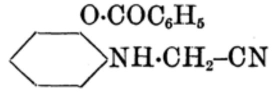
9. Diacetyl-o-hydroxyanilidoacetonitrile.



When the pure nitrile was acetylated with acetic anhydride and sodium acetate at room temperature, the diacetyl cempound was obtained. It consists of colorless needles which melt at 105–106° (uncorr.).

0.1203 gr. subst. gave 0.2715 gr. CO_2 and 0.0603 gr. H_2O. 0.1055 gr. subst. gave 10.8 c.c. N_2 (9.5°, 753.4 mm.). (Found; C=61.55; H=5.57; N=12.37. $C_{12}H_{12}O_3N_2$ raquires C=62.07; H=5.17; N=12.07%).

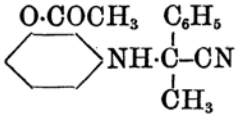
10. Benzoyl-o-hydroxyanilidoacetonitrile.



The nitrile was benzoylated by Schotten-Bauman's method. The benzoyl-o-hydroxyanilidoacetonitrile was obtained as fine white crystalline powder melting at 120–121° (uncorr.).

0.1121 gr. subst. gave 0.2942 gr. CO_2 and 0.0504 gr. H_2O. 0.1337 gr. subst. gave 12.7 c.c. N_2 (13°, 755.8 mm.). (Found: C=71.56; H=5.00; N=11.33. $C_{15}H_{12}O_2N_2$ requires C=71.43; H=4.76; N=11.11%).

11. Acetyl-m-hydroxyanilidophenylmethylacetonitrile.

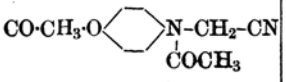
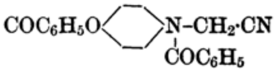
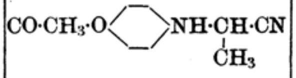
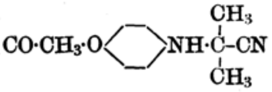
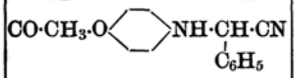
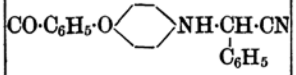
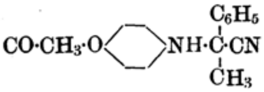
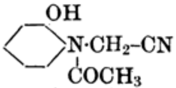
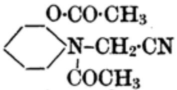
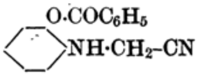
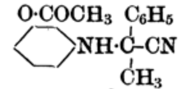


When the nitrile was acetylated by acetic anhydride and sodium acetate, the acetyl compound was obtained which was purified by dilute alcohol. It melts at 123–124° (uncorr.).

0.1199 gr. subst. gave 0.3182 gr. CO_2 and 0.0630 gr. H_2O. 0.1059 gr. subst. gave 8.9 c.c. N_2 (11°, 766.5 mm.). (Found: C=72.38; H=5.88; N=10.42. $C_{17}H_{16}O_2N_2$ requires C=72.86; H=5.71; N=10.00%).

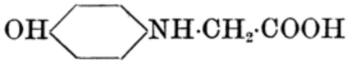
The solubilities of the acetyl or benzoyl derivatives of hydroxyphenylglycinenitriles in organic solvents and also in acids or alkalies are mentioned in Table 1.

TABLE 1.

Substance.	Acetone, alcohol, acetic ester, or glac. acetic acid.	Benzene, ether or chloroform.	Ligroin or water.	Caustic alkalies or mineral acids.
 m.p. 94–95°	soluble.	soluble. spar. sol. in ether.	sol. in hot water.	insoluble.
 m.p. 129–130°	soluble.	soluble.	insoluble.	insoluble.
 m p. 129–131°	soluble.	soluble.	spar. soluble.	sol. in acid. insol. in alkali.
 m.p. 77–78°	soluble.	soluble.	insoluble.	sol. in acid. insol. in alkali.
 m.p. 119–120°	soluble.	soluble.	insoluble.	insoluble.
 m.p. 200°	soluble.	soluble. spar. sol. in ether.	insoluble.	insoluble.
 m.p. 142–143°	soluble.	soluble.	insoluble.	insoluble.
 m.p. 167–168°	soluble.	spar. sol.	spar. sol. in water.	soluble in alkali. insol. in acid.
 m.p. 105–106°	soluble.	soluble.	spar. sol.	insoluble.
 m.p. 120–121°	soluble.	spar. sol. sol. in chloroform.	insol. in water.	sol.in conc. HCl. insol. in alkali.
 m.p. 123–124°	soluble.	soluble.	insoluble.	insoluble.

Derivatives of Hydrophenylglycine.

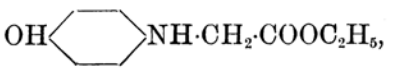
1. p-Hydroxyanilidoacetic Acid.
(p-Hydroxyphenylglycine.)



This substance was obtained from p-hydroxyanilidoacetonitrile by saponifying with dilute caustic soda in 84.2% yield of the theory.

0.1822 gr. subst. gave 0.3823 gr. CO_2 and 0.0885 gr. H_2O. 0.1537 gr. subst. gave 10.7 c.c. N_2 (10°, 764 mm.). (Found: C=57.28; H=5.40; N=8.48. $C_8H_9O_3N$ requires C=57.49; H=5.39; N=8.38%).

2. Ethyl and Methyl Ester of p-Hydroxyanilidoacetic Acid.

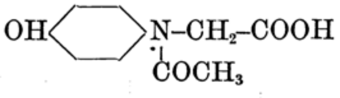


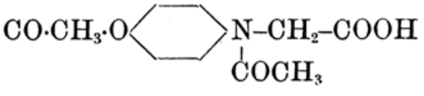
p-Hydroxyanilidoacetic acid yield the ethyl and methyl ester when dry hydrogen chloride gas was passed into the corresponding alcoholic solution of the acid, and then neutralising hydrochloride of the ester with sodium carbonate solution. The ethyl ester, thus obtained, was white leaflets, melting at 78–79° (uncorr.) and methyl ester at 97–98° (uncorr.).

0.1663 gr. of the ethyl ester gave 0.3748 gr. CO_2 and 0.0989 gr. H_2O. 0.1932 gr. of the subst. gave 12.25 c.c. N_2 (19°, 751.4 mm.). (Found: C=61.47; H=6.61; N=7.36. $C_{10}H_{13}O_3N$ requires C=61.54; H=6.67: N=7.18%).

0.1695 gr. of the methyl ester gave 0.3696 gr. CO_2 and 0.0910 gr. H_2O. 0.1562 gr. of the subst. gave 10.6 c.c. N_2 (20°, 753 mm.). (Found: C=59.47; H=5.97; N=7.87. $C_9H_{11}O_3N$ requires C=59.67; H=6.08; N=7.74%).

3. Mono-and Di-acetyl-p-hydroxyanilidoacetic Acid.

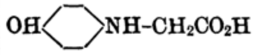
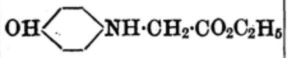
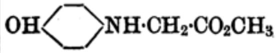
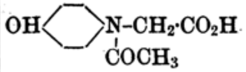
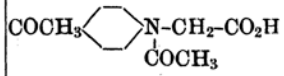
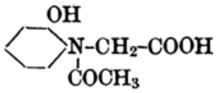




When p-hydroxyanilidoacetic acid is treated with acetic anhydride in alkaline solution, it yields diacetyl-p-hydroxyanilidoacetic acid which melts at 174–175° (uncorr.). When, however, ethereal solution of acetic anhydride is used as an acetylation agent monoacetyl derivative is formed, which crystallizes from hot aqueous solution in white prisms, melting at 203–204° (uncorr.).

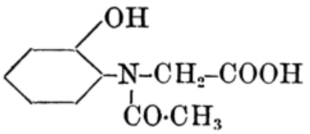
0.1566 gr. of the diacetyl subst. gave 0.3263 gr. CO_2 and 0.0736 gr. H_2O. 0.1728 gr. of the subst. gave 8.6 c.c. N_2 (18°, 753.5 mm.). (Found: C=56.81; H=5.22; N=5.82. $C_{12}H_{13}O_5N$ requires C=57.37; H=5.18; N=5.58%).

TABLE 2.

Substance.	Solubility.			Color Reaction.		
	Acetone, alcohol, ether, chloroform, acetic ester, benzene, or glac. acetic acid.	Water.	Caustic alkalies or mineral acids.	Ferric chloride.	Silver nitrate.	Am. silver nitrate.
	sparingly soluble.	spar. sol.	soluble.	violet-red.	greyish black ppt.	pale brownish yellow → blue colloidal.
 m.p. 78–79°  m.p. 97–98°	soluble.	sol. in hot. spar. sol. in cold.	soluble.	reddish violet.	pale reddish violet producing white ppt.	yellowish green colloidal → dirty green → greyish black ppt.
 m.p. 203–204°	sparingly soluble. sol. in alcohol or acetone.	sol. in hot. spar. sol. in cold.	soluble in alkali.	pale dirty violet.		
 m.p. 174–175°	soluble. spar. sol. in ether or benzene.	sol. in hot. spar. sol. in cold.	soluble in alkali.			
 m.p. 201–202°	soluble. spar. sol. in ether, chloroform or benzene.	spar. sol.	soluble in alkali. insoluble in acid.	pale reddish violet.		

0.1844 gr. of the monoacetyl subst. gave 0.3868 gr. CO_2 and 0.0857 gr. H_2O. 0.1721 gr. of the subst. gave 10.1 c.c. N_2 (18.5°, 753.9 mm.). (Found ; C=57.21; H=5.16 : N=6.85. $C_{10}H_{11}O_4N$ requires C=57.41 ; H=5.26 ; N=6.70%).

4. Acetyl-o-hydroxyanilidoacetic Acid (Acetyl-o-hydroxyphenylglycine).



Acetyl-o-hydroxyanilidoacetonitrile was boiled with dilute caustic soda until the evolution of ammonia had ceased, and then the solution was acidified with hydrochloric acid, whereby slightly brown-coloured sandy crystals were deposited.

Acetyl-o-hydroxyphenylglycine recrystallised from boiling water is colourless monoclinic crystals and melt at 201–202° (uncorr.) with slight decomposition.

0.1112 gr. subst. gave 0.2324 gr. CO_2 and 0.0537 gr. H_2O. 0.1267 gr. subst. gave 7.5 c.c. N_2 (13°, 755.5 mm.). (Found : C=57.00 ; H=5.40; N=7.08. $C_{10}H_{11}O_4N$ requires C=57.41 ; H=5.36 ; N=6.70%).

The solubility and the colour reactions of the derivatives of hydroxyphenylglycine are mentioned in Table 2.

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Daini, Osaka.