449. *Hydroxamic Acids. Part II. The Synthesis and Structure of Cyclic Hydroxamic Acids from Pyridine and Quinoline.*

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By the general methods devloped in Part I (*J.*, 1948, 1864), several pyridine and quinoline cyclic hydroxamic acids have been prepared. A study of the ultra-violet absorption spectra of the known pyridine cyclic hydroxamic acids and related derivatives leads to the conclusion that in ethanolic solution the acids are 1-hydroxy-2-keto-1 : 2-dihydropyridines and not 2-hydroxypyridine 1-oxides.

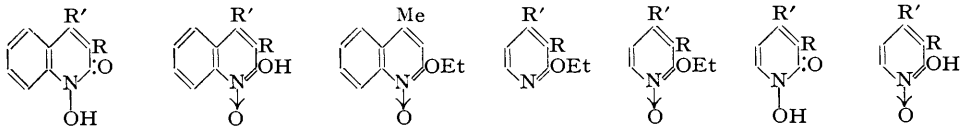
In Part I of this series Newbold and Spring (*J.*, 1948, 1864) described the preparation of 1-hydroxy-2-keto-1 : 2-dihydropyridine (IV*a*; R = R′ = H) [2-hydroxypyridine 1-oxide (IV*b*; R = R′ = H)] and of 1-hydroxy-2-keto-1 : 2-dihydroquinoline (I*a*; R = R′ = H) [2-hydroxyquinoline 1-oxide (I*b*; R = R′ = H)] by oxidation of 2-ethoxypyridine and of 2-ethoxyquinoline to yield the respective *N*-oxides, followed by acid hydrolysis of the oxides. 1-Hydroxy-2-keto-1 : 2-dihydroquinoline possesses a pronounced *in vitro* inhibitory effect on the growth of *Strep. hæmolyticus*, *Staph. aureus*, and *B. coli*. Subsequent curative tests using mice infected with a mouse-virulent hæmolytic streptococcus, however, showed that death was not delayed by administration of 5 mg. of this compound by oral, intraperitoneal, or subcutaneous routes. The compound was too toxic to allow of the administration of larger doses. The present paper describes the synthesis of a number of related cyclic hydroxamic acids which was undertaken with a view to their antibacterial evaluation.

2-*Bromo*-3-*methylpyridine* and 2-*bromo*-4-*methylpyridine* were converted into 2-*ethoxy*-3-*methyl*- (II; R = Me, R′ = H) and 2-*ethoxy*-4-*methyl*-*pyridine* (II; R = H, R′ = Me), respectively. Treatment of 2-ethoxy-3-methylpyridine with hydrogen peroxide, followed by hydrolysis of the product with dilute mineral acid, gave the hydroxamic acid, 1-*hydroxy*-2-*keto*-3-*methyl*-1 : 2-*dihydropyridine* (IV*a*; R = Me, R′ = H), which gives a crystalline copper salt and a positive reaction with ferric chloride. In the case of 2-ethoxy-4-methylpyridine, oxidation with peracetic acid gives 2-*ethoxy*-4-*methylpyridine* 1-*oxide* (III; R = H, R′ = Me) which immediately liberates iodine from an acidified potassium iodide solution and was characterised by a *picrate*. Hydrolysis of the oxide with mineral acid yields 1-*hydroxy*-2-*keto*-4-*methyl*-1 : 2-*dihydropyridine* (IV*a*; R = H, R′ = Me) which shows the characteristic properties of a cyclic hydroxamic acid. Although 2-*ethoxy*-6-*methylpyridine* was successfully oxidised to 2-*ethoxy*-6-*methylpyridine* 1-*oxide*, characterised as its *picrate*, we were unable to isolate the corresponding cyclic hydroxamic acid from the solution obtained after treatment of the oxide with mineral acid although this gave a deep red colour with ferric chloride.

1-*Hydroxy*-2-*keto*-4-*methyl*-1 : 2-*dihydroquinoline* (I*a*; R = H, R′ = Me) has been obtained from 4-methylcarbostyril which was converted into 2-ethoxy-4-methylquinoline following the method of Knorr (*Annalen*, 1886, **236**, 102). Oxidation of the last compound with peracetic acid yielded 2-*ethoxy*-4-*methylquinoline* 1-*oxide*, hydrolysis of which with mineral acid gave the required hydroxamic acid. A different route was employed to synthesise 1-*hydroxy*-2-*keto*-3-*methyl*-1 : 2-*dihydroquinoline* (I*a*; R = Me, R′ = H). In this, *ethyl* β-o-*nitrophenyl*-α-*methyl*l *acrylate* was reduced with ammonium sulphide to give a mixture from which 3-methylcarbostyri- and the required hydroxamic acid were isolated.

In Part I, the simple hydroxamic acid derived from quinoline was described as 2-hydroxyquinoline 1-oxide (I*b*; R = R′ = H) and not as 1-hydroxy-2-keto-1 : 2-dihydroquinoline (I*a*; R = R′ = H). Similarly the cyclic hydroxamic acid derived from pyridine was described as 2-hydroxypyridine 1-oxide (IV*b*; R = R′ = H) and not as 1-hydroxy-2-keto-1 : 2-dihydropyridine (IV*a*; R = R′ = H); comment was made upon the arbitrary nature of this choice. It became of some interest to attempt to differentiate between these two structure-types and, with this in view, a study has been made of the ultra-violet absorption spectra of pyridine cyclic hydroxamic acids and related compounds.

The ultra-violet absorption spectra of various pyridine derivatives are shown in Table I. The unsubstituted pyridine cyclic hydroxamic acid and the corresponding 3- and 4-methyl homologues each show absorption maxima of fairly high intensity at approximately 2300 and 3050 A. This type of absorption spectrum corresponds very closely to that of 2-keto-1 : 2-dihydropyridine and that of 1-methyl-2-keto-1 : 2-dihydropyridine, and is markedly different from that of 2-methoxypyridine and of 2-ethoxy-6-methylpyridine. These results indicate



(I*a*.) (I*b*.) (V.) (II.) (III.) (IV*a*.) (IV*b*.)

that in ethanolic solution the pyridine cyclic hydroxamic acids examined possess the 1-hydroxy-2-keto-1 : 2-dihydro-structure and not the 2-hydroxy 1-oxide structure.

TABLE I.

Ultra-violet Absorption Spectra in Ethanol.

	Max. 1.		Max. 2.	
	A.	ε.	A.	ε.
1-Hydroxy-2-keto-1 : 2-dihydropyridine	2280	6500	3050	4000
1-Hydroxy-2-keto-3-methyl-1 : 2-dihydropyridine	2300	2500	3050	5000
1-Hydroxy-2-keto-4-methyl-1 : 2-dihydropyridine	2300	5000	3030	6700
2-Keto-1 : 2-dihydropyridine [1]	2290	7000	3000	5000
1-Methyl-2-keto-1 : 2-dihydropyridine	2300	6000	3050	5000
2-Methoxypyridine	2700	3500	—	—
2-Ethoxy-6-methylpyridine	2730	6400	—	—

[1] Cf. Specker and Gawrosch, *Ber.*, 1942, **75**, 1338.

The results of antibacterial tests on some of the cyclic hydroxamic acids described in this paper, together with those on some simpler hydroxamic acids, are shown in Table II.

TABLE II.

Minimal Inhibitory Concentration in Mg. per 100 *c.c. of Culture Medium.*

	Strep. haem.		*Staph. aureus.*		*B. coli.*	
	Broth.	Blood.	Broth.	Synthetic.	Broth.	Synthetic.
1-Hydroxy-2-keto-3-methyl-1 : 2-dihydropyridine	0·5	5	2	1	1	1
1-Hydroxy-2-keto-4-methyl-1 : 2-dihydropyridine	2	20	20	10	20	2
1-Hydroxy-2-keto-4-methyl-1 : 2-dihydroquinoline	0·5	>5	5	5	2	1
Glycine hydroxamic acid	20	—	50	—	200	—
DL-Alanine hydroxamic acid	20	—	50	—	200	—
DL-Valine hydroxamic acid	>10	—	>10	—	>10	>10
DL-*iso*Leucine hydroxamic acid	5	—	>50	—	50	—
DL-Phenylalanine hydroxamic acid	20	>20	>20	—	>20	>20
Benzhydroxamic acid	20	—	200	—	200	—
p-Aminobenzhydroxamic acid	10	—	20	—	20	—

In publications which appeared after the manuscript of this paper was completed, Shaw (*J. Amer. Chem. Soc.*, 1949, **71**, 67) and Lott and Shaw (*ibid.*, p. 70) have described the synthesis of 1-hydroxy-2-keto-1 : 2-dihydropyridine and of 1-hydroxy-2-keto-4-methyl-1 : 2-dihydropyridine by essentially the method described by Newbold and Spring (*loc. cit.*); in addition they have obtained the first-named compound in poor yield by the oxidation of 2-pyridone with perbenzoic acid. These authors also describe the ultra-violet spectrum of the unsubstituted pyridine hydroxamic acid and they conclude that it is 1-hydroxy-2-keto-1 : 2-dihydropyridine and not 2-hydroxypyridine-1-oxide.

EXPERIMENTAL.

2-Bromo-3-methylpyridine.—2-Amino-3-methylpyridine (18 g.) was added at 15° to hydrobromic acid (48%; 82·5 c.c.). The solution was cooled to −10° and treated with bromine (25·1 c.c.) added dropwise during 1 hour. A solution of sodium nitrite (28·8 g.) in water (42 c.c.) was added during 2 hours, and the mixture stirred for a further hour. The mixture was treated with a solution of sodium

hydroxide (63 g.) in water (65 c.c.), the temperature being kept below 20°. The solution was extracted with ether, and the extract dried (KOH). After removal of the ether the product was distilled; *2-bromo-3-methylpyridine* was obtained as a colourless oil (22·3 g.), b. p. 81—83·5°/10 mm., n_D^{15} 1·5472 (Found: C, 41·8; H, 3·4. C_6H_6NBr requires C, 41·9; H, 3·5%).

2-Bromo-4-methylpyridine was obtained by the same method starting from 2-amino-4-methylpyridine (yield, 80%). It is a colourless, highly refracting oil, b. p. 87°/10 mm., n_D^{15} 1·5625 (Found: C, 42·0; H, 3·3. C_6H_6NBr requires C, 41·9; H, 3·5%). The *picrate* separates as prisms, m. p. 108°, from ethanol (Found: N, 13·7. $C_{12}H_9O_7N_4Br$ requires N, 14·0%).

2-Ethoxy-3-methylpyridine.—2-Bromo-3-methylpyridine (20·4 g.) was added to a solution of sodium ethoxide in ethanol (from 7 g. of sodium and 140 c.c. of dry ethanol), and the solution heated under reflux for 14 hours. The mixture was concentrated, diluted with water, and extracted with ether. The extract was dried (Na_2SO_4) and distilled. Two main fractions, b. p. 58—63°/9 mm. (9·5 g.) and 70—80°/9 mm. (4·3 g.), were collected. The higher-boiling fraction was 2-bromo-3-methylpyridine. Redistillation of the lower-boiling fraction gave *2-ethoxy-3-methylpyridine* as a colourless oil, b. p. 59—61°/9 mm., n_D^{15} 1·4981 (Found: C, 69·7; H, 7·6. $C_8H_{11}ON$ requires C, 70·1; H, 8·0%). With allowance for recovered starting material, the yield was 59%. The *picrate* separates from ethanol as needles, m. p. 117° (Found: C, 46·5; H, 4·3. $C_{14}H_{14}O_8N_4$ requires C, 45·9; H, 3·8%).

2-Ethoxy-4-methylpyridine was obtained from 2-bromo-4-methylpyridine by the same method, as a colourless oil, b. p. 70°/10 mm., n_D^{16} 1·5005 (yield, with allowance for recovered starting material, 75%) (Found: C, 69·7; H, 7·9. $C_8H_{11}ON$ requires C, 70·1; H, 8·0%). The *picrate* separates from ethanol as leaflets, m. p. 145° (Found: N, 15·1. $C_{14}H_{14}O_8N_4$ requires N, 15·3%).

2-Ethoxy-6-methylpyridine was obtained from 2-bromo-6-methylpyridine (Willink and Wibaut, *Rec. Trav. chim.*, 1934, **53**, 417) in 47% yield by the method described above, as a colourless oil, b. p. 59—60°/10 mm., n_D^{14} 1·4997 (Found: C, 70·5; H, 8·0. $C_8H_{11}ON$ requires C, 70·1; H, 8·0%).

2-Ethoxy-4-methylpyridine 1-Oxide.—An aqueous solution of peracetic acid was prepared by heating equal volumes of hydrogen peroxide (100 vol.) and glacial acetic acid at 90° for 2 hours. The solution was cooled and treated with 2-ethoxy-4-methylpyridine (22 g.), and the mixture maintained at 45° for 24 hours. The solution was evaporated at 25 mm. and finally at 2—5 mm. (bath temp., 40°). The residue was cooled in a freezing mixture and cautiously neutralised with cold 5N-sodium hydroxide. The cold mixture was extracted with chloroform (3 × 50 c.c.), and the dried (Na_2SO_4) extract evaporated under reduced pressure to give an oil which rapidly solidified. The solid (7·0 g.) was collected and recrystallised from dioxan from which *2-ethoxy-4-methylpyridine 1-oxide* separates as hygroscopic needles, m. p. 101—102° (Found: N, 8·4. $C_8H_{11}O_2N,H_2O$ requires N, 8·2%). It immediately liberates iodine in the cold from a solution of potassium iodide acidified with acetic acid. Light absorption in ethanol: Maxima at 2610 A., ε = 5300, and 3040 A., ε = 3000. The *picrate* separates from ethanol as needles, m. p. 139° (Found: C, 44·1; H, 3·9; N, 14·3. $C_{14}H_{14}O_9N_4$ requires C, 44·0; H, 3·7; N, 14·7%).

2-Ethoxy-6-methylpyridine 1-Oxide.—A solution of 2-ethoxy-3-methylpyridine (9·5 g.) in glacial acetic acid (70 c.c.) was treated with hydrogen peroxide (100 vol.; 70 c.c.) and kept at 56° for 19 hours. The solution was concentrated at 30° under reduced pressure, and the residue made alkaline by the addition of 3N-potassium hydroxide at 0°. The solution was extracted with chloroform (6 × 35 c.c.), and the extract dried (Na_2SO_4) and evaporated. The residue was crystallised from benzene–light petroleum (b. p. 60—80°) from which *2-ethoxy-6-methylpyridine 1-oxide* separated as plates, m. p. 102—103° (Found: C, 63·3; H, 7·3; N, 9·2. $C_8H_{11}O_2N$ requires C, 62·7; H, 7·2; N, 9·1%). Light absorption in ethanol: Maxima at 2610 A., ε = 3600, and 2990 A., ε = 1500. The *picrate* separated from ethanol as prisms, m. p. 88—89° (Found: N, 14·9. $C_{14}H_{14}O_9N_4$ requires N, 14·7%).

1-Hydroxy-2-keto-3-methyl-1 : 2-dihydropyridine.—A solution of 2-ethoxy-3-methylpyridine (9·5 g.) in glacial acetic acid (70 c.c.) was treated with hydrogen peroxide (100 vol.; 70 c.c.), and the solution maintained at 56° for 19 hours. The mixture was concentrated at 2 mm. (bath temperature below 30°) and the residue cooled to 0° and made alkaline with 3N-potassium hydroxide. The solution was then extracted with chloroform (6 × 35 c.c.), the extract dried (Na_2SO_4), and the solvent removed under reduced pressure. 2-Ethoxy-3-methylpyridine (0·9 g.) was removed by distillation. The residual viscous oil (2·26 g.) was dissolved in 3N-hydrochloric acid (25 c.c.), and the solution heated under reflux for 2 hours. The solution, which gave a deep cherry-red colour with aqueous ferric chloride, was evaporated under reduced pressure. The residue partly crystallised when kept. The mixture was triturated with ice-water and filtered. The crystalline solid (*A*), which gave a positive ferric chloride test, was collected and the filtrate made alkaline with sodium hydrogen carbonate and extracted with chloroform (3 × 40 c.c.). Acidification of the aqueous phase with hydrochloric acid, followed by extraction with chloroform (6 × 30 c.c.) and evaporation of the extract, yielded a solid which gave a positive ferric test. The solid was combined with solid (*A*) and sublimed at 80—85°/10^{-3} mm. The sublimate was crystallised from acetone to yield *1-hydroxy-2-keto-3-methyl-1 : 2-dihydropyridine* as needles, m. p. 138—139° (Found: C, 57·9; H, 5·6; N, 11·4; equiv., 130. $C_6H_7O_2N$ requires C, 57·6; H, 5·6; N, 11·2%; equiv., 125). The compound gave a copper salt, m. p. 276—278°, which separated from dioxan as needles.

1-Hydroxy-2-keto-4-methyl-1 : 2-dihydropyridine.—2-Ethoxy-4-methylpyridine 1-oxide (5·0 g.) was heated under reflux with hydrochloric acid (3N.; 100 c.c.) for 3 hours. The solution was evaporated under reduced pressure and the residue neutralised with sodium hydrogen carbonate solution. A slight excess of saturated copper acetate solution was added. The precipitated copper salt [2·0 g., m. p. 280° (decomp.)] was crystallised from dioxan from which it separated as prisms, m. p. 292° (decomp.). A solution of the copper salt (1·5 g.) in dioxan (100 c.c.) and water (100 c.c.) was treated with hydrogen sulphide. The mixture was evaporated to small bulk under reduced pressure and filtered (filter-aid). Evaporation of the filtrate to dryness gave a crystalline solid (0·7 g.) which, after crystallisation from acetone and sublimation at 100°/10^{-3} mm., gave *1-hydroxy-2-keto-4-methyl-1 : 2-dihydropyridine* (0·5 g.) as needles, m. p. 131—133° (Found: C, 57·7; H, 5·4; N, 10·8. $C_6H_7O_2N$ requires C, 57·6; H, 5·6; N, 11·2%).

Ethyl β-o-Nitrophenyl-α-methylacrylate.—A mixture of *o*-nitrobenzaldehyde (10·1 g.), propionic

anhydride (14 c.c.), and anhydrous sodium propionate (6·4 g.) was heated at 150° for 15 hours. The reaction mixture was poured into water, and the solid filtered off and extracted with dilute alkali. Acidification of the alkaline extract gave β-*o*-nitrophenyl-α-methylacrylic acid (9·4 g.) which separated from aqueous ethanol as needles, m. p. 194°. Edeleano (*Ber.*, 1887, **20**, 616) gives m. p. 208°, and Ranfaldi (*Rend. R. Accad. Scienze Fis. Mat. Napoli*, 1910, 3, **16**, 226) gives m. p. 198° for this acid. A solution of the acid (4·2 g.) in dry ethanol (50 c.c.) containing dry hydrogen chloride (2·0 g.) was boiled under reflux for 2 hours. The mixture was evaporated under reduced pressure, the oil mixed with ice-water, and the mixture neutralised with concentrated sodium carbonate solution. The solid was collected, washed with water, and crystallised from aqueous ethanol, to give *ethyl β-o-nitrophenyl-α-methylacrylate* (4·5 g.) as prisms, m. p. 60° (Found: C, 61·7; H, 5·9; N, 5·6. $C_{12}H_{13}O_4N$ requires C, 61·3; H, 5·5; N, 6·0%).

1-*Hydroxy*-2-*keto*-3-*methyl*-1 : 2-*dihydroquinoline*.—Ethyl β-*o*-nitrophenyl-α-methylacrylate (4·3 g.) in ethanol (20 c.c.) was added to an aqueous ethanolic solution of ammonium sulphide prepared by saturating a mixture of ethanol (20 c.c.) and aqueous ammonia (*d*, 0·88; 5 c.c.) with hydrogen sulphide at 0°. The solution was heated in a closed vessel at 100° for 2 hours. The reaction mixture was evaporated to dryness under reduced pressure, and the solid extracted with warm 2N-sodium hydroxide solution. The combined extracts were acidified with dilute hydrochloric acid, and the yellow-brown solid (1·4 g.) extracted with cold 0·5N-sodium hydroxide. The insoluble residue, on treatment with water, gave 3-methylcarbostyril, m. p. 235° (1·1 g.); Ornstein (*Ber.*, 1907, **40**, 1095) gives m. p. 234—235°. Acidification of the alkaline extract with dilute hydrochloric acid gave a brown solid, m. p. 140—160° (200 mg.). The solid was twice sublimed at 140°/10^{-3} mm. to give 1-*hydroxy*-2-*keto*-3-*methyl*-1 : 2-*dihydroquinoline*, m. p. 182°, which separated from ethanol as prisms (Found: C, 68·4; H, 5·5; equiv., 180. $C_{10}H_9O_2N$ requires C, 68·6; H, 5·1%; equiv., 175). It gives a deep red colour in aqueous alcoholic ferric chloride.

2-*Ethoxy*-4-*methylquinoline* 1-*Oxide*.—A solution of 2-ethoxy-4-methylquinoline (3·3 g.; Knorr, *Annalen*, 1886, **236**, 102) in peracetic acid (80 c.c., prepared as described above) was maintained at 50° for 48 hours. The reaction mixture was evaporated (reduced pressure), the cold residue made alkaline with 3N-potassium hydroxide solution, and the mixture extracted with chloroform (6 × 35 c.c.). The dried (Na_2SO_4) extract was evaporated and the viscous oil dissolved in the minimum quantity of ethanol and treated with ethanolic picric acid. 2-*Ethoxy*-4-*methylquinoline* 1-*oxide picrate* (2·1 g.) separated from ethanol as prismatic needles, m. p. 144—145° (Found: C, 50·0; H, 3·9; N, 12·9. $C_{18}H_{16}O_9N_4$ requires C, 50·0; H, 3·7; N, 13·0%). Decomposition of the picrate by the method of Burger (*J. Amer. Chem. Soc.*, 1945, **67**, 1615) gave 2-*ethoxy*-4-*methylquinoline* 1-*oxide* as slightly yellow plates, m. p. 61°, from acetone–light petroleum (b. p. 40—60°) (Found: N, 6·9. $C_{12}H_{13}O_2N$ requires N, 6·9%); yield, 550 mg.

1-*Hydroxy*-2-*keto*-4-*methyl*-1 : 2-*dihydroquinoline*.—A solution of 2-ethoxy-4-methylquinoline 1-oxide (260 mg.) in ethanol (5 c.c.) and hydrochloric acid (3N.; 6 c.c.) was heated under reflux for 2 hours. The mixture was evaporated to dryness. Sublimation of the residue at 120°/10^{-3} mm., followed by crystallisation from acetone, gave 1-*hydroxy*-2-*keto*-4-*methyl*-1 : 2-*dihydroquinoline* as needles, m. p. 225—227° (Found: C, 68·6; H, 5·1; N, 7·95; equiv., 167. $C_{10}H_9O_2N$ requires C, 68·6; H, 5·1; N, 8·0%; equiv., 175). A solution of the acid in ethanol gave a deep red colour with aqueous ferric chloride.

DL-*Alanine Hydroxamic Acid*.—A solution of hydroxylamine [from the hydrochloride (1·5 g.) and sodium (0·5 g.) in absolute methyl alcohol (50 c.c.)] was cooled to −10° and added slowly to a solution of DL-alanine methyl ester [from the hydrochloride (3·06 g.) and sodium (0·46 g.) in methyl alcohol (40 c.c.)] also at −10°. The mixture was kept at 0° overnight and concentrated to small bulk. The solid (1·4 g.) was collected and crystallised from aqueous ethanol, from which DL-*alanine hydroxamic acid* separated as small needles, m. p. 163—164° (Found: C, 34·7; H, 7·7; N, 27·2. $C_3H_8O_2N_2$ requires C, 34·6; H, 7·7; N, 26·9%). The acid gives a wine-red colour with aqueous ferric chloride, a property common to the hydroxamic acids described below.

By the same method, glycine hydroxamic acid was obtained as small prisms from aqueous methyl alcohol, m. p. 137° (decomp.) (Found: C, 27·1; H, 6·85. Calc. for $C_2H_6O_2N_2$: C, 26·7; H, 6·7%). Ley and Mannchen (*Ber.*, 1913, **46**, 754) give m. p. 107°, and Jones and Sneed (*J. Amer. Chem. Soc.*, 1917, **39**, 673) give m. p. 140° (decomp.).

DL-*Valine hydroxamic acid* separated from water as prisms, m. p. 180° (Found: C, 45·5; H, 9·3. $C_5H_{12}O_2N_2$ requires C, 45·5; H, 9·1%).

DL-iso*Leucine hydroxamic acid* formed very small needles, m. p. 171—172° (decomp.), from water (Found: C, 49·5; H, 9·3. $C_6H_{14}O_2N_2$ requires C, 49·3; H, 9·6%).

DL-*Phenylalanine hydroxamic acid* separated from water as very small plates, m. p. 180° (decomp.) (Found: C, 59·5; H, 6·4. $C_9H_{12}O_2N_2$ requires C, 60·0; H, 6·7%).

p-*Aminobenzhydroxamic acid* separated as prismatic needles, m. p. 184—185° (decomp.), from methyl alcohol–ethyl acetate (Found: C, 55·6; H, 5·4; N, 18·7. $C_7H_8O_2N_2$ requires C, 55·3; H, 5·3; N, 18·4%).

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