L 57471-65

ACCESSION NR: AR5016448

year. A study was made of the behavior of the sporadic E and E_s layers and of their relationship to meteoric activity. In accordance with the determined values

RUBTSOV, L.N.

Preliminary results of a vertical sounding of the ionosphere above Tadzhikistan. Biul. Inst. astrofiz. AN Tadzh. SSR no.33: 3-11 '62. (MIRA 17:11)

VOLOVCHENKO, I.; METELEV, V.; BANNIKOV, N.; LAPIDUS, M.; MOROZOV, P.; RUBTSOV, M.; BATSANOV, N.; PRYANISHNIKOV, D.N., akademik; TULAYKOV, N.M., akademik; BEREZIN, I.A., red.; AVDEYEVA, V.A., tekhn. red.

[Strong crops] Moguchie kul'tury. Moskva, Sovetskaia Rossiia, 1962. 222 p. (Truzhenikam sela - ob intensivnoi sisteme zemledeliia, no.2) (MIRA 16:9)

(Field crops)

RUBTSOV, M.G.

NIKITSKAYA, Ye.S.; RUBTSOV, M.G.

Hydrogenation of 4-(β,β-dicarbethoxyvinyl)-pyridine in the presence of the nickel-skeleton catalyst. Zhur.ob.khim.26 no.11:3119-3123 N'56. (MIRA 10:1)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S.Ordzhonikidze.
(Pyridine) (Hydrogenation)

S/072/63/000/003/001/004
B101/B186

AUTHORS: Garif'yanov, N. S., Candidate of Physics and Mathematics, Rubtsov, M. I., Physicist, Ryshmanov, Yu. M., Physicist

TITLE: E.p.r. spectra in silicate glasses containing three-valent titanium

PERIODICAL: Steklo i keramika, no. 3, 1963, 11-12

TEXT: The e.p.r. spectra of some silicate glasses containing 0-20% TiO_2 were taken at 9320 and 450 Mc/sec. Results:

glass	TiO_2,%	450 Mc/sec H,oerst. 300°K	77°K	g factor	9320 Mc/sec H,oerst. 300°K	77°K	g factor
M-519	0	-	-	-	-	-	-
M-519	1	-	-	-	-	-	-
M-519	10	-	7	1.9	-	-	-
M-519	15	9	13	1.9	71	71	1.946
M-519	20	-	8	1.9	-	-	-
no.6	7.5	-	5	1.9	-	-	-
no.11	4	-	-	-	-	-	-

Card 1/3

It was found in an earlier paper (ZhETF, 1960, v.39) that supercooled solutions of Ti^{3+} compounds have similar e.p.r. spectra. It is therefore concluded that when the glass is melted, the Ti^{4+} is partially reduced to Ti^{3+}. In M-519(M-519) glass the octahedral crystal field, formed by six oxygen atoms, splits the five-fold orbital level of Ti^{3+} into an upper doublet and a lower triplet. The low-symmetry fields produced by distortions of the oxygen octahedron and by particles of the second sphere of coordinates split the orbital triplet into a lower singlet and doublet. Since the narrow e.p.r. line in M-519 glass containing 15% TiO_2 is observed even at room temperature, the value Δ of the splitting of the orbital triplet must be rather high. The resonance line at 450 Mc/sec in glasses containing 7.5,10 and 20% TiO_2 is observed only at 77°K. This is explained by the fact that in this case the Ti^{3+} ions are in a symmetric field and the e.p.r. line becomes so wide at room temperature that it cannot be observed any more. The strong broadening of the line at 9320 Mc/sec is explained by the presence of two local fields. This causes a superposition, leading to

a broad e.p.r. peak independent of temperature. The Ti^{3+} concentration in M-519 glass (15% TiO_2) was found to be 3% by comparing the area of the e.p.r. curves at 77°K in supercooled solutions of Ti^{3+} of known concentration with the areas of the e.p.r. spectra for the glasses. The paramagnetic ion content of the glasses can be determined quantitatively in this way. There are 1 figure and 1 table.

ASSOCIATION: Fiziko-tekhnicheskiy institut Kazanskogo filiala AN SSSR (Physicotechnical Institute of the Kazan' Branch AS USSR) (N.S. Garif'yanov); Saratovskiy filial Instituta stekla (Saratov Branch of the Institute of Glass)(M.I. Rubtsov); Institut organicheskoy khimii AN SSSR (Institute of Organic Chemistry AS USSR)(Yu.M.Ryzhmanov)

GARIF'YANOV, N. S., kand. fiz.-matemat. nauk; RUBTSOV, M. I., fizik; RYZHMANOV, Yu. M., fizik

Electron paramagnetic resonance in silicate glasses containing trivalent titanium. Stek. i ker. 20 no.3:11-12 Mr '63. (MIRA 16:4)

1. Fiziko-tekhnicheskiy institut Kazanskogo filiala AN SSSR (for Garif'yanov). 2. Saratovskiy filial Instituta stekla (for Rubtsov). 3. Institut organicheskoy khimii AN SSSR (for Ryzhmanov).

(Paramagnetic resonance and relaxation)
(Glass) (Titanium)

PAVLOV, Ivan Petrovich, prof. Prinimali uchastiye: TATARINTSEV, A.S., prof.; VIDENIN, K.F., dots.; RUBTSOV, M.I., dots.; YERMILOVA, A.A., dots.; BYKOVA, M.G., red.

[Breeding and seed production of vegetable crops] Selektsiia i semenovodstvo ovoshchnykh kul'tur. Moskva, Sel'khozizdat, 1963. 279 p. (MIRA 17:11)

1. Plodoovoshchnyy institut im. I.V.Michurina (for Tatarintsev, Videnin, Rubtsov, Yermilova).

RUBTSOV, M.I., dots.; YERMILOVA, A.A., dots.; CHEREPOVA, O.M., kand. sel'khoz.nauk; SKRIPNIKOV, Yu.G., dots.; DOROKHOV, A.A., kand. sel'khoz.nauk; LITVINOVA, M.K., assistent; MUSTAFIN, A.M., prepodavatel'; PESHKOV, V.P., red.; POPOV, V.N., tekhn. red.

[Growing vegetables in the Central Chernozem Region of the U.S.S.R.]Vyrashchivanie ovoshchei v TSentral'noi chernozemnoi zone SSSR. Tambov, Tambovskoe knizhnoe izd-vo, 1962. 110 p. (MIRA 16:2)

1. Sotrudniki kafedry ovoshchevodstva Michurinskogo plodoovoshchnogo instituta im.I.V.Michurina (for all except Peshkov, Popov).
(Central Chernozem Region--Vegetable gardening)

"Fundamentals of the Growing of Seedling Tomatoes in Sheltered Ground Warmed by Steam." Cand Agr Sci, Moscow Order of Lenin Agricultural Acad imeni K. A. Timiryazev, Moscow, 1955. (KL, No 16, Apr 55)

SO: Sum. No. 704, 2 Nov 55 - Survey of Scientific and Technical Dissertations Defended at USSR Higher Educational Institutions (16).

RUBTSOV, M.K.; YELIASHVILI, A.I., inzh.; PASHCHENKO, I.N., inzh.; YAKUNIN, V.I., inzh.; MERKULOV, Ye.M., inzh., obshchiy red.; GOLUBEVA, I.A., red.; USHKOVA, M., tekhn.red.

[Simplest methods for making bricks] Prosteishie sposoby izgotovleniia kirpicha. Moskva, 1958. 69 p. (MIRA 12:8)

1. Russia (1923- U.S.S.R.) Ministerstvo sel'skogo khozyaystva. Upravleniye kapital'nogo stroitel'stva.
(Brickmaking)

Nutritive Requirements and The Composition

RUBTSOV, M. K. Cand Agr Sci -- (diss) "On the Levels of ~~the~~ ~~General~~ and Protein ~~Nourishment~~ ~~Contained in~~ the Rations ~~given to~~ Pregnant and Dry Cows." Mos, 1957. 22 pp 22 cm. (Mos Order of Lenin Agricultural Academy im K. A. Timiryazev), 120 copies (KL, 26-57, 111)

RUBTSOV, M.K., kand.sel'skokhozyaystvennykh nauk (Moskva);
BAZHANOV, B.D., inzh. (Moskva); BELYAYEV, G.S., ekonomist (Moskva)

Pressing problems of agricultural electrification. Elektrichestvo no.6:1-5 Je '62. (MIRA 15:6)
(Rural electrification)

Q-2

USSR / Farm Animals. Cattle

Abs Jour: Ref Zhur-Biol., No 3, 1958, 12067

Author : Rubtsov M. K.
Inst :
Title : On the Composition of Feed Rations for Pregnant Dry Cows (O strukture kormoyykh ratsionov dla stel'nykh sukhostoynykh korov)

Orig Pub: Sovkoznoye proiz-vo, 1957, No 5, 49-54

Abstract: An experiment was carried out on five groups of the pregnant-dry cows of the East Friesian breed. The beetroot-silage group was fed rations containing 16.6 kg. of beetroot and 8.8 kg. of silage; the silage group - 16.6 kg. of silage; the beetroot group - 25 kg. of beetroot; the potato group - 10.5 kg. of potatoes; the "dryration" group - 12 kg. of beetroot. All group rations included 11.6 to 12 kg. of

Card 1/2

USSR

...rm Animals. Cattle

Abs Jour: Ref Zhur-Biol., No 3, 1958, 12067 Q-2

Abstract: hay each, and 2.5 to 4.6 kg. of concentrates. As a result of the experiment, the live weight of cows during dry period increased in all five groups by 51-41-42-56-53.7 kg. respectively; on the 3-5th day after calving it decreased by 77-89-87-74-70 kg.; the Hb of the blood, during 1st month od fry period increased by 4-3-3-0-5%; the milk yield for the 60 days of lactation was 1,457-1,257, 1,317-1,574-1,360 kg., and for 300 days constituted 5,317-4,936-5,092-5,915-4,848 kg., respectively. On the basis of the data provided by the experiments the conclusion was drawn that succulent rations were advantageous in the preparation of the cows for calving. The beet-root-silage ration was the best.

Card 2/2

SHEVCHENKO, A.S.; KAVUN, P.K., red.; RUBTSOV, M.K., red.; PROKOF'YEVA, L.N., tekhn. red.

[Corn; make way for extensive exchange of experience] Kukuruza; dlia obmena opytom dveri shiroko otkryty. Izd.2., dop. Moskva, Izd-vo sel'khoz. lit-ry, zhurnalov i plakatov, 1961. 413 p. (MIRA 14:10)
(Corn (Maize))

NIKITSKAYA, Ye.S.; LEVKOYEVA, Ye.I.; USOVSKAYA, V.S.; RUBTSOV, M.V.

Synthesis of 7-hydroxy-9-methyl-3,9-diazabicyclo [3,3,1] nonane and some of its derivatives. Zhur. org. khim. 1 no.1:174-182 Ja '65. (MIRA 18:5)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S.Ordzhonikidze.

MIKHLINA, Ye.Ye.; VOROB'YEVA, V.Ya.; SHEDCHENKO, V.I.; RUBTSOV, M.V.

Structure of 3-quinuclidinone rearrangement products according to the Schmidt and Beckmann reactions. Zhur. org. khim. 1 no.7:1336-1337 Jl '65. (MIRA 18:11)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S.Ordzhonikidze i Institut khimii prirodnykh soyedineniy AN SSSR.

5(3)
AUTHORS: Mikhlina, Ye. Ye., Rubtsov, M. V. SOV/79-29-7-50/83

TITLE: Synthesis of 3-Oxy-3-alkyl(aryl)-quinuclidines and Their Esters (Sintez 3-oksi-3-alkil(aril)-khinuklidinov i ikh efirov)

PERIODICAL: Zhurnal obshchey khimii, 1959, Vol 29, Nr 7, pp 2337-2343 (USSR)

ABSTRACT: Rubtsov and coworkers demonstrated in earlier reports (Refs 1, 2) that some 2-mono- and 2,3-disubstituted quinuclidines are of high biological activity. With the object of examining the less investigated 3-substituted quinuclidines, the authors carried out the synthesis of a number of 3-oxy-3-alkyl(aryl) quinuclidines and their esters. For the synthesis the authors used quinuclidone-3 which gave compounds (I) by reaction with organo-magnesium compounds. In some instances the tertiary alcohols were obtained in considerably higher yields by the use of organo-lithium compounds. Thus, the reaction of quinuclidone-3 with methyl-magnesium iodide yielded 27% 3-oxy-3-methylquinuclidine, while the yield was 81% when methyl-lithium was used (Scheme 1). The conversion of the compounds (I) into the esters (II) was effected by heating the corresponding tertiary alcohols with acid chlorides. The best results were attained when chloroform solutions were used for the reaction.

Card 1/2

Synthesis of 3-Oxy-3-alkyl(aryl)-quinuclidines and Their Esters

SOV/79-29-7-50/83

On heating (Id) for some time with acid chlorides without a solvent the compound (IIIa) was obtained instead of the corresponding esters. The ready transformation of (Id) to (IIIa) induced the authors to study the effect of other desiccating reagents on the quinuclidines (I). For this purpose thionyl chloride and sulfuric acid were used. It was found that (Id) on short treatment with thionyl chloride (15 mol) gave a mixture of (IIIa) with 3-phenyl-3-chloroquinuclidine which was difficult to separate. Heating this mixture with alcoholic alkali hydroxide yielded (IIIa) only. On heating (Id) with 70% sulfuric acid (Id) gave (IIIa) in 90% yield. The substance (Ia) remained unaffected by heating with 70% sulfuric acid, but became completely resinous with 80% acid. On heating (Ia) for a short time with thionyl chloride (equimolar proportions) in benzene (IIIb) was formed (Scheme 2). The esters of the 3-oxy-3-alkyl(aryl) quinuclidines have slight pharmacological activity. There are 6 references, 2 of which are Soviet.

ASSOCIATION: Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S. Ordzhonikidze (All-Union Scientific Chemico-pharmaceutical Research Institute imeni S. Ordzhonikidze)

SUBMITTED: May 15, 1958

Card 2/2

RUBTSOV, M. N.

SOV/122-58-5-25/26

AUTHOR: Podurayev, V.N., Candidate of Technical Sciences, Dotsent

TITLE: Inter-Vuz Conference on Technology
(Mezhvuzovskaya tekhnologicheskaya konferentsiya)

PERIODICAL: Vestnik Mashinostroyeniya, 1958, Nr 5, p 84 (USSR).

ABSTRACT: An inter-vuz conference took place in January, 1958 at the MVTU (Moscow Technical University) imeni Bauman , devoted to manufacturing problems in the engineering and instrument industries. 22 universities and representatives of research institutes in the main engineering and instrument branches took part. Over 50 papers were read. The following papers were devoted to the state of knowledge of the theoretical foundations of production engineering. "The Basic Trends of Development in Engineering Manufacture" by Satel Ye.A., "The Fundamental Theoretical Problems in the Development of Casting", by Rubtsov, M.N., "Current Problems of Metallurgy and Heat Treatment of Metals" by Sidorin, I.I., Professor, "Accuracy and Interchangeability in Engineering" by Prof. B.S. Balakshin and "Present State of the Theory of Plastic Deformation in Press-forming Manufacture" by Ye.A. Popov, Doctor of Technical Sciences. In these papers, the main attention was devoted to

Card 1/3

Inter-Vuz Conference on Technology

manufacturing methods which could be performed by small, light, universal and economic plants. New production methods capable of improving the life of machine components are needed. The trends of increasing power of machine tools, greater expansion of high-speed manufacturing processes and the need to ensure the greatest precision in manufacture were emphasized. The theory of interchangeability of machine components requires further development primarily in its application to pneumatic, hydraulic and electrical elements. In several papers, the inadequate use made in the theory of manufacturing methods of modern achievements in science was deprecated. Further developments in the several branches of engineering science needed in connection with topical manufacturing problems were indicated. Widespread automation and overall mechanisation of manufacture were discussed in the following papers: "Trends of Development in Automatic Welding" by Nikolayev, G.A., Professor, Corresponding Member of the Academy of Architecture and Building [illegible] "The Automation of Manufacturing Processes in Engineering" by Prof. G.A. Shaumyan, "The Part Played by Electronics in the Solution of Automation Problems" by Kugushev, A.M., Professor, "The Configuration and Classification of Automatic Production

Inter-Vuz Conference on Technology

Machines and Their Basic Elements" by Prof. S.I. Artobolevskiy, "The Basic Trends of Development in the Theory of Automatic Regulating and Control" by Solodvnikov, A.V. Professor, "The Application of Electronic Devices to the Programme Control of Metal Cutting Machine Tools" by B.V. Anisimov. In the present state of its development, automation must ensure not only an increased productivity of labour but also a high accuracy in the performance of its individual operation and the constancy of its properties in time. Problems of the evaluation of the economic effectiveness of introducing any form of automation under given manufacturing conditions must be further elucidated. The flexibility of automated production should be given attention. The problems set by these developments must be solved to an increasing degree by the methods of automatic electronic regulating and control and by programme control systems.

Card 3/3 1. Industrial Production--USSR 2. Engineering--USSR 3. Instruments --Production

YAKHONTOV, L.N.; RUBTSOV, M.V.

7-Azaindole derivatives. New type of closure of the pyrroline ring in the reaction of trichlorocollidine with secondary amines. Zhur. ob.khim. 30 no.10:3300-3306 O '61. (MIRA 14:4)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S.Ordzhonikidze.
(Pyridine) (Cyclization)

NIKITSKAYA, Ye.S.; USOVSKAYA, V.S.; RUBTSOV, M.V.

Bicyclic compounds based on 2,6-lutidine. Part 4: 3-Substituted derivatieves of 9-methyl-3,9-diazabicyclo [3.3.1]nonane. Zhur.ob. khim. 30 no.10:3306-3315 O '61. (MIRA 14:4)
(Diazabicyclononane)

5(3)
AUTHORS: Yakhontov, L. N., Rubtsov, M. V. SOV/79-29-7-51/83

TITLE: Aminoacids of the Quinuclidine Series
(Aminokisloty ryada khinuklidina)

PERIODICAL: Zhurnal obshchey khimii, 1959, Vol 29, Nr 7, pp 2343-2348 (USSR)

ABSTRACT: No data on the synthesis and biological activity of the above-mentioned acids is given in publications. The following amino acids were synthesized in this investigation: α-Aminomethyl-β-(quinuclidyl-2)-propionic acid (III), β-(quinuclidyl-2)-β-aminopropionic acid (VII), and 3-aminoquinuclidine-2-carboxylic acid (XII). (I) was used as an initial compound for the preparation of (III)(Ref 2)(Scheme 1). The Knoevenagel condensation of the aldehyde (I) gave (II) in quantitative yield. The hydrogenation of the double bond and the cyano group in (II) was effected with the Pt catalyst according to Adams and was a one-step reaction. The obtained esters of acid (III) was saponified without previous isolation. (IV) was used for the preparation of (VII)(Scheme 2). The Claisen condensation of (IV) with ethyl acetate (Ref 3) gave the sodium derivative [enol form(V)] . (V) dissolved in water only within 24 hours, yielding the sodium salt of β-(quinuclidyl-2)- β-ketopropionic

Card 1/2

acid after hydrolysis. The oxime (VI) of this keto acid was prepared by the reaction of the sodium salt of the acid with an equimolar amount of hydroxylamine hydrochloride in absolute alcohol. (VI) was converted to (VII) by the Adams reduction. The synthesis of (XII) was carried out as shown in scheme 3. Against all expectations only one diastereo-isomer of each of the three aminoacids synthesized was obtained, instead of the three theoretically possible isomers. There are 4 references, 2 of which are Soviet.

ASSOCIATION: Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevtiches-kiy institut imeni S. Ordzhonikidze (All-Union Scientific Chemico-pharmaceutical Research Institute imeni S. Ordzhonikidze)

SUBMITTED: May 15, 1958

RUBTSOVA, M.S.

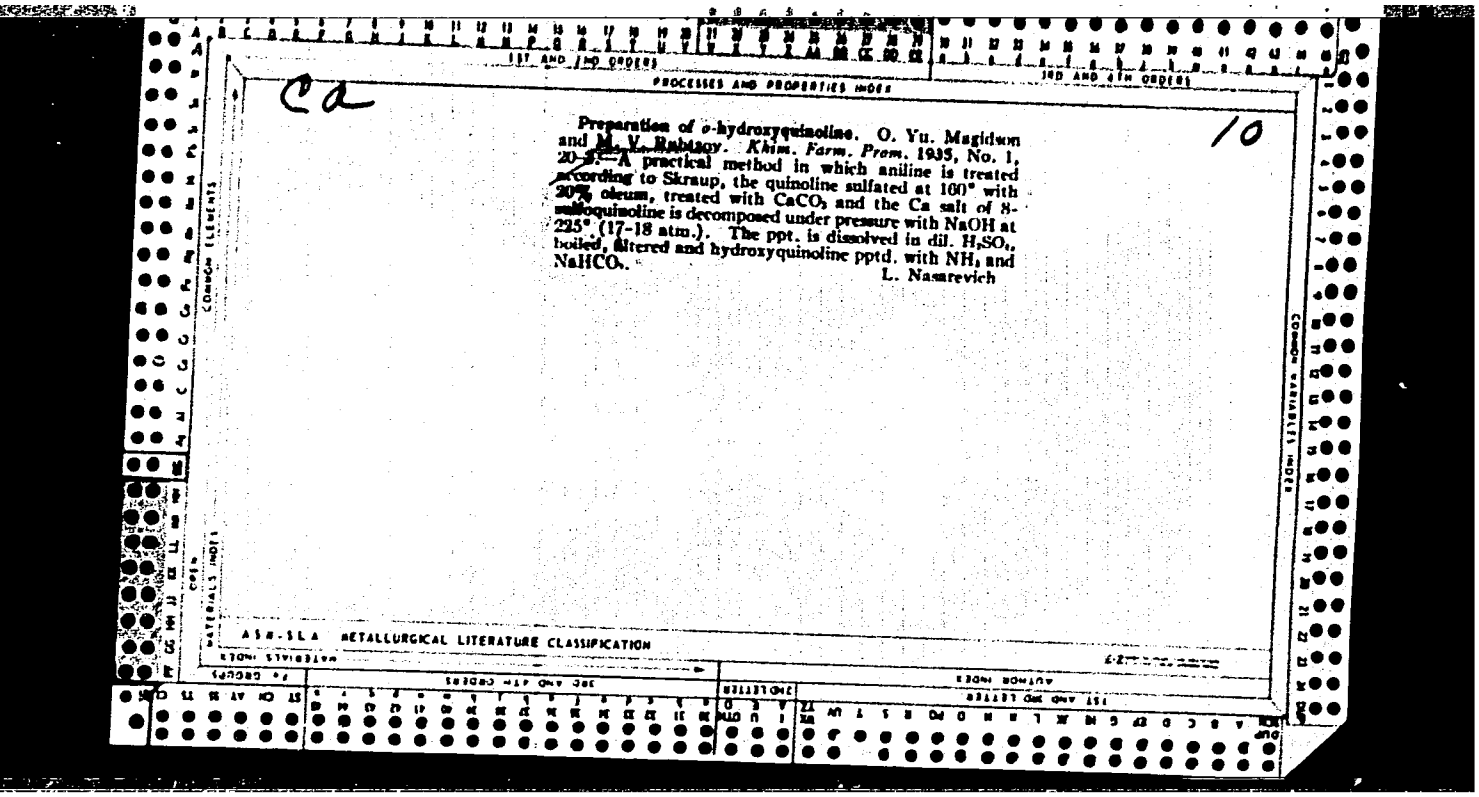
Some physiological characteristics of hybrids and parental self-pollinated lines of corn. Fiziol. rast. 7 no.6:695-700 '60. (MIRA 14:1)

1. Gorky Agricultural Institute.
(Corn breeding)

RUBTSOV, M.V.; YAKHONTOV, L.N.; MIKHLINA, Ye.Ye.

Hofmann degradation of 1,4-bispentamethylene piperazinium dichloride by means of a methanol solution of caustic potash. Zhur. ob. khim. 35 no.4:621 Ap '65. (MIRA 18:5)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S. Ordzhonikidze.



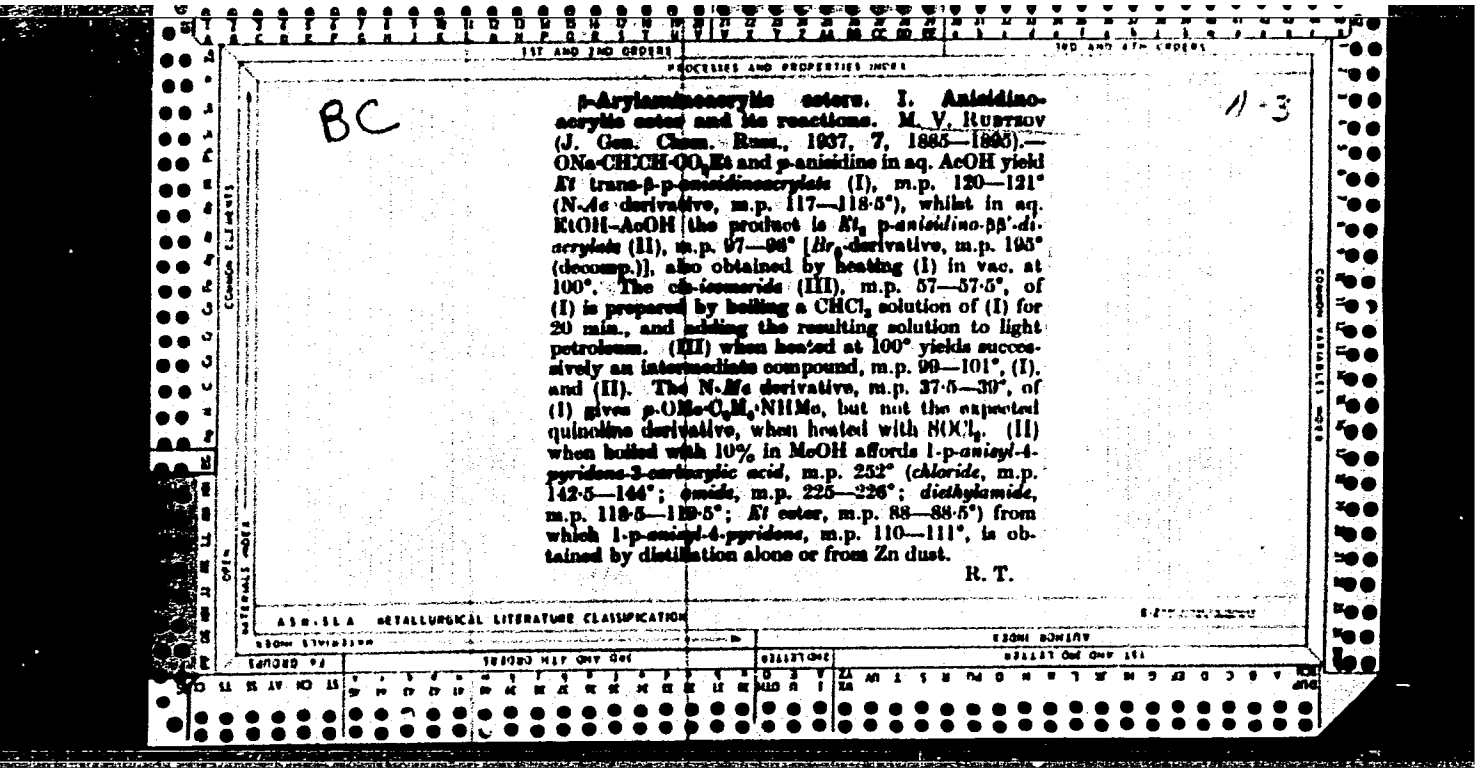
Ca

10

Preparation of o-hydroxyquinoline. O. Yu. Magidson and M. V. Rabinov. *Khim. Farm. Prom.* 1935, No. 1, 20–3.—A practical method in which aniline is treated according to Skraup, the quinoline sulfated at 160° with 20% oleum, treated with $CaCO_3$ and the Ca salt of 8-sulfoquinoline is decomposed under pressure with NaOH at 225° (17–18 atm.). The ppt. is dissolved in dil. H_2SO_4, boiled, filtered and hydroxyquinoline pptd. with NH_4 and $NaHCO_3$.

L. Nasarevich

ASM-SLA METALLURGICAL LITERATURE CLASSIFICATION

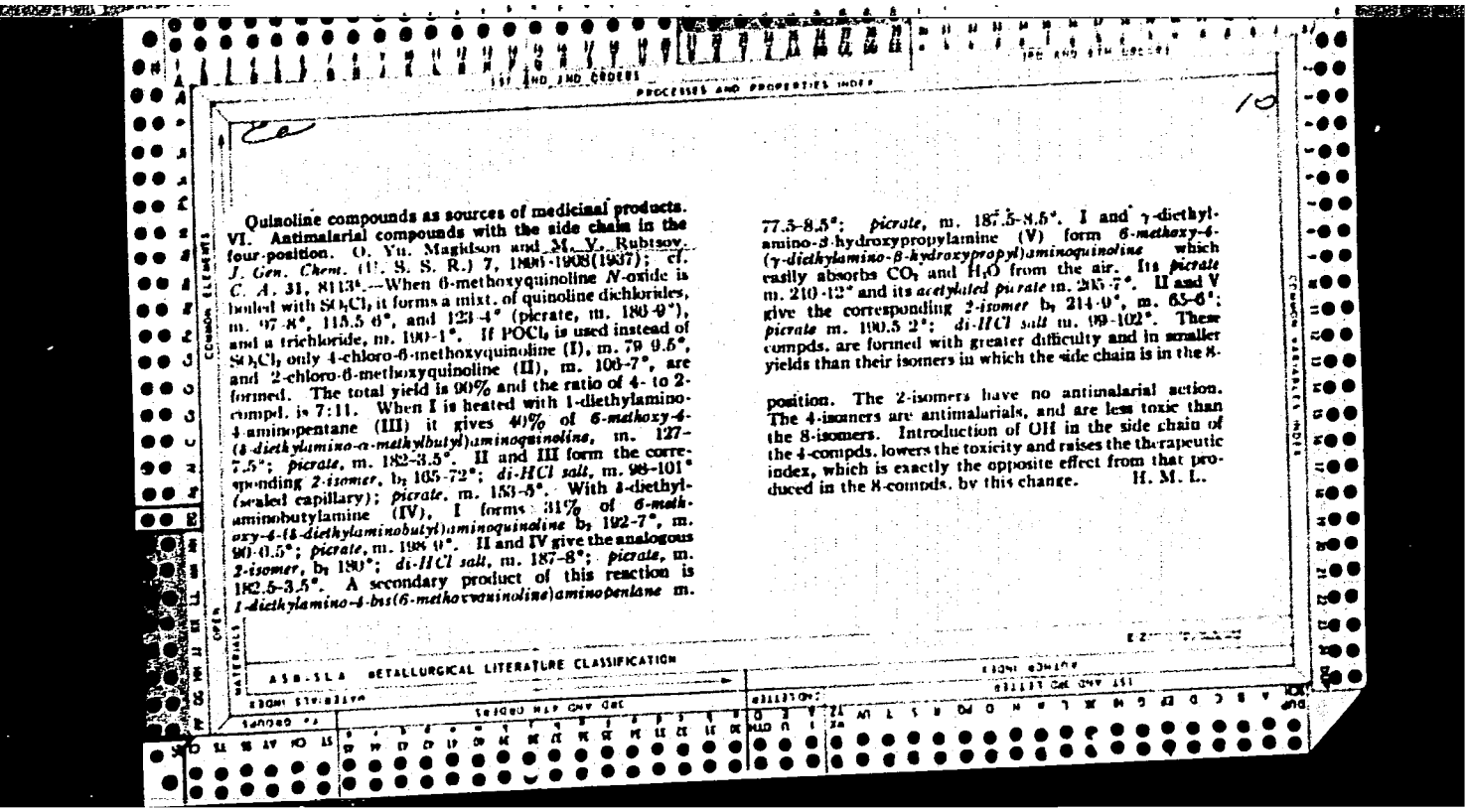


BC

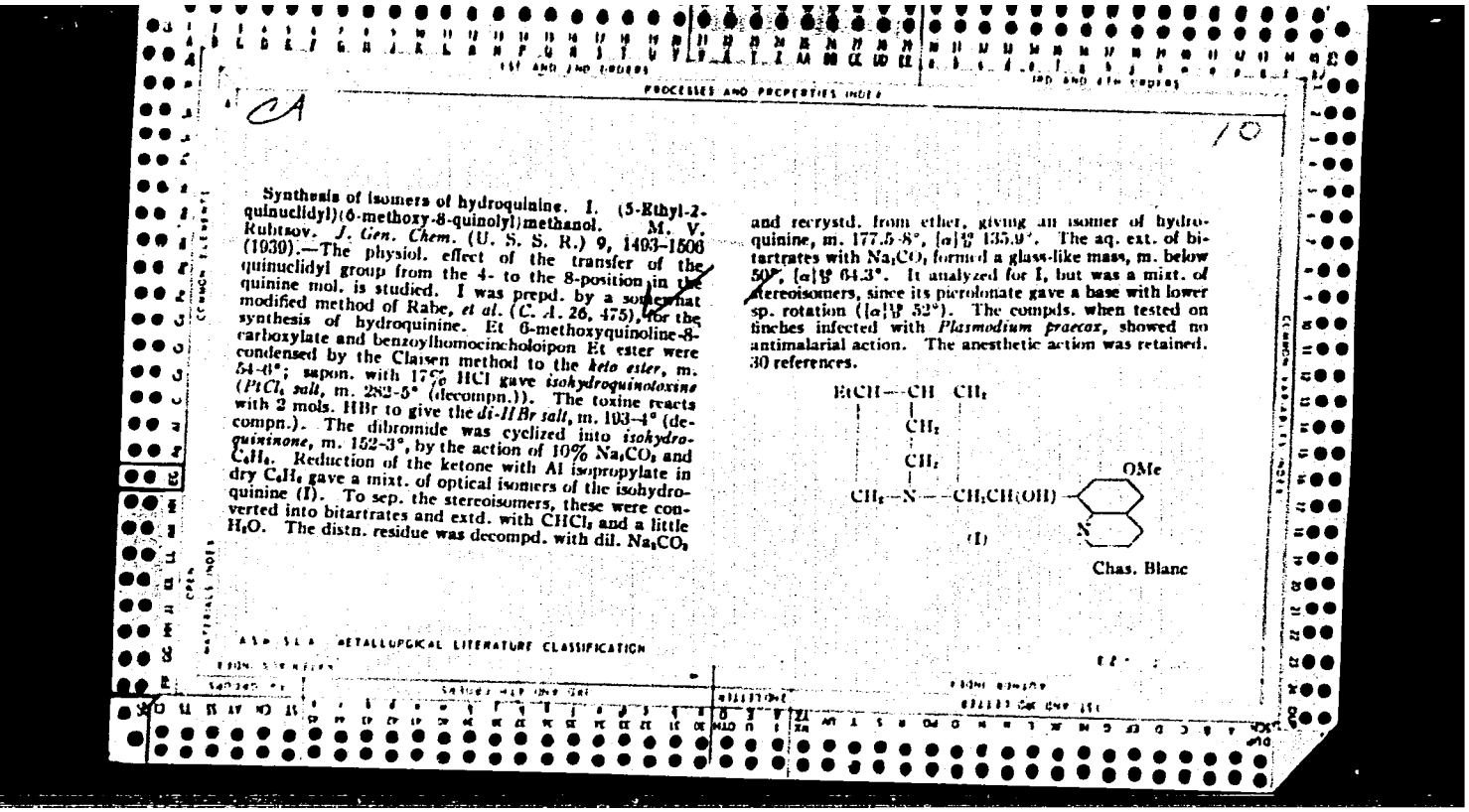
11-3

β-Arylaminoacrylic esters. I. Anisidinoacrylic ester and its reactions. M. V. Rubtsov (J. Gen. Chem. Russ., 1937, 7, 1885—1895).—ONa·CH:CH·CO_2Et and *p*-anisidine in aq. AcOH yield *Et trans-β-p-anisidinoacrylate* (I), m.p. 120—121° (*N-Ac* derivative, m.p. 117—118·5°), whilst in aq. EtOH–AcOH the product is Et_2 *p-anisidino-ββ'-diacrylate* (II), m.p. 97—98° [Et_2 *Br*$_2$-derivative, m.p. 195° (decomp.)], also obtained by heating (I) in vac. at 100°. The *cis-isomeride* (III), m.p. 57—57·5°, of (I) is prepared by boiling a $CHCl_3$ solution of (I) for 20 min., and adding the resulting solution to light petroleum. (III) when heated at 100° yields successively an intermediate compound, m.p. 99—101°, (I), and (II). The *N-Me* derivative, m.p. 37·5—39°, of (I) gives *p*-OMe·C_6H_4·NHMe, but not the expected quinoline derivative, when heated with $NOCl_3$. (II) when boiled with 10% in MeOH affords *1-p-anisyl-4-pyridone-3-carboxylic acid*, m.p. 252° (*chloride*, m.p. 142·5—144°; *amide*, m.p. 225—226°; *diethylamide*, m.p. 118·5—119·5°; *Et* ester, m.p. 88—88·5°) from which *1-p-anisyl-4-pyridone*, m.p. 110—111°, is obtained by distillation alone or from Zn dust.

R. T.



Quinoline compounds as sources of medicinal products. VI. Antimalarial compounds with the side chain in the four-position. O. Yu. Magidson and M. V. Rubtsov. *J. Gen. Chem.* (U. S. S. R.) 7, 1805-1908(1937); cf. *C. A.* 31, 8113⁴.—When 6-methoxyquinoline *N*-oxide is boiled with SO_2Cl_2 it forms a mixt. of quinoline dichlorides, m. 97-8°, 115.5-6°, and 123-4° (picrate, m. 180-9°), and a trichloride, m. 190-1°. If $POCl_3$ is used instead of SO_2Cl_2 only 4-chloro-6-methoxyquinoline (I), m. 79-9.5°, and 2-chloro-6-methoxyquinoline (II), m. 100-7°, are formed. The total yield is 90% and the ratio of 4- to 2-compd. is 7:11. When I is heated with 1-diethylamino-4-aminopentane (III) it gives 40% of *6-methoxy-4-(δ-diethylamino-α-methylbutyl)aminoquinoline*, m. 127-7.5°; *picrate*, m. 182-3.5°. II and III form the corresponding *2-isomer*, b_3 165-72°; *di-HCl salt*, m. 98-101° (sealed capillary); *picrate*, m. 153-5°. With 3-diethylaminobutylamine (IV), I forms 31% of *6-methoxy-4-(β-diethylaminobutyl)aminoquinoline* b_3 192-7°, m. 90-0.5°; *picrate*, m. 198-9°. II and IV give the analogous *2-isomer*, b_3 180°; *di-HCl salt*, m. 187-8°; *picrate*, m. 182.5-3.5°. A secondary product of this reaction is *1-diethylamino-4-bis(6-methoxyquinoline)aminopentane* m. 77.5-8.5°; *picrate*, m. 187.5-8.5°. I and γ-diethylamino-β-hydroxypropylamine (V) form *6-methoxy-4-(γ-diethylamino-β-hydroxypropyl)aminoquinoline* which easily absorbs CO_2 and H_2O from the air. Its *picrate* m. 210-12° and its *acetylated picrate* m. 215-7°. II and V give the corresponding *2-isomer* b_3 214-9°, m. 65-6°; *picrate* m. 190.5-2°; *di-HCl salt* m. 99-102°. These compds. are formed with greater difficulty and in smaller yields than their isomers in which the side chain is in the 8-position. The 2-isomers have no antimalarial action. The 4-isomers are antimalarials, and are less toxic than the 8-isomers. Introduction of OH in the side chain of the 4-compds. lowers the toxicity and raises the therapeutic index, which is exactly the opposite effect from that produced in the 8-compds. by this change. H. M. L.



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Synthesis of isomers of hydroquinine. I. (5-Ethyl-2-quinuclidyl)(6-methoxy-8-quinolyl)methanol. M. V. Rubtsov. *J. Gen. Chem.* (U. S. S. R.) 9, 1493–1506 (1939).—The physiol. effect of the transfer of the quinuclidyl group from the 4- to the 8-position in the quinine mol. is studied. I was prepd. by a somewhat modified method of Rabe, *et al.* (*C. A.* 26, 475), for the synthesis of hydroquinine. Et 6-methoxyquinoline-8-carboxylate and benzoylhomocincholoipon Et ester were condensed by the Claisen method to the *keto ester*, m. 54–6°; sapon. with 17% HCl gave *isohydroquinoloxine* (*PtCl₄ salt*, m. 283–5° (decompn.)). The toxine reacts with 2 mols. HBr to give the *di-HBr salt*, m. 193–4° (decompn.). The dibromide was cyclized into *isohydroquininone*, m. 152–3°, by the action of 10% Na_2CO_3 and C_6H_6. Reduction of the ketone with Al isopropylate in dry C_6H_6 gave a mixt. of optical isomers of the isohydroquinine (I). To sep. the stereoisomers, these were converted into bitartrates and extd. with $CHCl_3$ and a little H_2O. The distn. residue was decompd. with dil. Na_2CO_3 and recrystd. from ether, giving an isomer of hydroquinine, m. 177.5–8°, $[\alpha]_D^{19}$ 135.9°. The aq. ext. of bitartrates with Na_2CO_3 formed a glass-like mass, m. below 50°, $[\alpha]_D^{19}$ 64.3°. It analyzed for I, but was a mixt. of stereoisomers, since its picrolonate gave a base with lower sp. rotation ($[\alpha]_D^{19}$ 52°). The compds. when tested on finches infected with *Plasmodium praecox*, showed no antimalarial action. The anesthetic action was retained. 30 references.

(I)

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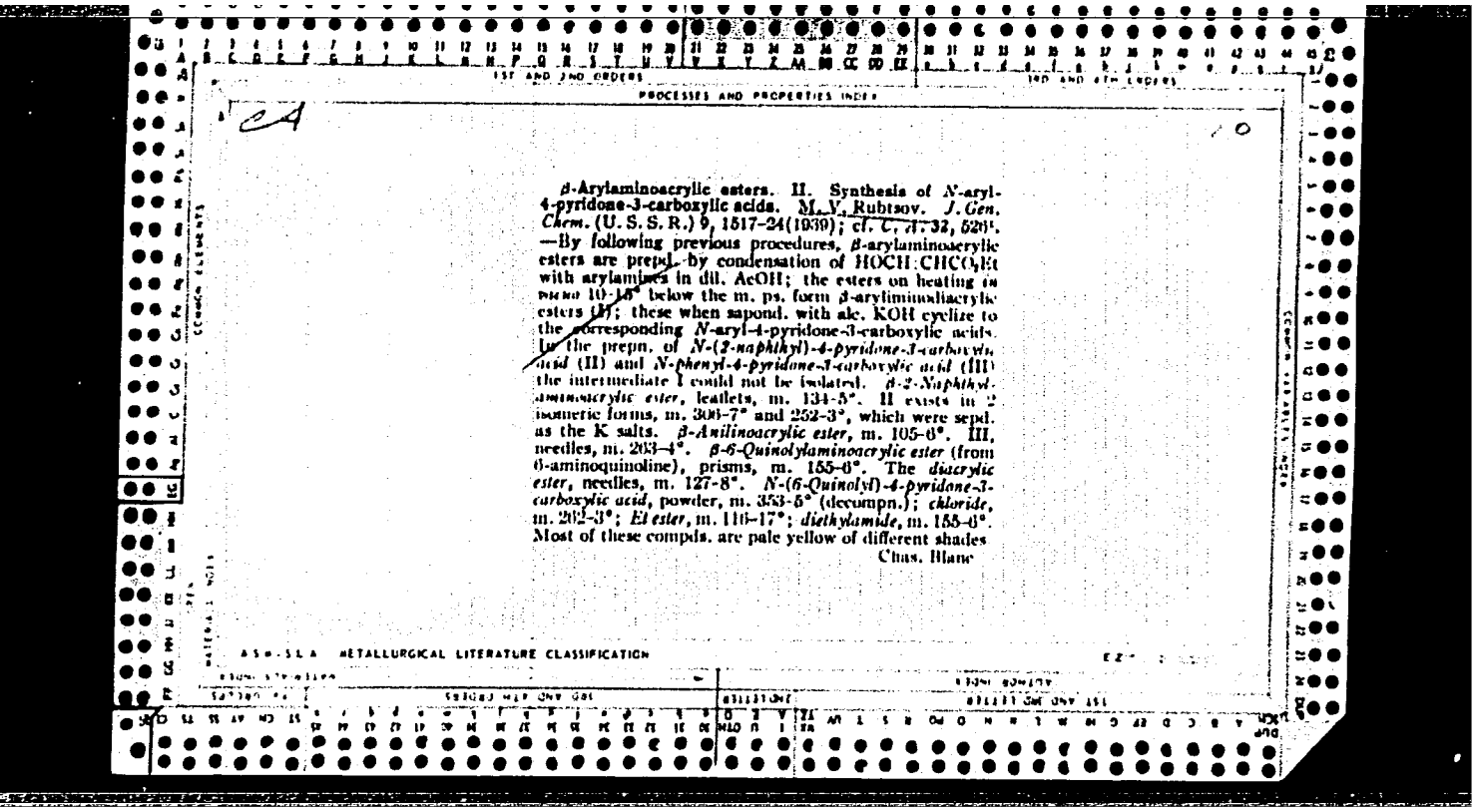

PROCESSES AND PROPERTIES INDEX

CA

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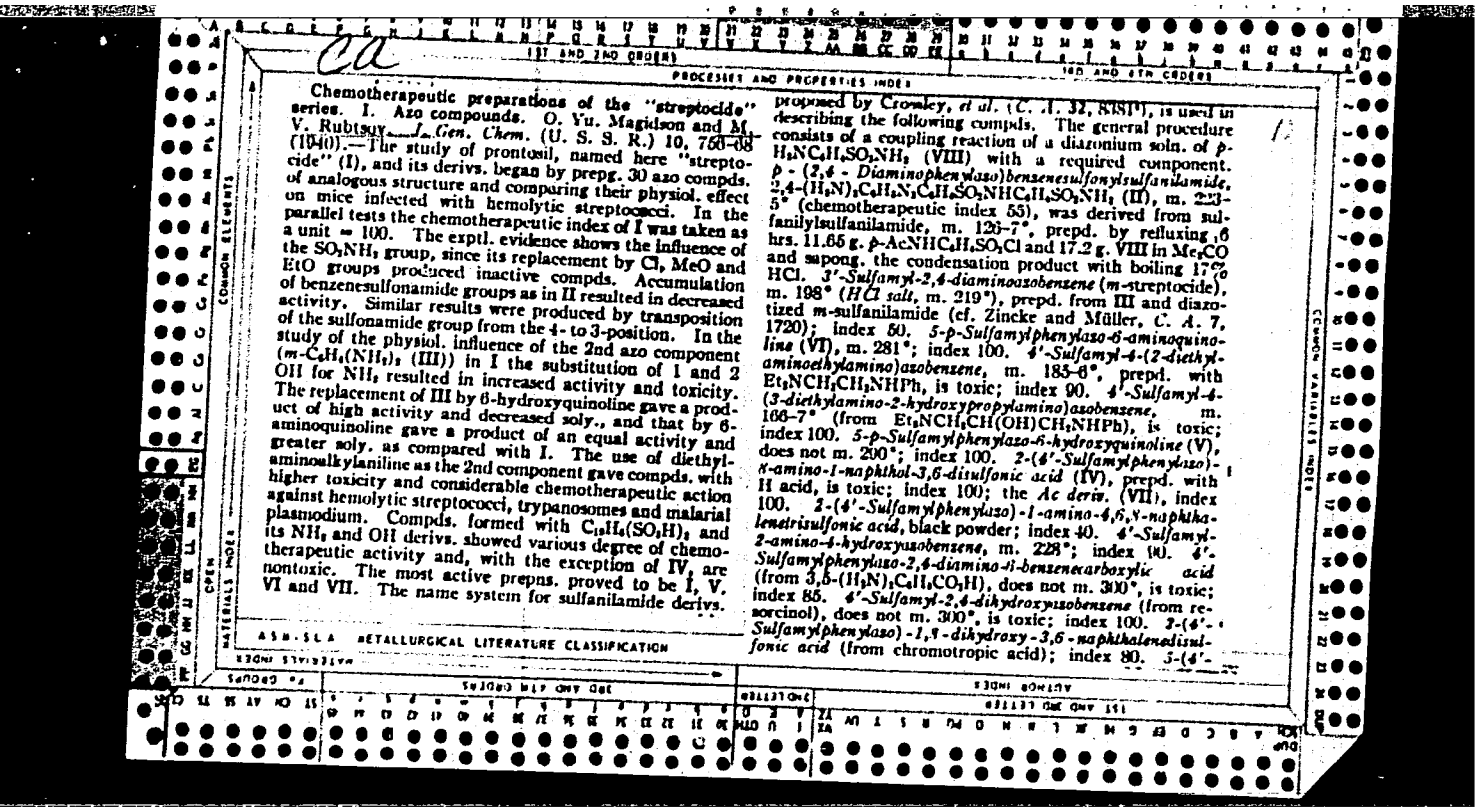
β-Arylaminoacrylic esters. II. Synthesis of *N*-aryl-4-pyridone-3-carboxylic acids. M. V. Rubtsov. *J. Gen. Chem.* (U. S. S. R.) 9, 1517–24(1939); cf. *C. A.* 32, 6201.—By following previous procedures, β-arylaminoacrylic esters are prepd. by condensation of HOCH:CHCO$_2$Et with arylamines in dil. AcOH; the esters on heating in vacuo 10–15° below the m. ps. form β-arylaminoallacrylic esters (II); these when saponf. with alc. KOH cyclize to the corresponding *N*-aryl-4-pyridone-3-carboxylic acids. In the prepn. of *N-(2-naphthyl)-4-pyridone-3-carboxylic acid* (II) and *N-phenyl-4-pyridone-3-carboxylic acid* (III) the intermediate I could not be isolated. *β-2-Naphthylaminoacrylic ester*, leaflets, m. 134–5°. II exists in 2 isomeric forms, m. 301–7° and 252–3°, which were sepd. as the K salts. *β-Anilinoacrylic ester*, m. 105–6°. III, needles, m. 203–4°. *β-6-Quinolylaminoacrylic ester* (from 6-aminoquinoline), prisms, m. 155–6°. The *diacrylic ester*, needles, m. 127–8°. *N-(6-Quinolyl)-4-pyridone-3-carboxylic acid*, powder, m. 353–5° (decompn.); *chloride*, m. 202–3°; *Et ester*, m. 116–17°; *diethylamide*, m. 155–6°. Most of these compds. are pale yellow of different shades

Chas. Blanc

A S M - S L A METALLURGICAL LITERATURE CLASSIFICATION



Chemotherapeutic preparations of the "streptocide" series. I. Azo compounds. O. Yu. Magidson and M. V. Rubtsov. *J. Gen. Chem.* (U. S. S. R.) 10, 760–68 (1940).—The study of prontosil, named here "streptocide" (I), and its derivs. began by prepg. 30 azo compds. of analogous structure and comparing their physiol. effect on mice infected with hemolytic streptococci. In the parallel tests the chemotherapeutic index of I was taken as a unit = 100. The exptl. evidence shows the influence of the SO_2NH_2 group, since its replacement by Cl, MeO and EtO groups produced inactive compds. Accumulation of benzenesulfonamide groups as in II resulted in decreased activity. Similar results were produced by transposition of the sulfonamide group from the 4- to 3-position. In the study of the physiol. influence of the 2nd azo component (m-$C_6H_4(NH_2)_2$ (III)) in I the substitution of 1 and 2 OH for NH_2 resulted in increased activity and toxicity. The replacement of III by 6-hydroxyquinoline gave a product of high activity and decreased soly., and that by 6-aminoquinoline gave a product of an equal activity and greater soly. as compared with I. The use of diethylaminoalkylaniline as the 2nd component gave compds. with higher toxicity and considerable chemotherapeutic action against hemolytic streptococci, trypanosomes and malarial plasmodium. Compds. formed with $C_6H_4(SO_2H)_2$ and its NH_2 and OH derivs. showed various degree of chemotherapeutic activity and, with the exception of IV, are nontoxic. The most active prepns. proved to be I, V, VI and VII. The name system for sulfanilamide derivs. proposed by *Crowley, et al.* (*C. A.* 32, 8181[1]), is used in describing the following compds. The general procedure consists of a coupling reaction of a diazonium soln. of p-$H_2NC_6H_4SO_2NH_2$ (VIII) with a required component. *p - (2,4 - Diaminophenylazo)benzenesulfonylsulfanilamide*, 2,4-$(H_2N)_2C_6H_3N_2C_6H_4SO_2NHC_6H_4SO_2NH_2$ (II), m. 223–5° (chemotherapeutic index 55), was derived from sulfanilylsulfanilamide, m. 126–7°, prepd. by refluxing 6 hrs. 11.65 g. p-$AcNHC_6H_4SO_2Cl$ and 17.2 g. VIII in Me_2CO and sapong. the condensation product with boiling 17% HCl. *3'-Sulfamyl-2,4-diaminoazobenzene* (m-streptocide), m. 198° (*HCl salt*, m. 219°), prepd. from III and diazotized m-sulfanilamide (cf. Zincke and Müller, *C. A.* 7, 1720); index 80. *5-p-Sulfamylphenylazo-6-aminoquinoline* (VI), m. 281°; index 100. *4'-Sulfamyl-4-(2-diethylaminoethylamino)azobenzene*, m. 185–6°, prepd. with $Et_2NCH_2CH_2NHPh$, is toxic; index 90. *4'-Sulfamyl-4-(3-diethylamino-2-hydroxypropylamino)azobenzene*, m. 166–7° (from $Et_2NCH_2CH(OH)CH_2NHPh$), is toxic; index 100. *5-p-Sulfamylphenylazo-6-hydroxyquinoline* (V), does not m. 290°; index 100. *2-(4'-Sulfamylphenylazo)-8-amino-1-naphthol-3,6-disulfonic acid* (IV), prepd. with H acid, is toxic; index 100; the *Ac deriv.* (VII), index 100. *2-(4'-Sulfamylphenylazo)-1-amino-4,6,8-naphthalenetrisulfonic acid*, black powder; index 40. *4'-Sulfamyl-2-amino-4-hydroxyazobenzene*, m. 228°; index 90. *4'-Sulfamylphenylazo-2,6-diamino-3-benzenecarboxylic acid* (from 3,5-$(H_2N)_2C_6H_3CO_2H$), does not m. 300°, is toxic; index 85. *4'-Sulfamyl-2,4-dihydroxyazobenzene* (from resorcinol), does not m. 300°, is toxic; index 100. *2-(4'-Sulfamylphenylazo)-1,8-dihydroxy-3,6-naphthalenedisulfonic acid* (from chromotropic acid); index 80. *5-(4'-*

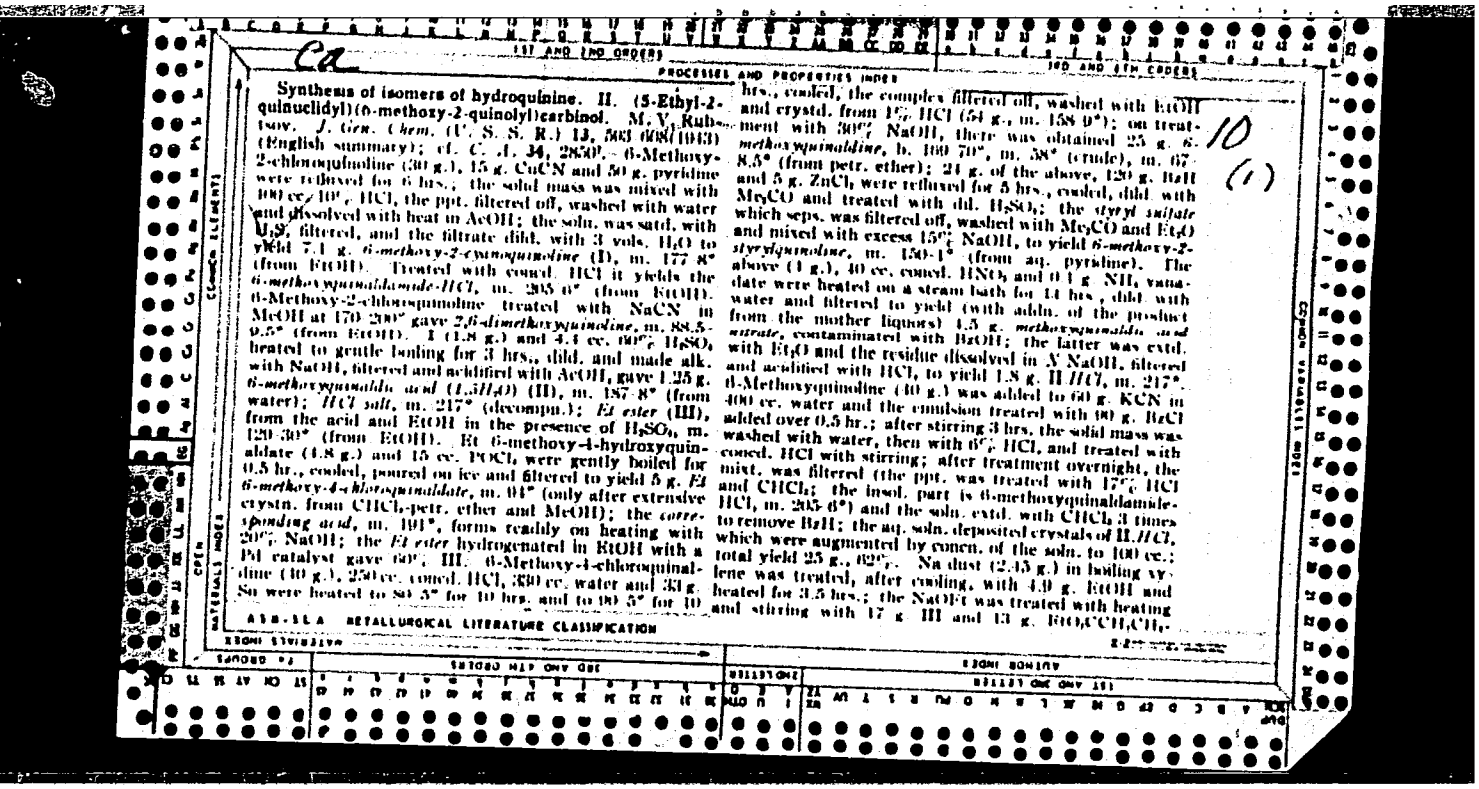
Sulfamylphenylazo)-2-hydroxybenzoic acid (from salicylic acid), m. 220° (decompn.); index 100. *5-(4'-Sulfamylphenylazo)-2-aminobenzoic acid* (from anthranilic acid), m. 235–6°; index 50. H. M. V. Rubtsov. *Ibid.* 831–43. —Derivs. of VIII with substituents in the amino and sulfamyl groups were prepd. and their physiol. actions were compared. In the parallel tests the chemotherapeutic index of VIII was taken as a unit = 80. In general, the therapeutic effect varied with the nature of the substituent in the amino group. Introduction of diethylaminoalkyls decreased greatly the therapeutic action and increased the toxicity. Acid radicals, linked by means of a methylene group, increased the activity and soly. as in IX. The benzyl group showed but little effect on the activity (X). Of the substituents in the sulfamyl group benzyl produced an insignificant change (XI), while sulfanilyl and *p*-H_2N-$C_6H_4SO_2NH$ greatly reduced the activity. The *p*-$H_2NC_6H_4$ group increased the activity (XII and XIII), which again was reduced by the presence of SO_3H in the substituent (XIV and XV). *p-Sulfamylphenylbenzylamine* (X), m. 174.5–76°, was prepd. from 7.3 g. BzH, 16 g. VIII.HCO_2H and 7.5 g. of 85% HCO_2H by heating the mixt. at 120–5° in an oil bath for 3 hrs. and dilg. with 30 ml. alc. The crude product was purified by heating it with 15% HCl, treating the soln. with dil. Na_2CO_3 and recrystg. from Me_2CO; index 70. *1-(p-Sulfamylphenylamino)-3-diethylaminopropane*, m. 140–2°, prepd. from $ClCH_2CH_2CH_2NEt_2.HCl$ and VIII by heating at 120° for 5 hrs., is toxic; index 45. *1-(p-Sulfamylphenylamino)-2-hydroxy-3-diethylaminopropane* (from $ClCH_2CH(OH)CH_2NEt_2.HCl$), m. 112°, is toxic; index 10. *p-Sulfamylphenylglycine* (IX), m. 295–6° (decompn.), was prepd. by gently heating 7 g. CH_2ClCO_2H in 15 ml. of 20% NaOH dild. with 20 ml. H_2O, 7.5 g. of cryst. NaOAc and 8.6 g. VIII and recrystg. from 50% alc.; index 125. *p-Sulfamylphenylglycinamide*, m. 203–4°, was prepd. by refluxing VIII and $CH_2ClCONH_2$ in C_5H_5N for 2.5 hrs., dilg. with 2 vols. H_2O and acidifying with HCl to Congo red; index 85. *Na p-sulfamylphenylsulfamate* was prepd. by introducing 9 g. $ClSO_3H$ and 8.6 g. VIII into 50 g. C_5H_5N at 30–40°, treating the mixt. with 7.3 g. NaOH in 15 ml. H_2O, evapg. *in vacuo* to dryness, dissolving in 40 ml. H_2O and crystg. at 32°; index 20. *p-$H_2NO_2SC_6H_4NHCH_2SO_3Na$* was formed by treating 17.2 g. VIII and 26.7 g. of 50% $NaHSO_3$ with 9.6 g. of 38.2% HCHO in 38 ml. H_2O and stirring the mixt. at 50° for 3 hrs.; index 90. *p-$NH_2C_6H_4SO_2NHCH_2Ph$* (XI), m. 119–9.5°, was prepd. in 84% yield by sapon. of *p*-AcNHC$_6$H$_4$SO$_2$NHCH$_2$Ph obtained by treating 11.7 g. *p*-ClO_2S-C_6H_4NHAc and 10.7 g. $PhCH_2NH_2$ and recrystg. from 60% alc.; index 65. *Disulfanilimide*, m. 295–6° (decompd.), was prepd. by a modified method of Crossley, *et al.* (loc. cit.); index 5. *2-Amino-5-sulfanilamidobenzenesulfonic acid* (XIV) (cf. Crossley, *loc. cit.*), index 60. *p*-$NH_2C_6H_4SO_2NHC_6H_4NH_2$-*p* (XII), m. 158–8.5°, index 100. *p-Bis(sulfanilamido)benzene* (XIII), m. 268–9° (decompn.), index 100. *2,5-Bis(sulfanilamido)benzenesulfonic acid* (XV), index 25.

Chas. Blanc

RUBTSOV, M.V.

"Chemo-Therapeutic Substances of the Streptocide Series-II." Zhur. Obshch, KHim. 10 No. 9, 1940. Synthetic Dept., Scientific-Research Chemico-Pharmaceutical Inst. Imeni Ordzhonikidze. Moscos. Received 20, Nov. 1939

Report U-1627, 11 Jan. 52



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PROCESSES AND PROPERTIES INDEX

Synthesis of isomers of hydroquinine. II. (5-Ethyl-2-quinuclidyl)(6-methoxy-2-quinolyl)carbinol. M. V. Rubtsov. *J. Gen. Chem.* (U. S. S. R.) **13**, 503-608(1943) (English summary); cf. *C. A.* **34**, 2850⁹. 6-Methoxy-2-chloroquinoline (30 g.), 15 g. CuCN and 50 g. pyridine were refluxed for 6 hrs.; the solid mass was mixed with 100 cc. 10% HCl, the ppt. filtered off, washed with water and dissolved with heat in AcOH; the soln. was satd. with H_2S, filtered, and the filtrate dild. with 3 vols. H_2O to yield 7.1 g. *6-methoxy-2-cyanoquinoline* (I), m. 177.8° (from EtOH). Treated with concd. HCl it yields the *6-methoxyquinaldamide-HCl*, m. 205.6° (from EtOH). 6-Methoxy-2-chloroquinoline treated with NaCN in MeOH at 170-200° gave *2,6-dimethoxyquinoline*, m. 88.5-9.5° (from EtOH). I (1.8 g.) and 4.4 cc. 60% H_2SO_4 heated to gentle boiling for 3 hrs., dild. and made alk. with NaOH, filtered and acidified with AcOH, gave 1.25 g. *6-methoxyquinaldic acid* (*1,5H,O*) (II), m. 187-8° (from water); *HCl salt*, m. 217° (decompn.); *Et ester* (III), from the acid and EtOH in the presence of H_2SO_4, m. 120-30° (from EtOH). Et 6-methoxy-4-hydroxyquinaldate (1.8 g.) and 15 cc. $POCl_3$ were gently boiled for 0.5 hr., cooled, poured on ice and filtered to yield 5 g. *Et 6-methoxy-4-chloroquinaldate*, m. 94° (only after extensive crystn. from $CHCl_3$-petr. ether and MeOH); the *corresponding acid*, m. 191°, forms readily on heating with 20% NaOH; the *Et ester* hydrogenated in EtOH with a Pd catalyst gave 60% III. 6-Methoxy-4-chloroquinaldine (10 g.), 250 cc. concd. HCl, 350 cc. water and 33 g. Sn were heated to 80.5° for 10 hrs. and to 90.5° for 10 hrs., cooled, the complex filtered off, washed with EtOH and crystd. from 1% HCl (54 g., m. 158.9°); on treatment with 30% NaOH, there was obtained 25 g. *6-methoxyquinaldine*, b. 100-7°, m. 38° (crude), m. 67-8.5° (from petr. ether); 21 g. of the above, 120 g. BzH and 5 g. $ZnCl_2$ were refluxed for 5 hrs., cooled, dild. with Me_2CO and treated with dil. H_2SO_4; the *styryl sulfate* which seps. was filtered off, washed with Me_2CO and Et_2O and mixed with excess 15% NaOH, to yield *6-methoxy-2-styrylquinoline*, m. 150-1° (from aq. pyridine). The above (1 g.), 40 cc. concd. HNO_3 and 0.1 g. NH_4 vanadate were heated on a steam bath for 1.4 hrs., dild. with water and filtered to yield (with addn. of the product from the mother liquors) 1.5 g. *methoxyquinaldic acid nitrate*, contaminated with BzOH; the latter was extd. with Et_2O and the residue dissolved in N NaOH, filtered and acidified with HCl, to yield 1.8 g. II *HCl*, m. 217°. 6-Methoxyquinoline (40 g.) was added to 60 g. KCN in 400 cc. water and the emulsion treated with 80 g. BzCl added over 0.5 hr.; after stirring 3 hrs. the solid mass was washed with water, then with 6% HCl, and treated with concd. HCl with stirring; after treatment overnight, the mixt. was filtered (the ppt. was treated with 17% HCl and $CHCl_3$; the insol. part is 6-methoxyquinaldamide-HCl, m. 205.6°) and the soln. extd. with $CHCl_3$ 3 times to remove BzH; the aq. soln. deposited crystals of II *HCl*, which were augmented by concn. of the soln. to 100 cc.; total yield 25 g., 62%. Na dust (2.45 g.) in boiling xylene was treated, after cooling, with 4.9 g. EtOH and heated for 3.5 hrs.; the NaOEt was treated with heating and stirring with 17 g. III and 13 g. $EtO_2CCH_2CH_2$-

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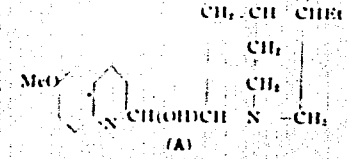
(1)

A58-31A METALLURGICAL LITERATURE CLASSIFICATION

$CH_2:CH_2.NBz.CH_2.CHEt$; after 7 hrs. at 80-90°, the mass was cooled and mixed with 200 cc. 18% HCl, filtered, acidified from xylene and gently boiled for 4 hrs., extd. with Et_2O and the aq. soln. made alk. with 40% NaOH; the resulting *isohydroquinotoxine* extd. with Et_2O and purified through the *di-HBr salt* (m. 192-3°), recrystd. from EtOH, m. 195-6°; *dipicrate*, m. 167-8°; *mono-HCl salt*, m. 226.5-8°. Isohydroquinotoxine-2HBr (5.17 g.) in 16 cc. 48% HBr was treated at 65-70° with 10.1 g. of 9.43% Br in 48% HBr which was added dropwise over 20 min.; the mixt. was heated to 80° and stirred at this temp. for 20 min., and the excess HBr removed *in vacuo* at 50°; the residue treated with 10% NaOH and extd. with benzene, yielded on evapn. of the latter and recrystn. from Et_2O 3.7 g. *3-ethyl-2-quinuclidyl-6-methoxy-2-quinolyl ketone*, m. 125-6° (from ligroin); a freshly prepd. soln. of this compd. (*isohydroquinhanone*) in 80% EtOH has $[\alpha]_D^{\text{H}}$ 163.4°, which after 18 hrs. standing stabilizes at $[\alpha]_D^{\text{H}}$ 92.0°. The above (2.62 g.) in 16 cc. *N* HCl was treated with 2 cc. 2% $PdCl_2$; after shaking, until the yellow ppt. was thoroughly dispersed, 8 cc. H_2O and 0.25 g. activated charcoal were added and the mixt. hydrogenated at room temp. under mild H pressure; on completion, removal of the catalyst and addn. of alkali the product was extd. with Et_2O, which on evapn. yielded a glassy mixture of isomeric *isohydroquinines* (probably stereoisomers of A).



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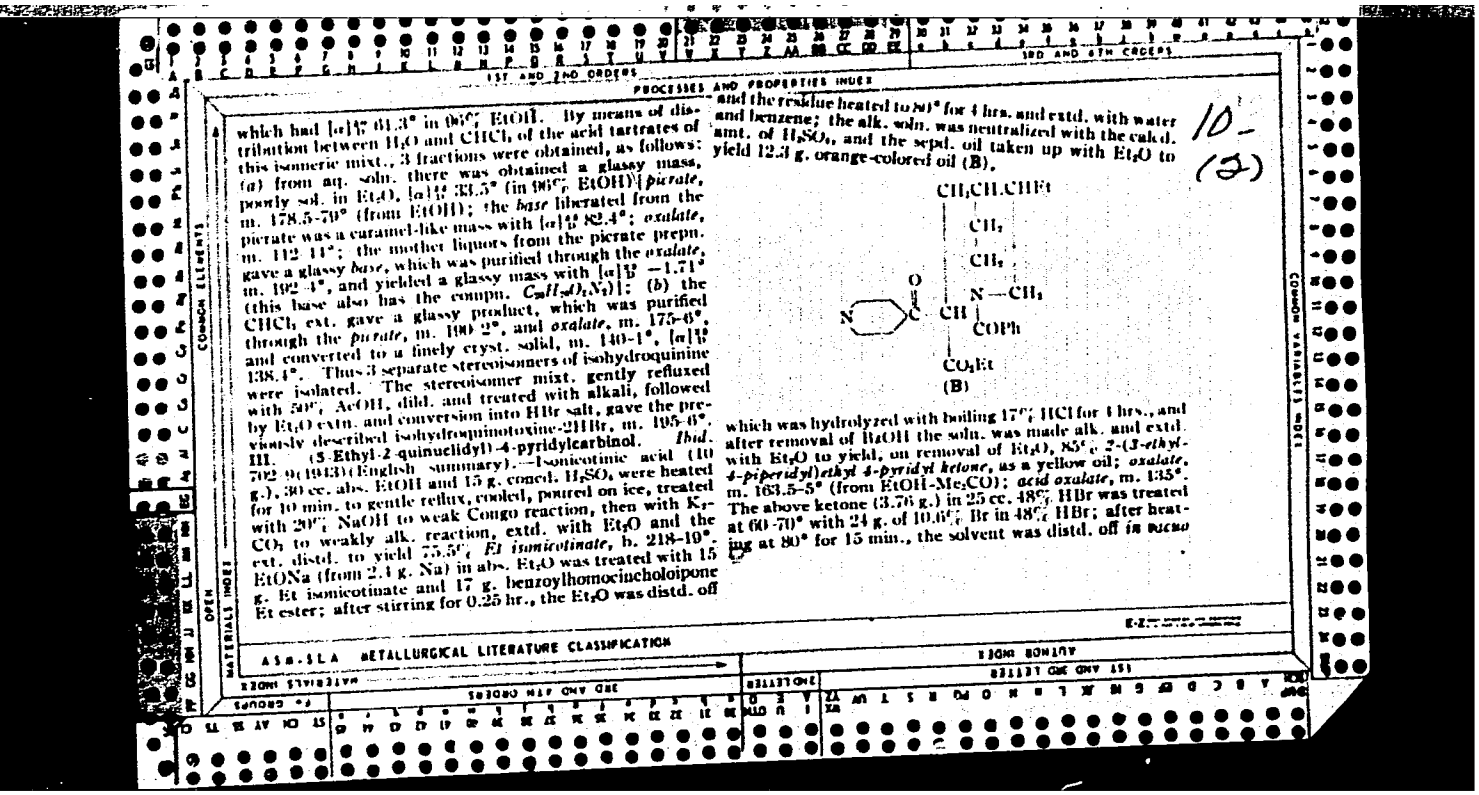


PROCESSES AND PROPERTIES INDEX

which had $[\alpha]_D^{17}$ 81.3° in 96% EtOH. By means of distribution between H_2O and $CHCl_3$ of the acid tartrates of this isomeric mixt., 3 fractions were obtained, as follows: (*a*) from aq. soln. there was obtained a glassy mass, poorly sol. in Et_2O, $[\alpha]_D^{18}$ 33.5° (in 96% EtOH) [*picrate*, m. 178.5-79° (from EtOH); the *base* liberated from the picrate was a caramel-like mass with $[\alpha]_D^{18}$ 82.4°; *oxalate*, m. 112-14°; the mother liquors from the picrate prepn. gave a glassy *base*, which was purified through the *oxalate*, m. 192-4°, and yielded a glassy mass with $[\alpha]_D^{18}$ −1.71° (this base also has the compn. $C_{20}H_{24}ON_2$)]; (*b*) the $CHCl_3$ ext. gave a glassy product, which was purified through the *picrate*, m. 190-2°, and *oxalate*, m. 175-6°, and converted to a finely cryst. solid, m. 140-1°, $[\alpha]_D^{18}$ 138.4°. Thus 3 separate stereoisomers of isohydroquinine were isolated. The stereoisomer mixt. gently refluxed with 50% AcOH, dild. and treated with alkali, followed by Et_2O extn. and conversion into HBr salt, gave the previously described isohydroquinotoxine-2HBr, m. 195-6°. III. (5-Ethyl-2-quinuclidyl)-4-pyridylcarbinol. *Ibid.* 702-9(1943)(English summary).—Isonicotinic acid (10 g.), 30 cc. abs. EtOH and 15 g. concd. H_2SO_4 were heated for 10 min. to gentle reflux, cooled, poured on ice, treated with 20% NaOH to weak Congo reaction, then with K_2CO_3 to weakly alk. reaction, extd. with Et_2O and the ext. distd. to yield 75.5% *Et isonicotinate*, b. 218-19°. EtONa (from 2.4 g. Na) in abs. Et_2O was treated with 15 g. Et isonicotinate and 17 g. benzoylhomocincholoipone Et ester; after stirring for 0.25 hr., the Et_2O was distd. off and the residue heated to 80° for 4 hrs. and extd. with water and benzene; the alk. soln. was neutralized with the calcd. amt. of H_2SO_4, and the sepd. oil taken up with Et_2O to yield 12.5 g. orange-colored oil (**B**).

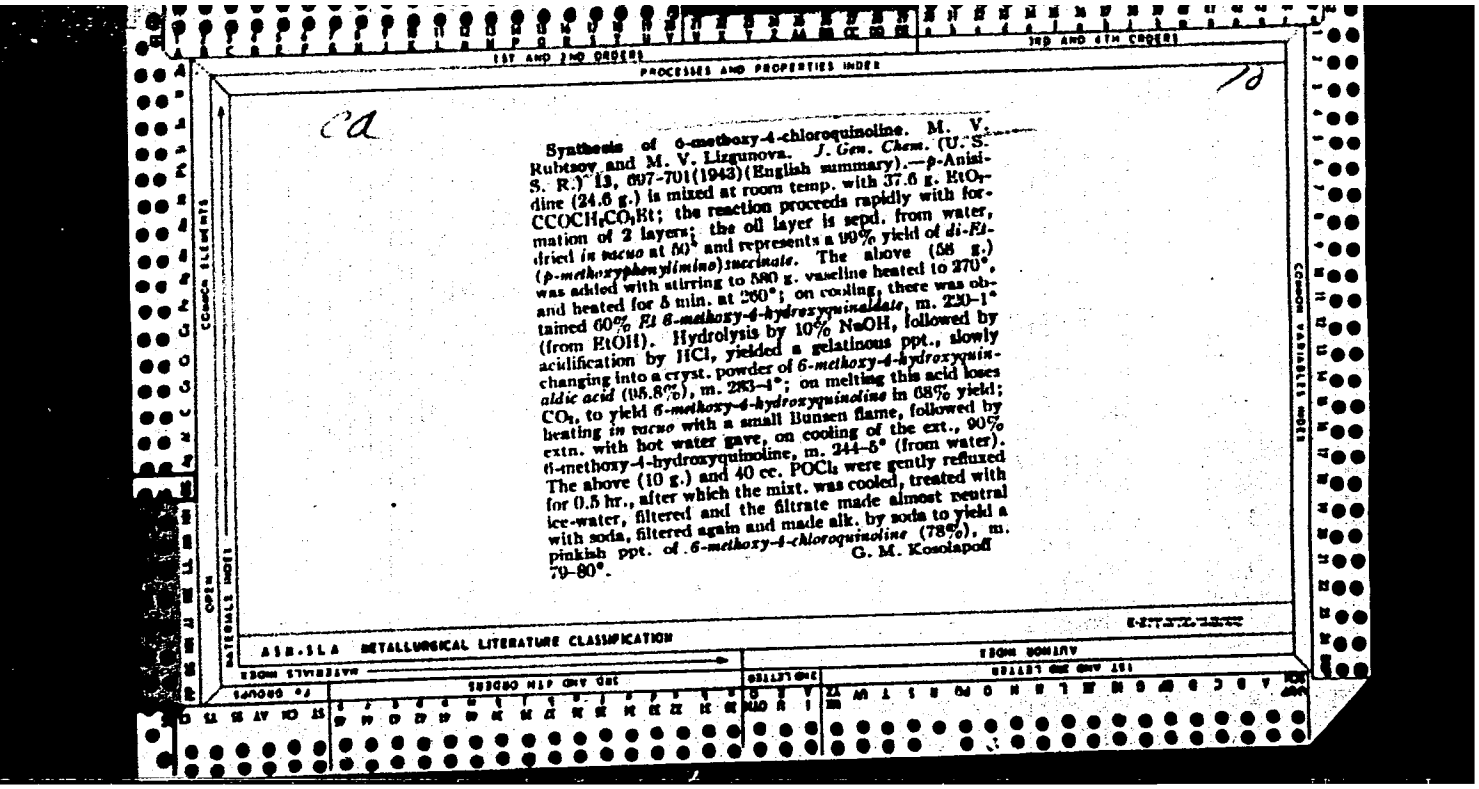
10-(2)

(B)

which was hydrolyzed with boiling 17% HCl for 4 hrs., and after removal of EtOH the soln. was made alk. and extd. with Et_2O to yield, on removal of Et_2O, 85% *2-(3-ethyl-4-piperidyl)ethyl 4-pyridyl ketone*, as a yellow oil; *oxalate*, m. 163.5-5° (from EtOH-Me_2CO); *acid oxalate*, m. 135°. The above ketone (3.76 g.) in 25 cc. 48% HBr was treated at 60-70° with 24 g. of 10.6% Br in 48% HBr; after heating at 80° for 15 min., the solvent was distd. off *in vacuo*

and the residue mixed with 10% Na_2CO_3 and Et_2O; evapn. of Et_2O gave 2.9 g. crude product, purified by warm petr. ether to give 2.2 g. pure *5-ethyl-3-quinuclidyl 4-pyridyl ketone*, m. 91–2°; the fresh soln. has $[\alpha]_D^{25}$ 81.6°; after 48 hrs. $[\alpha]_D^{25}$ 97.5°. The corresponding *carbinol* was prepd. by hydrogenation in the presence of $PdCl_2$ and activated charcoal in *N* HCl at room temp.; the resulting mixt. of optical isomers of the carbinol was obtained as a viscous mass with $[\alpha]_D^{25}$ 61.4°. Sepn. was effected through *d*-camphorsulfonic acid salts and distribution between water and $CHCl_3$. The 3 isomers of the (*5-ethyl-3-quinuclidyl*)-*4-pyridylmethanol* thus obtained had the following consts.: (*a*) m. 171–2° (from Me_2CO), $[\alpha]_D^{25}$ 87.3° (*di-HCl salt* m. 212–13.5° (from EtOH)); (*b*) m. 110–11°, $[\alpha]_D^{25}$ 34.3° (*di-HCl salt*, m. 202–3° (from EtOH)); and (*c*) m. 91–2° (from petr. ether), $[\alpha]_D^{25}$ 126.9° (*di-HCl salt*, m. 198–9° (from EtOH-Me_2CO)).

G. M. Kosolapoff



PROCESSES AND PROPERTIES INDEX

Ca

Synthesis of 6-methoxy-4-chloroquinoline. M. V. Rubtsov and M. V. Lizgunova. *J. Gen. Chem.* (U. S. S. R.) 13, 697-701(1943)(English summary).—*p*-Anisidine (24.6 g.) is mixed at room temp. with 37.6 g. $EtO_2CCOCH_2CO_2Et$; the reaction proceeds rapidly with formation of 2 layers; the oil layer is sepd. from water, dried *in vacuo* at 80° and represents a 99% yield of *di-Et (p-methoxyphenylimino)succinate*. The above (58 g.) was added with stirring to 580 g. vaseline heated to 270°, and heated for 5 min. at 260°; on cooling, there was obtained 60% *Et 6-methoxy-4-hydroxyquinaldate*, m. 220–1° (from EtOH). Hydrolysis by 10% NaOH, followed by acidification by HCl, yielded a gelatinous ppt., slowly changing into a cryst. powder of *6-methoxy-4-hydroxyquinaldic acid* (95.8%), m. 283–4°; on melting this acid loses CO_2, to yield *6-methoxy-4-hydroxyquinoline* in 68% yield; heating *in vacuo* with a small Bunsen flame, followed by extn. with hot water gave, on cooling of the ext., 90% 6-methoxy-4-hydroxyquinoline, m. 244–5° (from water). The above (10 g.) and 40 cc. $POCl_3$ were gently refluxed for 0.5 hr., after which the mixt. was cooled, treated with ice-water, filtered and the filtrate made almost neutral with soda, filtered again and made alk. by soda to yield a pinkish ppt. of *6-methoxy-4-chloroquinoline* (78%), m. 79–80°.

G. M. Kosolapoff

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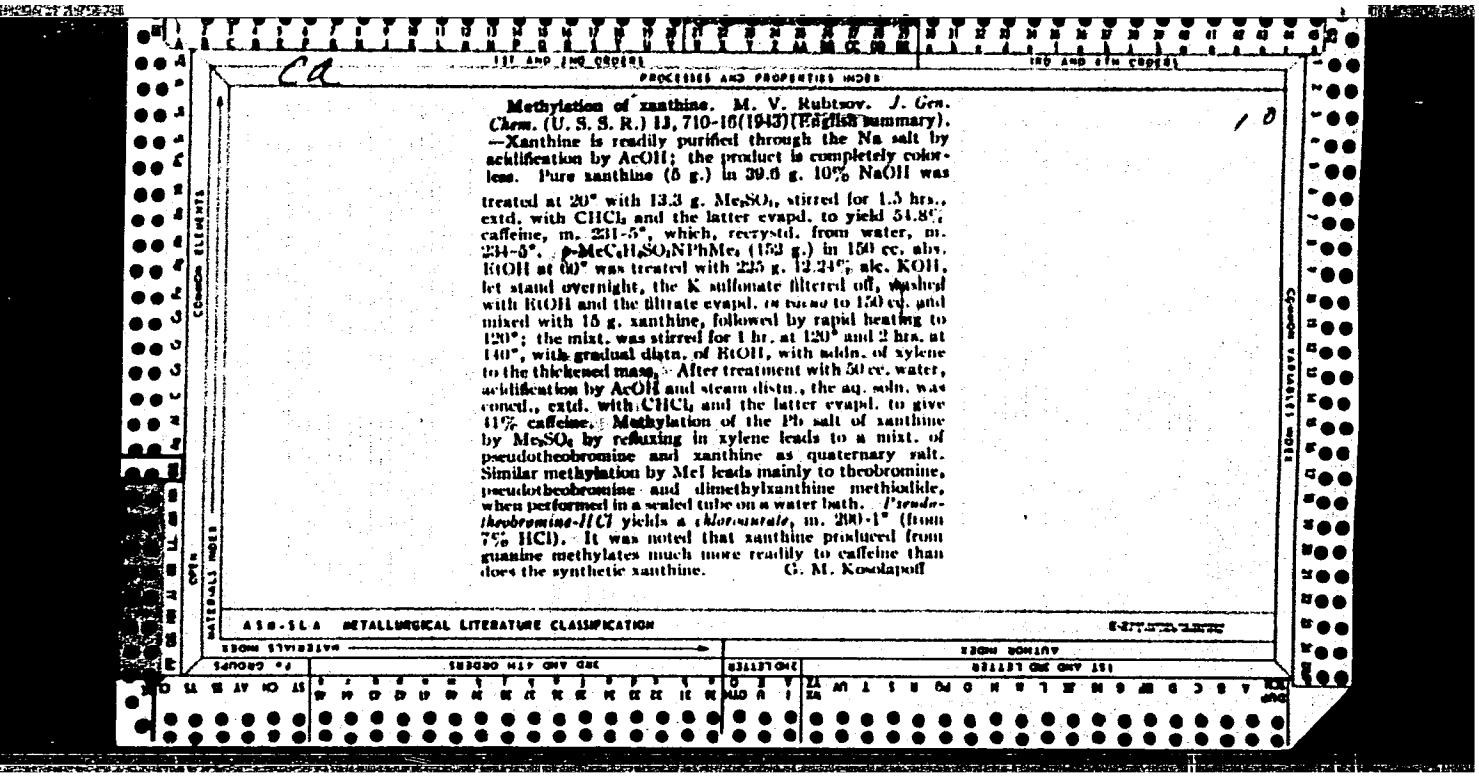
ASB-SLA METALLURGICAL LITERATURE CLASSIFICATION

RUBTZOV, M. V.

"Synthesis of Compounds of the Quinine Type. III. /5-Ethyl-quinuclidyl-(2)-/Pyridyl-(4)-/ -Carbinol". Rubtzov, M. V. (p.702)

SO: Journal of General Chemistry (Zhurnal Obshchei Khimii) 1943, Volume 13, no. 9-10.

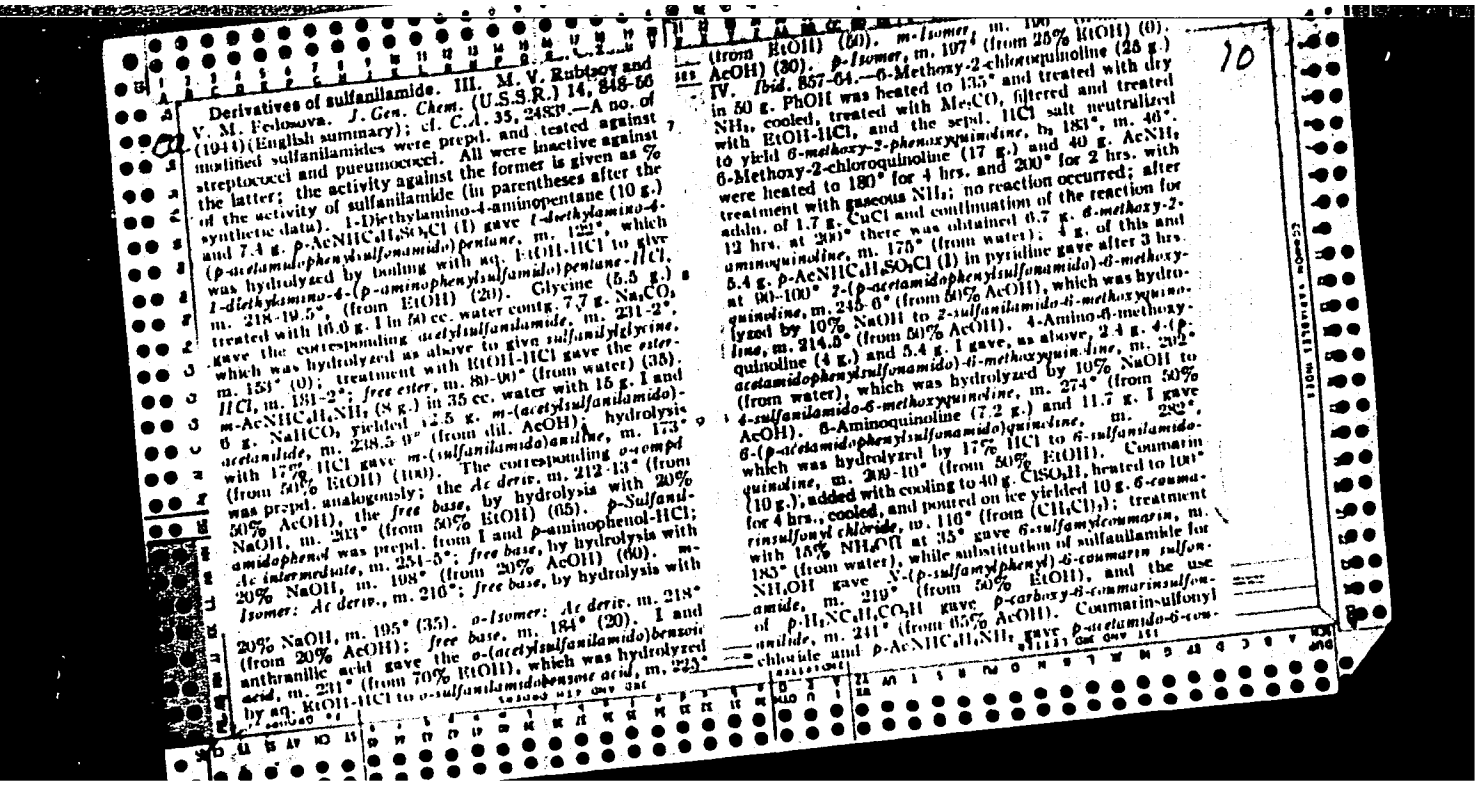


Ca

PROCESSES AND PROPERTIES INDEX

Methylation of xanthine. M. V. Rubtsov. *J. Gen. Chem.* (U. S. S. R.) 13, 710-16(1943)(English summary). —Xanthine is readily purified through the Na salt by acidification by AcOH; the product is completely colorless. Pure xanthine (5 g.) in 39.6 g. 10% NaOH was treated at 20° with 13.3 g. Me_2SO_4, stirred for 1.5 hrs., extd. with $CHCl_3$ and the latter evapd. to yield 54.8% caffeine, m. 231-5°, which, recrystd. from water, m. 234-5°. *p*-$MeC_6H_4SO_3NPhMe_2$ (153 g.) in 150 cc. abs. EtOH at 60° was treated with 225 g. 12.24% alc. KOH, let stand overnight, the K sulfonate filtered off, washed with EtOH and the filtrate evapd. *in vacuo* to 150 cc. and mixed with 15 g. xanthine, followed by rapid heating to 120°; the mixt. was stirred for 1 hr. at 120° and 2 hrs. at 140°, with gradual distn. of EtOH, with addn. of xylene to the thickened mass. After treatment with 50 cc. water, acidification by AcOH and steam distn., the aq. soln. was concd., extd. with $CHCl_3$ and the latter evapd. to give 41% caffeine. **Methylation** of the Pb salt of xanthine by Me_2SO_4 by refluxing in xylene leads to a mixt. of pseudotheobromine and xanthine as quaternary salt. Similar methylation by MeI leads mainly to theobromine, pseudotheobromine and dimethylxanthine methiodide, when performed in a sealed tube on a water bath. *Pseudotheobromine-HCl* yields a *chloroaurate*, m. 200-1° (from 7% HCl). It was noted that xanthine produced from guanine methylates much more readily to caffeine than does the synthetic xanthine. G. M. Kosolapoff

A S M - S L A METALLURGICAL LITERATURE CLASSIFICATION



Derivatives of sulfanilamide. III. M. V. Rubtsov and V. M. Fedosova. *J. Gen. Chem.* (U.S.S.R.) 14, 848-66 (1944)(English summary); cf. *C.A.* 35, 2483⁹.—A no. of modified sulfanilamides were prepd. and tested against streptococci and pneumococci. All were inactive against the latter; the activity against the former is given as % of the activity of sulfanilamide (in parentheses after the synthetic data). 1-Diethylamino-4-aminopentane (10 g.) and 7.4 g. *p*-AcNHC$_6$H$_4$SO$_2$Cl (I) gave *1-diethylamino-4-(p-acetamidophenylsulfonamido)pentane*, m. 122°, which was hydrolyzed by boiling with aq. EtOH-HCl to give *1-diethylamino-4-(p-aminophenylsulfamido)pentane-HCl*, m. 218-19.5°, (from EtOH) (20). Glycine (5.5 g.) in 10.6 g. 1 in 50 cc. water contg. 7.7 g. Na_2CO_3 treated with 16.0 g. I in 50 cc. water contg. 7.7 g. Na_2CO_3 gave the corresponding *acetylsulfanilamide*, m. 231-2°, which was hydrolyzed as above to give *sulfanilylglycine*, m. 153° (0); treatment with EtOH-HCl gave the *ester-HCl*, m. 181-2°; *free ester*, m. 80-90° (from water) (35). *m*-AcNHC$_6$H$_4$NH$_2$ (8 g.) in 35 cc. water with 15 g. I and 6 g. $NaHCO_3$ yielded 12.5 g. *m-(acetylsulfanilamido)-acetanilide*, m. 248.5-9° (from dil. AcOH); hydrolysis with 17% HCl gave *m-(sulfanilamido)aniline*, m. 173° (from 50% EtOH) (100). The corresponding *o*-compd. was prepd. analogously; the *Ac deriv.* m. 212-13° (from 50% AcOH), the *free base*, by hydrolysis with 20% NaOH, m. 203° (from 50% EtOH) (65). *p-Sulfanilamidophenol* was prepd. from I and *p*-aminophenol-HCl; *Ac intermediate*, m. 254-5°; *free base*, by hydrolysis with 20% NaOH, m. 198° (from 20% AcOH) (60). *m-Isomer*: *Ac deriv.*, m. 216°; *free base*, by hydrolysis with 20% NaOH, m. 195° (35). *o-Isomer*: *Ac deriv.* m. 218° (from 20% AcOH); *free base*, m. 184° (20). I and anthranilic acid gave the *o-(acetylsulfanilamido)benzoic acid*, m. 231° (from 70% EtOH), which was hydrolyzed by aq. EtOH-HCl to *o-sulfanilamidobenzoic acid*, m. 225° (from EtOH) (50). *m-Isomer*, m. 190° (from 25% EtOH) (30). *p-Isomer*, m. 197° (from 25% EtOH) (0).

IV. *Ibid.* 857-64.—6-Methoxy-2-chloroquinoline (25 g.) in 50 g. PhOH was heated to 135° and treated with dry NH_3, cooled, treated with Me_2CO, filtered and treated with EtOH-HCl, and the sepd. HCl salt neutralized to yield *6-methoxy-2-phenoxyquinoline*, b$_{15}$ 183°, m. 46°. 6-Methoxy-2-chloroquinoline (17 g.) and 40 g. AcNH$_2$ were heated to 180° for 4 hrs. and 200° for 2 hrs. with treatment with gaseous NH_3; no reaction occurred; after addn. of 1.7 g. CuCl and continuation of the reaction for 12 hrs. at 200° there was obtained 0.7 g. *6-methoxy-2-aminoquinoline*, m. 175° (from water); 4 g. of this and 5.4 g. *p*-AcNHC$_6$H$_4$SO$_2$Cl (I) in pyridine gave after 3 hrs. at 90-100° *2-(p-acetamidophenylsulfonamido)-6-methoxyquinoline*, m. 245.6° (from 50% AcOH), which was hydrolyzed by 10% NaOH to *2-sulfanilamido-6-methoxyquinoline*, m. 214.5° (from 50% AcOH). 4-Amino-6-methoxyquinoline (4 g.) and 5.4 g. I gave, as above, 2.4 g. *4-(p-acetamidophenylsulfonamido)-6-methoxyquinoline*, m. 202° (from water), which was hydrolyzed by 10% NaOH to *4-sulfanilamido-6-methoxyquinoline*, m. 274° (from 50% AcOH). 6-Aminoquinoline (7.2 g.) and 11.7 g. I gave *6-(p-acetamidophenylsulfonamido)quinoline*, m. 282°, which was hydrolyzed by 17% HCl to *6-sulfanilamidoquinoline*, m. 209-10° (from 50% EtOH). Coumarin (10 g.), added with cooling to 40 g. $ClSO_3H$, heated to 100° for 4 hrs., cooled, and poured on ice yielded 10 g. *6-coumarinsulfonyl chloride*, m. 110° (from $(CH_2Cl)_2$); treatment with 15% NH_4OH at 35° gave *6-sulfamylcoumarin*, m. 185° (from water), while substitution of sulfanilamide for NH_4OH gave *N-(p-sulfamylphenyl)-6-coumarin sulfonamide*, m. 219° (from 50% EtOH), and the use of *p*-$H_2NC_6H_4CO_2H$ gave *p-carboxy-6-coumarinsulfonamide*, m. 241° (from 65% AcOH). Coumarinsulfonyl chloride and *p*-AcNHC$_6$H$_4$NH$_2$ gave *p-acetamido-6-cou-*

marinsulfonanilide, m. 280° (from 75% AcOH), which was hydrolyzed by 10% NaOH to *p-amino-6-coumarinsulfonanilide*, m. 300° (from 50% EtOH). 6-Aminocoumarin (2.9 g.) with 2.4 g. I in Me_2CO gave 3.5 g. *6-(p-acetamidophenylsulfonamido)coumarin*, m. 230° (from 75% AcOH), which was hydrolyzed with 10% NaOH to *6-sulfanilamidocoumarin*, m. 191° (from 80% EtOH). Only the last compd. showed promising activity against streptococci, pneumococci, and staphylococci.

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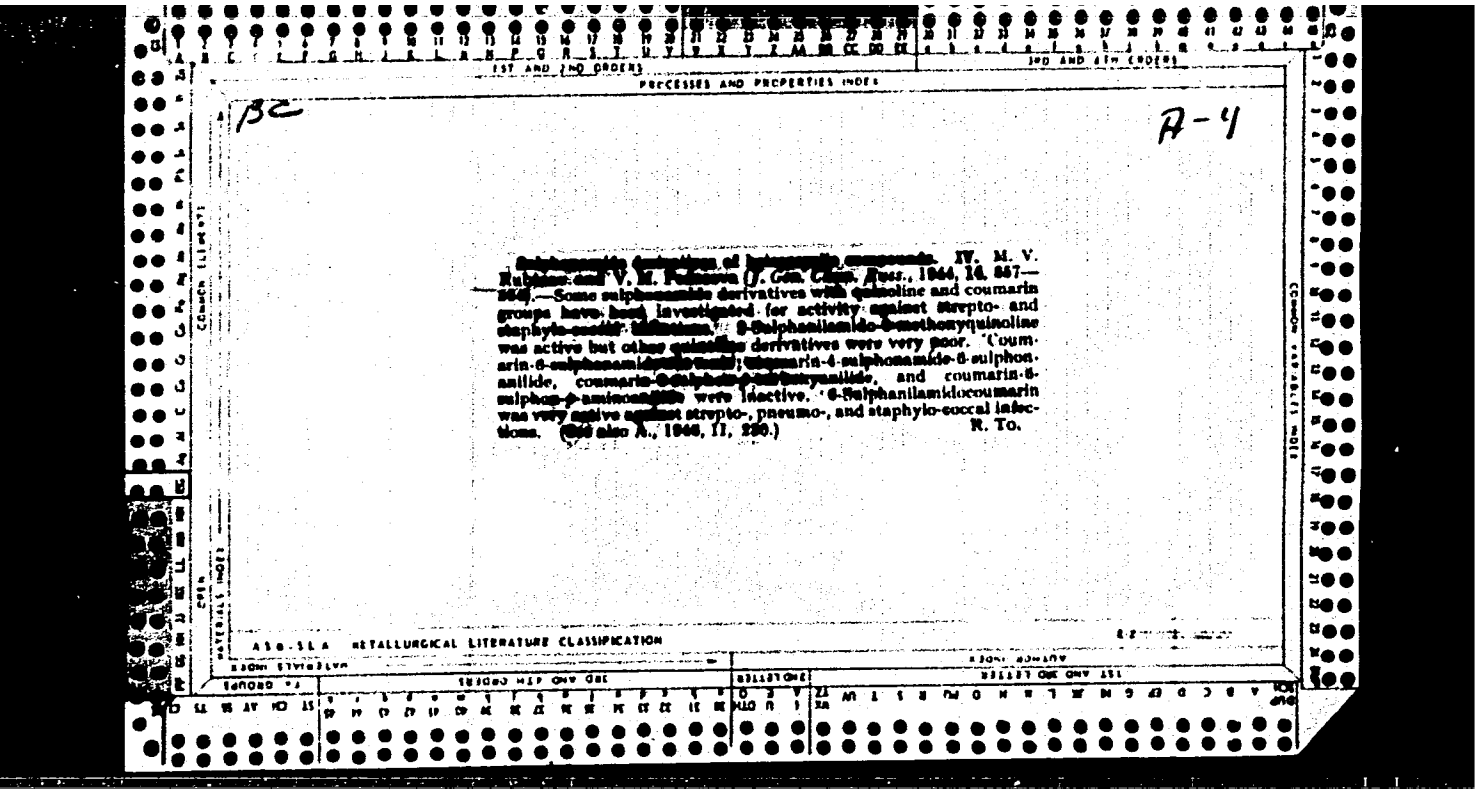

PROCESSES AND PROPERTIES INDEX

B2

A-4

Sulphonamide derivatives of heterocyclic compounds. IV. M. V. Rubtsov and V. M. Peshkova (*J. Gen. Chem. Russ.*, 1944, 14, 867—868).—Some sulphonamide derivatives with quinoline and coumarin groups have been investigated for activity against strepto- and staphylo-coccal infections. 6-Sulphanilamido-8-methoxyquinoline was active but other quinoline derivatives were very poor. Coumarin-6-sulphonamide; coumarin-4-sulphonamide-6-sulphonanilide, coumarin-6-sulphon-*p*-anisidyl, and coumarin-6-sulphon-*p*-aminoanilide were inactive. 6-Sulphanilamidocoumarin was very active against strepto-, pneumo-, and staphylo-coccal infections. (See also A., 1946, II, 230.) R. To.

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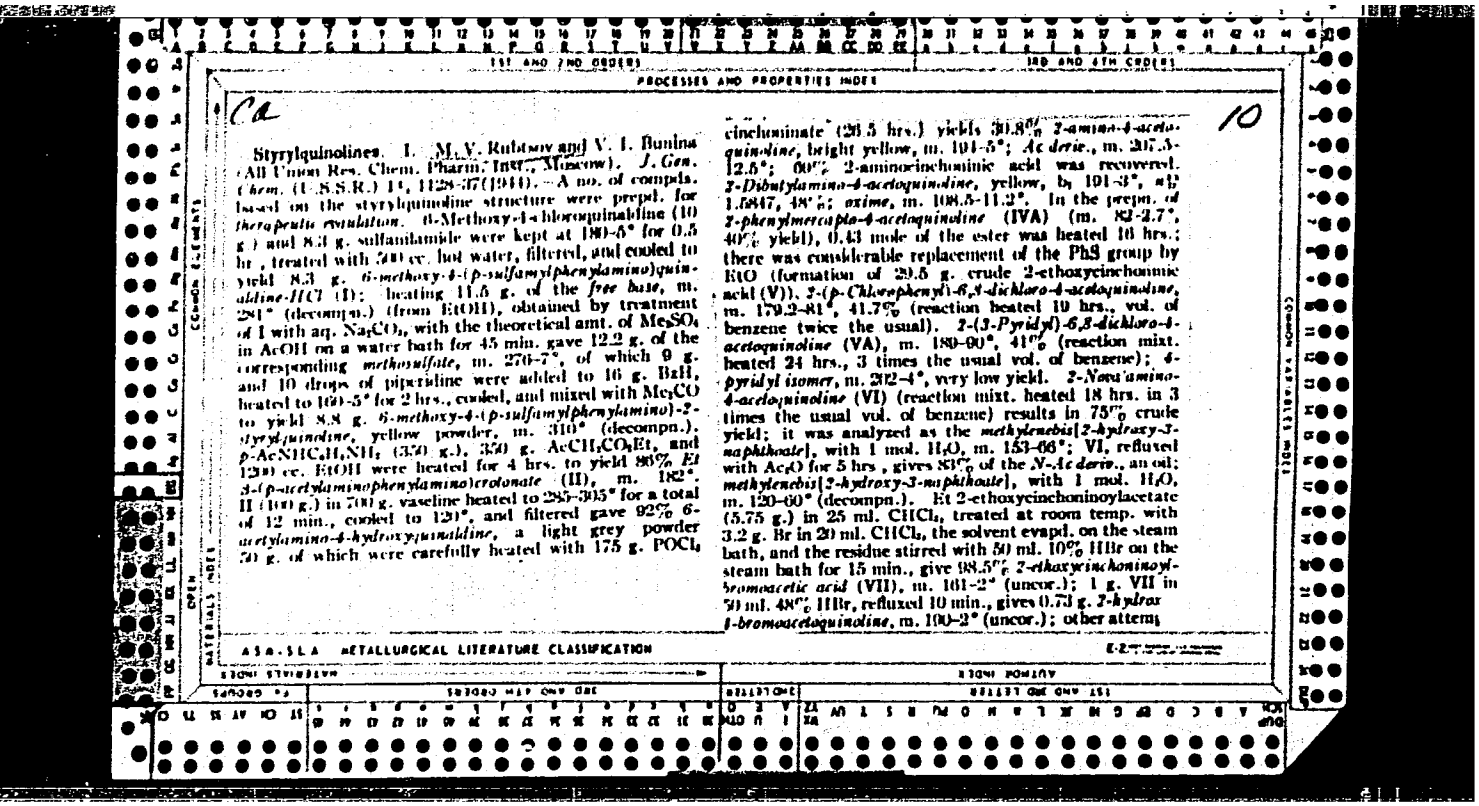

PROCESSES AND PROPERTIES INDEX

Ca

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Styrylquinolines. I. M. V. Rubtsov and V. I. Bunina (All Union Res. Chem. Pharm. Inst., Moscow). *J. Gen. Chem.* (U.S.S.R.) 14, 1128–37(1944).—A no. of compds. based on the styrylquinoline structure were prepd. for *therapeutic evaluation*. 6-Methoxy-4-chloroquinaldine (10 g.) and 8.3 g. sulfanilamide were kept at 180–5° for 0.5 hr., treated with 500 cc. hot water, filtered, and cooled to yield 8.3 g. *6-methoxy-4-(p-sulfamylphenylamino)quinaldine·HCl* (I); heating 11.5 g. of the *free base*, m. 281° (decompn.) (from EtOH), obtained by treatment of I with aq. Na_2CO_3, with the theoretical amt. of Me_2SO_4 in AcOH on a water bath for 45 min. gave 12.2 g. of the corresponding *methosulfate*, m. 270–7°, of which 9 g. and 10 drops of piperidine were added to 16 g. BzH, heated to 160–5° for 2 hrs., cooled, and mixed with Me_2CO to yield 8.8 g. *6-methoxy-4-(p-sulfamylphenylamino)-2-styrylquinoline*, yellow powder, m. 310° (decompn.). *p*-$AcNHC_6H_4NH_2$ (3.50 g.), 3.50 g. $AcCH_2CO_2Et$, and 120 cc. EtOH were heated for 4 hrs. to yield 98% *Et 3-(p-acetylaminophenylamino)crotonate* (II), m. 182°. II (100 g.) in 700 g. vaseline heated to 295–305° for a total of 12 min., cooled to 120°, and filtered gave 92% *6-acetylamino-4-hydroxyquinaldine*, a light grey powder 50 g. of which were carefully heated with 175 g. $POCl_3$ cinchoninate (28.5 hrs.) yields 30.8% *2-amino-4-acetoquinoline*, bright yellow, m. 191–5°; *Ac deriv.*, m. 207.5–12.5°; 60% 2-aminocinchoninic acid was recovered. *2-Dibutylamino-4-acetoquinoline*, yellow, b_5 191–3°, n_D^{25} 1.5847, 48%; *oxime*, m. 108.5–11.2°. In the prepn. of *2-phenylmercapto-4-acetoquinoline* (IVA) (m. 82–2.7°, 40% yield), 0.43 mole of the ester was heated 16 hrs.; there was considerable replacement of the PhS group by EtO (formation of 29.5 g. crude 2-ethoxycinchoninic acid (V)). *2-(p-Chlorophenyl)-6,8-dichloro-4-acetoquinoline*, m. 179.2–81°, 41.7% (reaction heated 19 hrs., vol. of benzene twice the usual). *2-(3-Pyridyl)-6,8-dichloro-4-acetoquinoline* (VA), m. 180–90°, 41% (reaction mixt. heated 24 hrs., 3 times the usual vol. of benzene); *4-pyridyl isomer*, m. 202–4°, very low yield. *2-Naphthylamino-4-acetoquinoline* (VI) (reaction mixt. heated 18 hrs. in 3 times the usual vol. of benzene) results in 75% crude yield; it was analyzed as the *methylenebis[2-hydroxy-3-naphthoate]*, with 1 mol. H_2O, m. 153–66°; VI, refluxed with Ac_2O for 5 hrs., gives 83% of the *N-Ac deriv.*, an oil; *methylenebis[2-hydroxy-3-naphthoate]*, with 1 mol. H_2O, m. 120–60° (decompn.). Et 2-ethoxycinchoninoylacetate (5.75 g.) in 25 ml. $CHCl_3$, treated at room temp. with 3.2 g. Br in 20 ml. $CHCl_3$, the solvent evapd. on the steam bath, and the residue stirred with 50 ml. 10% HBr on the steam bath for 15 min., give 98.5% *2-ethoxycinchoninoylbromoacetic acid* (VII), m. 161–2° (uncor.); 1 g. VII in 50 ml. 48% HBr, refluxed 10 min., gives 0.73 g. *2-hydroxy-4-bromoacetoquinoline*, m. 190–2° (uncor.); other attempts

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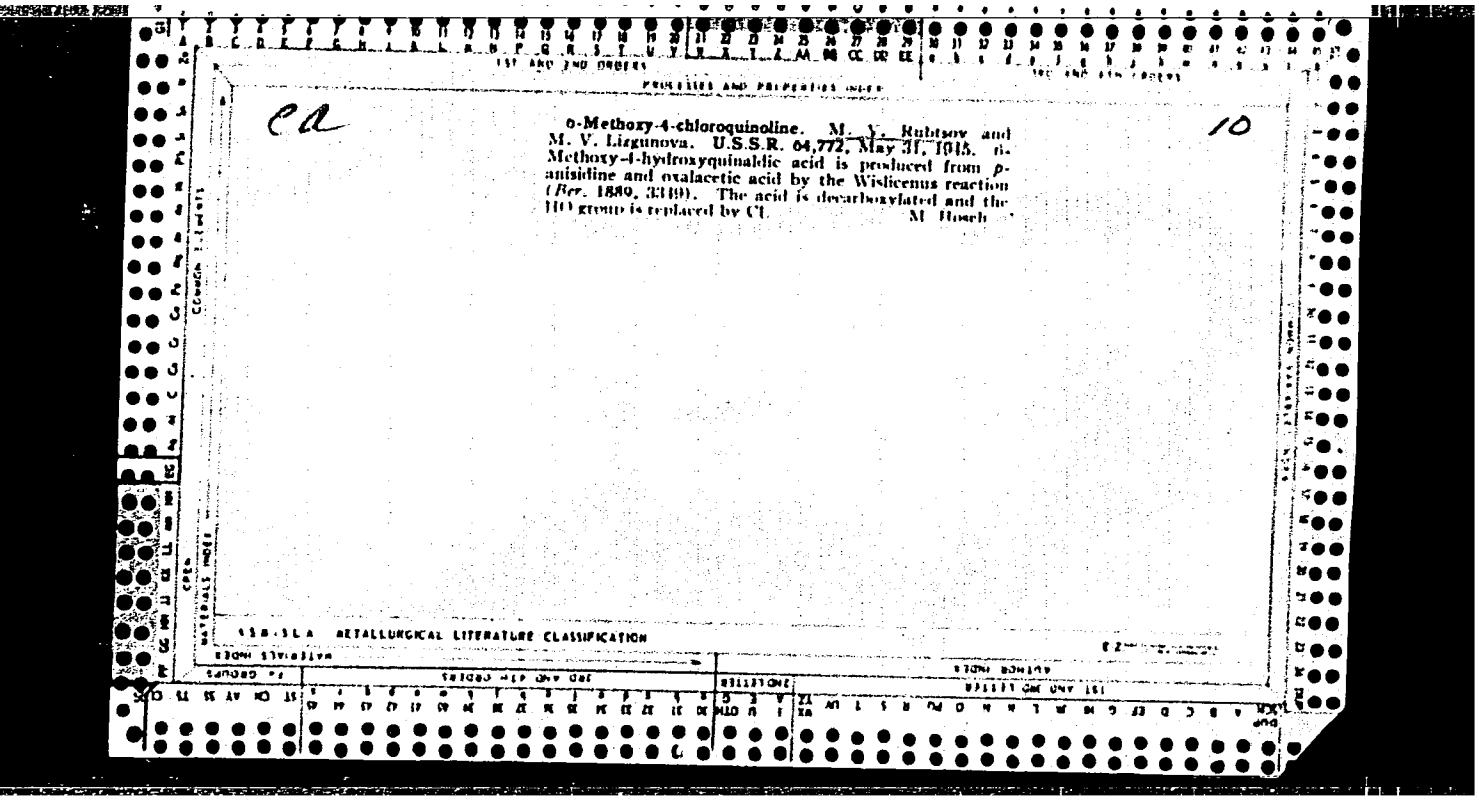

CA

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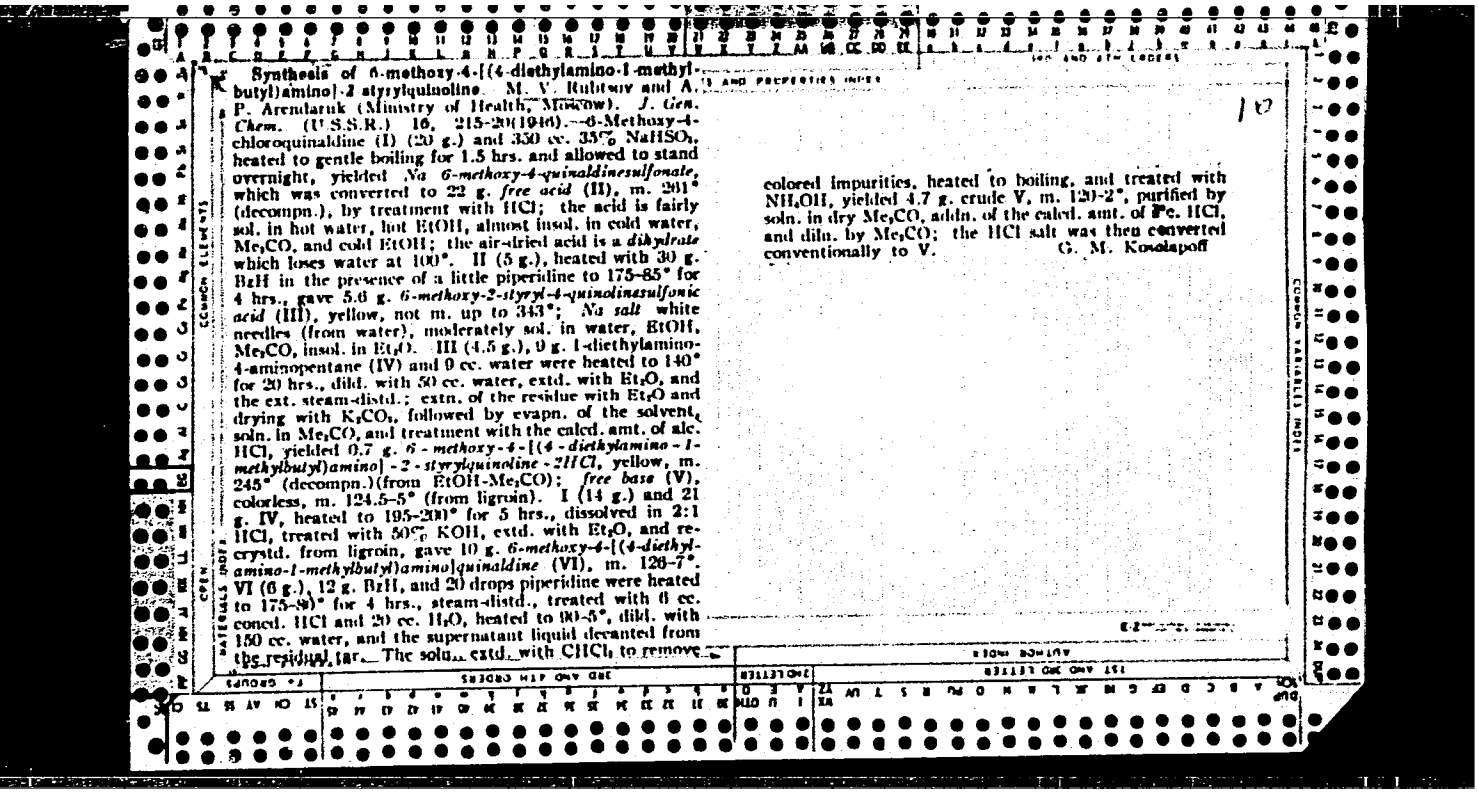
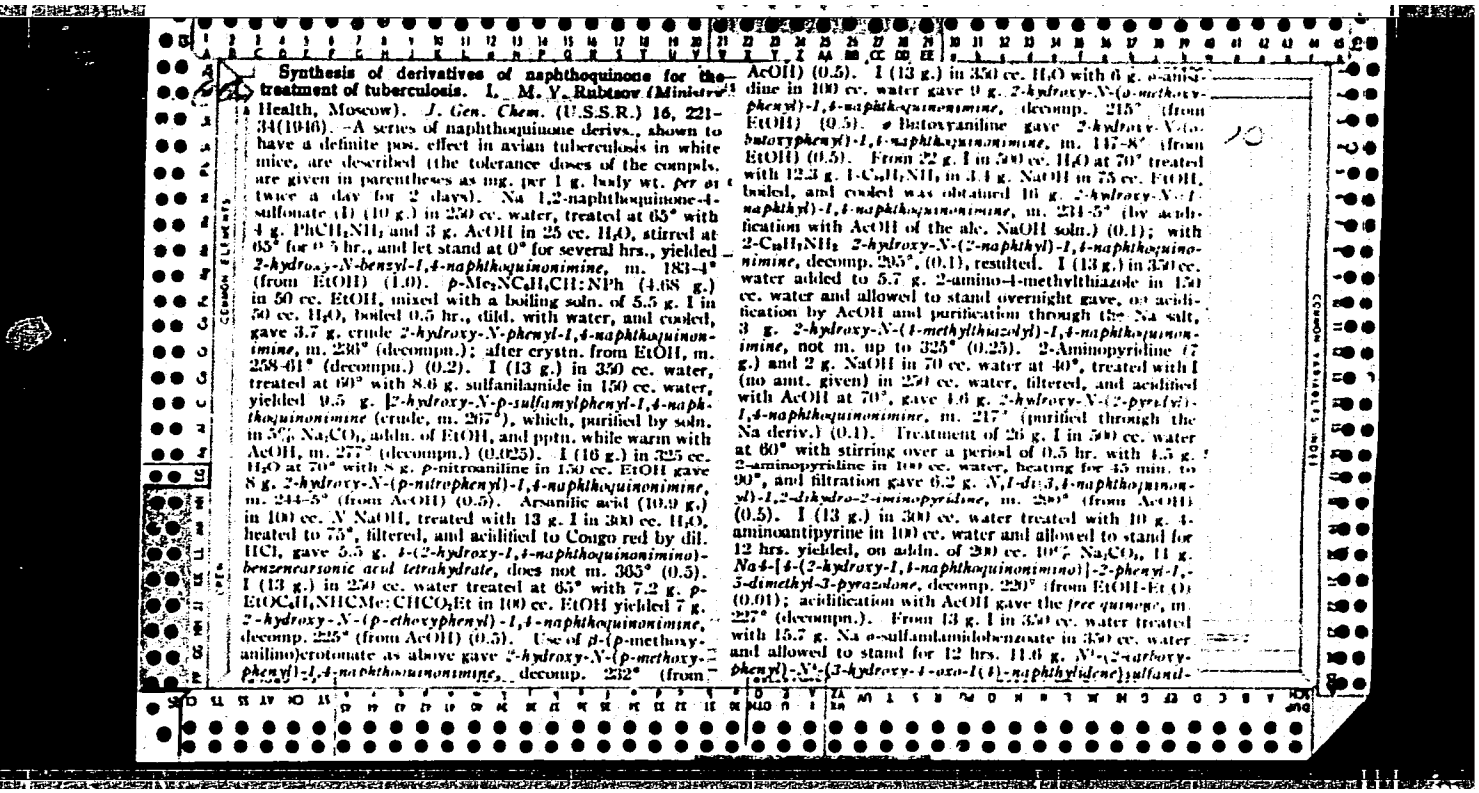
6-Methoxy-4-chloroquinoline. M. Y. Rubtsov and M. V. Lizgunova. U.S.S.R. 64,772, May 31, 1945. 6-Methoxy-4-hydroxyquinaldic acid is produced from *p*-anisidine and oxalacetic acid by the Wislicenus reaction (*Ber.* 1880, 3149). The acid is decarboxylated and the HO group is replaced by Cl. M. Hoch



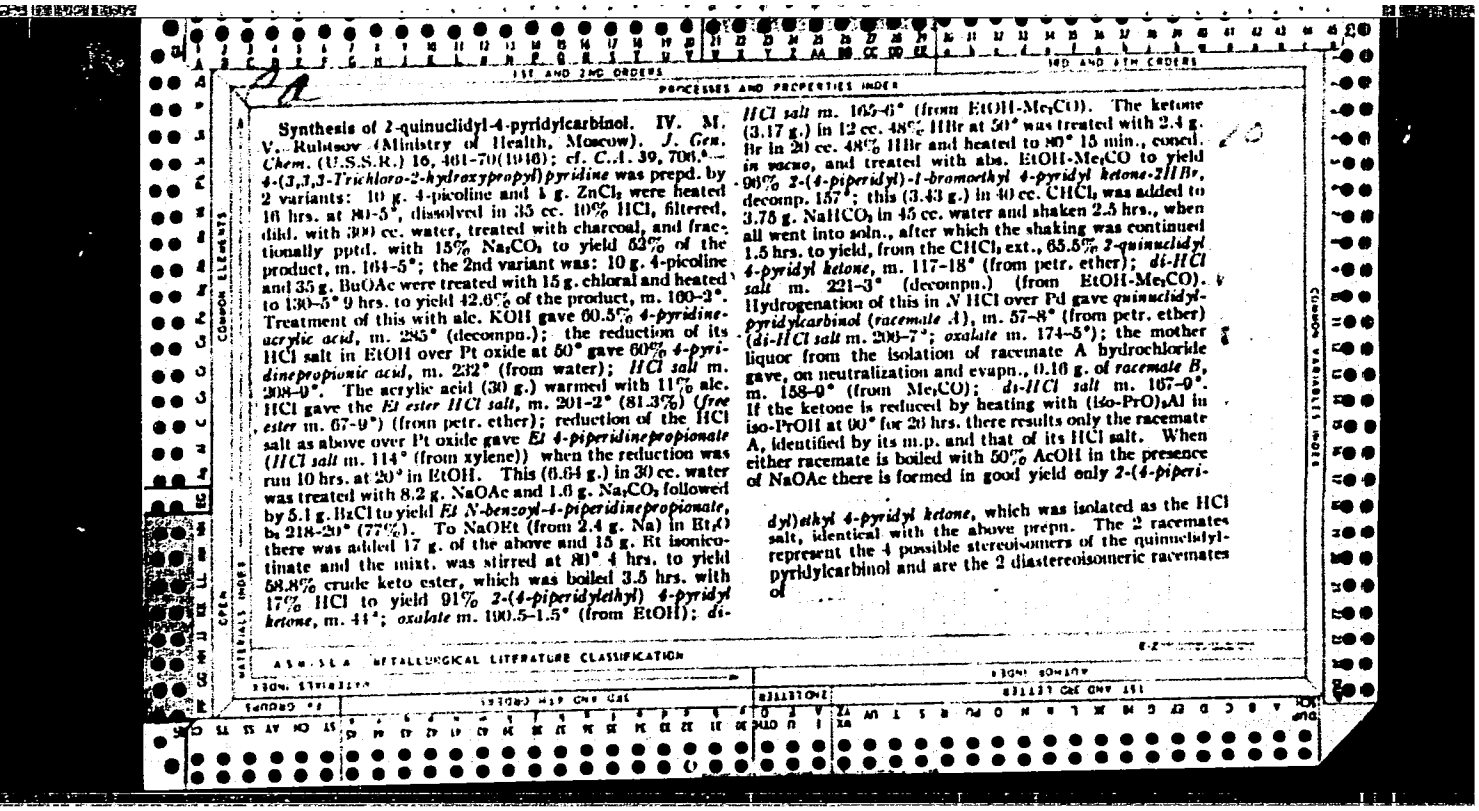
Synthesis of 6-methoxy-4-[(4-diethylamino-1-methylbutyl)amino]-2 styrylquinoline. M. V. Rubtsov and A. P. Arendaruk (Ministry of Health, Moscow). *J. Gen. Chem.* (U.S.S.R.) 16, 215-20(1946).—6-Methoxy-4-chloroquinaldine (I) (20 g.) and 350 cc. 35% $NaHSO_3$, heated to gentle boiling for 1.5 hrs. and allowed to stand overnight, yielded *Na 6-methoxy-4-quinaldinesulfonate*, which was converted to 22 g. *free acid* (II), m. 201° (decompn.), by treatment with HCl; the acid is fairly sol. in hot water, hot EtOH, almost insol. in cold water, Me_2CO, and cold EtOH; the air-dried acid is a *dihydrate* which loses water at 100°. II (5 g.), heated with 30 g. BzH in the presence of a little piperidine to 175–85° for 4 hrs., gave 5.6 g. *6-methoxy-2-styryl-4-quinolinesulfonic acid* (III), yellow, not m. up to 343°; *Na salt* white needles (from water), moderately sol. in water, EtOH, Me_2CO, insol. in Et_2O. III (4.5 g.), 9 g. 1-diethylamino-4-aminopentane (IV) and 9 cc. water were heated to 140° for 20 hrs., dild. with 50 cc. water, extd. with Et_2O, and the ext. steam-distd.; extn. of the residue with Et_2O and drying with K_2CO_3, followed by evapn. of the solvent, soln. in Me_2CO, and treatment with the calcd. amt. of alc. HCl, yielded 0.7 g. *6-methoxy-4-[(4-diethylamino-1-methylbutyl)amino]-2-styrylquinoline-2HCl*, yellow, m. 245° (decompn.)(from EtOH-Me_2CO); *free base* (V), colorless, m. 124.5–5° (from ligroin). I (14 g.) and 21 g. IV, heated to 195–200° for 5 hrs., dissolved in 2:1 HCl, treated with 50% KOH, extd. with Et_2O, and recrystd. from ligroin, gave 10 g. *6-methoxy-4-[(4-diethylamino-1-methylbutyl)amino]quinaldine* (VI), m. 126–7°. VI (6 g.), 12 g. BzH, and 20 drops piperidine were heated to 175–80° for 4 hrs., steam-distd., treated with 6 cc. concd. HCl and 20 cc. H_2O, heated to 90–5°, dild. with 150 cc. water, and the supernatant liquid decanted from the residual tar. The solu... extd. with $CHCl_3$ to remove...

colored impurities, heated to boiling, and treated with NH_4OH, yielded 4.7 g. crude V, m. 120–2°, purified by soln. in dry Me_2CO, addn. of the calcd. amt. of Pe. HCl, and dilu. by Me_2CO; the HCl salt was then converted conventionally to V.

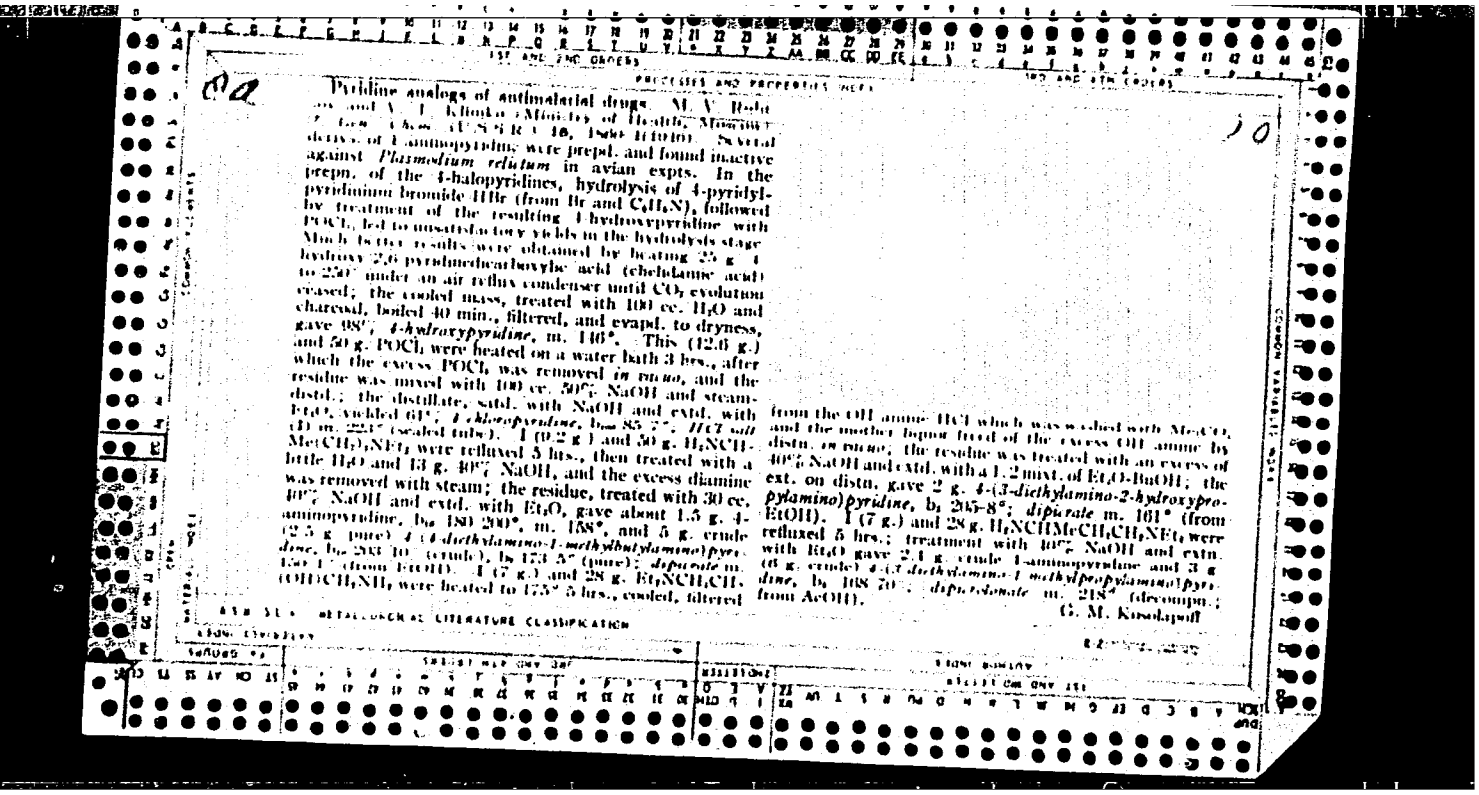
G. M. Kosolapoff



Synthesis of derivatives of naphthoquinone for the treatment of tuberculosis. I. M. Y. Rubtsov (Ministry Health, Moscow). *J. Gen. Chem.* (U.S.S.R.) **16**, 221–34(1946). —A series of naphthoquinone derivs., shown to have a definite pos. effect in avian tuberculosis in white mice, are described (the tolerance doses of the compds. are given in parentheses as mg. per 1 g. body wt. *per os* twice a day for 2 days). Na 1,2-naphthoquinone-4-sulfonate (I) (10 g.) in 250 cc. water, treated at 65° with 4 g. $PhCH_2NH_2$ and 3 g. AcOH in 25 cc. H_2O, stirred at 65° for 0.5 hr., and let stand at 0° for several hrs., yielded *2-hydroxy-N-benzyl-1,4-naphthoquinonimine*, m. 183–4° (from EtOH) (1.0). *p*-$Me_2NC_6H_4CH$:NPh (4.68 g.) in 50 cc. EtOH, mixed with a boiling soln. of 5.5 g. I in 50 cc. H_2O, boiled 0.5 hr., dild. with water, and cooled, gave 3.7 g. crude *2-hydroxy-N-phenyl-1,4-naphthoquinonimine*, m. 236° (decompn.); after crystn. from EtOH, m. 258–61° (decompn.) (0.2). I (13 g.) in 350 cc. water, treated at 60° with 8.6 g. sulfanilamide in 150 cc. water, yielded 9.5 g. *[2-hydroxy-N-p-sulfamylphenyl-1,4-naphthoquinonimine* (crude, m. 267°), which, purified by soln. in 5% Na_2CO_3, addn. of EtOH, and pptn. while warm with AcOH, m. 277° (decompn.) (0.025). I (16 g.) in 325 cc. H_2O at 70° with 8 g. *p*-nitroaniline in 150 cc. EtOH gave 8 g. *2-hydroxy-N-(p-nitrophenyl)-1,4-naphthoquinonimine*, m. 244–5° (from AcOH) (0.5). Arsanilic acid (10.9 g.) in 100 cc. N NaOH, treated with 13 g. I in 300 cc. H_2O, heated to 75°, filtered, and acidified to Congo red by dil. HCl, gave 5.5 g. *4-(2-hydroxy-1,4-naphthoquinonimino)-benzenarsonic acid tetrahydrate*, does not m. 305° (0.5). I (13 g.) in 250 cc. water treated at 65° with 7.2 g. *p*-$EtOC_6H_4NHCMe$:$CHCO_2Et$ in 100 cc. EtOH yielded 7 g. *2-hydroxy-N-(p-ethoxyphenyl)-1,4-naphthoquinonimine*, decomp. 225° (from AcOH) (0.5). Use of *β*-(*p*-methoxyanilino)crotonate as above gave *2-hydroxy-N-(p-methoxyphenyl)-1,4-naphthoquinonimine*, decomp. 232° (from AcOH) (0.5). I (13 g.) in 350 cc. H_2O with 6 g. *o*-anisidine in 100 cc. water gave 9 g. *2-hydroxy-N-(o-methoxyphenyl)-1,4-naphthoquinonimine*, decomp. 215° (from EtOH) (0.5). *o*-Butoxyaniline gave *2-hydroxy-N-(o-butoxyphenyl)-1,4-naphthoquinonimine*, m. 137–8° (from EtOH) (0.5). From 22 g. I in 500 cc. H_2O at 70° treated with 12.3 g. $1\text{-}C_{10}H_7NH_2$ in 3.4 g. NaOH in 75 cc. EtOH, boiled, and cooled was obtained 10 g. *2-hydroxy-N-(1-naphthyl)-1,4-naphthoquinonimine*, m. 234–5° (by acidification with AcOH of the alc. NaOH soln.) (0.1); with $2\text{-}C_{10}H_7NH_2$ *2-hydroxy-N-(2-naphthyl)-1,4-naphthoquinonimine*, decomp. 295°, (0.1), resulted. I (13 g.) in 350 cc. water added to 5.7 g. 2-amino-4-methylthiazole in 150 cc. water and allowed to stand overnight gave, on acidification by AcOH and purification through the Na salt, 3 g. *2-hydroxy-N-(4-methylthiazolyl)-1,4-naphthoquinonimine*, not m. up to 325° (0.25). 2-Aminopyridine (7 g.) and 2 g. NaOH in 70 cc. water at 40°, treated with I (no amt. given) in 250 cc. water, filtered, and acidified with AcOH at 70°, gave 4.6 g. *2-hydroxy-N-(2-pyridyl)-1,4-naphthoquinonimine*, m. 217° (purified through the Na deriv.) (0.1). Treatment of 26 g. I in 500 cc. water at 60° with stirring over a period of 0.5 hr. with 4.5 g. 2-aminopyridine in 100 cc. water, heating for 45 min. to 90°, and filtration gave 6.2 g. *N,1-di(3,4-naphthoquinonyl)-1,2-dihydro-2-aminopyridine*, m. 280° (from AcOH) (0.5). I (13 g.) in 300 cc. water treated with 10 g. 4-aminoantipyrine in 100 cc. water and allowed to stand for 12 hrs. yielded, on addn. of 200 cc. 10% Na_2CO_3, 11 g. *Na 4-[4-(2-hydroxy-1,4-naphthoquinonimino)]-2-phenyl-1,5-dimethyl-3-pyrazolone*, decomp. 220° (from EtOH-Et O) (0.01); acidification with AcOH gave the *free quinone*, m. 227° (decompn.). From 13 g. I in 350 cc. water treated with 15.7 g. Na *o*-sulfamidobenzoate in 350 cc. water and allowed to stand for 12 hrs. 11.6 g. *N'-(2-carboxyphenyl)-N'-[3-hydroxy-4-oxo-1(4)-naphthylidene]sulfanil-*

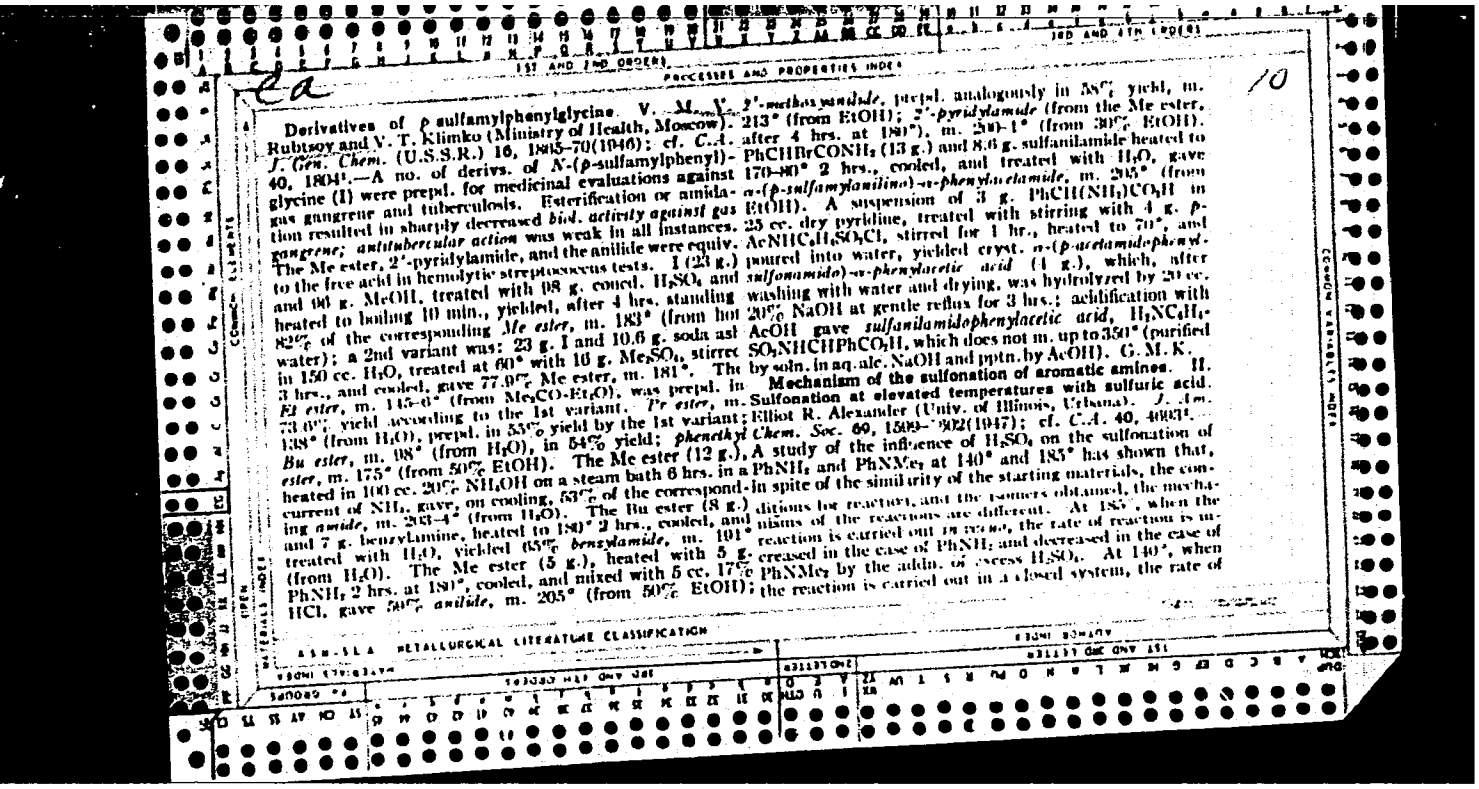


Synthesis of 2-quinuclidyl-4-pyridylcarbinol. IV. M. V. Rubtsov (Ministry of Health, Moscow). *J. Gen. Chem.* (U.S.S.R.) 16, 461-70(1946); *cf. C.A.* 39, 706.—*4-(3,3,3-Trichloro-2-hydroxypropyl)pyridine* was prepd. by 2 variants: 10 g. 4-picoline and 1 g. $ZnCl_2$ were heated 16 hrs. at 80-5°, dissolved in 35 cc. 10% HCl, filtered, dild. with 300 cc. water, treated with charcoal, and fractionally pptd. with 15% Na_2CO_3 to yield 52% of the product, m. 164-5°; the 2nd variant was: 10 g. 4-picoline and 35 g. BuOAc were treated with 15 g. chloral and heated to 130-5° 9 hrs. to yield 42.6% of the product, m. 160-2°. Treatment of this with alc. KOH gave 60.5% *4-pyridineacrylic acid*, m. 285° (decompn.); the reduction of its HCl salt in EtOH over Pt oxide at 50° gave 60% *4-pyridinepropionic acid*, m. 232° (from water); *HCl salt* m. 208-9°. The acrylic acid (30 g.) warmed with 11% alc. HCl gave the *Et ester HCl salt*, m. 201-2° (81.3%) (*free ester* m. 67-9°) (from petr. ether); reduction of the HCl salt as above over Pt oxide gave *Et 4-piperidinepropionate* (*HCl salt* m. 114° (from xylene)) when the reduction was run 10 hrs. at 20° in EtOH. This (6.64 g.) in 30 cc. water was treated with 8.2 g. NaOAc and 1.6 g. Na_2CO_3 followed by 5.1 g. BzCl to yield *Et N-benzoyl-4-piperidinepropionate*, b_5 218-20° (77%). To NaOEt (from 2.4 g. Na) in Et_2O there was added 17 g. of the above and 15 g. Et isonicotinate and the mixt. was stirred at 80° 4 hrs. to yield 58.8% crude keto ester, which was boiled 3.5 hrs. with 17% HCl to yield 91% *2-(4-piperidylethyl) 4-pyridyl ketone*, m. 44°; *oxalate* m. 190.5-1.5° (from EtOH); *di-HCl salt* m. 165-6° (from EtOH-Me_2CO). The ketone (3.17 g.) in 12 cc. 48% HBr at 50° was treated with 2.4 g. Br in 20 cc. 48% HBr and heated to 80° 15 min., concd. *in vacuo*, and treated with abs. EtOH-Me_2CO to yield 98% *2-(4-piperidyl)-1-bromoethyl 4-pyridyl ketone-2HBr*, decomp. 157°; this (3.43 g.) in 40 cc. $CHCl_3$ was added to 3.75 g. $NaHCO_3$ in 45 cc. water and shaken 2.5 hrs., when all went into soln., after which the shaking was continued 1.5 hrs. to yield, from the $CHCl_3$ ext., 65.5% *2-quinuclidyl 4-pyridyl ketone*, m. 117-18° (from petr. ether); *di-HCl salt* m. 221-3° (decompn.) (from EtOH-Me_2CO). Hydrogenation of this in N HCl over Pd gave *quinuclidyl-pyridylcarbinol* (*racemate A*), m. 57-8° (from petr. ether) (*di-HCl salt* m. 208-7°; *oxalate* m. 174-5°); the mother liquor from the isolation of racemate A hydrochloride gave, on neutralization and evapn., 0.16 g. of *racemate B*, m. 158-9° (from Me_2CO); *di-HCl salt* m. 167-9°. If the ketone is reduced by heating with $(iso\text{-}PrO)_3Al$ in iso-PrOH at 90° for 20 hrs. there results only the racemate A, identified by its m.p. and that of its HCl salt. When either racemate is boiled with 50% AcOH in the presence of NaOAc there is formed in good yield only *2-(4-piperidyl)ethyl 4-pyridyl ketone*, which was isolated as the HCl salt, identical with the above prepn. The 2 racemates represent the 4 possible stereoisomers of the quinuclidylpyridylcarbinol and are the 2 diastereoisomeric racemates of



Pyridine analogs of antimalarial drugs. M. V. Rubtsov and V. I. Klimko (Ministry of Health, Moscow). *Zhur. Obshchei Khim. (J. Gen. Chem.) U.S.S.R.* **10**, 1486–1500 (1940). Several derivs. of 4-aminopyridine were prepd. and found inactive against *Plasmodium relictum* in avian expts. In the prepn. of the 4-halopyridines, hydrolysis of 4-pyridylpyridinium bromide HBr (from Br and C_5H_5N), followed by treatment of the resulting 4-hydroxypyridine with $POCl_3$, led to unsatisfactory yields in the hydrolysis stage. Much better results were obtained by heating 25 g. 4-hydroxy-2,6-pyridinedicarboxylic acid (chelidamic acid) to 250° under an air reflux condenser until CO_2 evolution ceased; the cooled mass, treated with 100 cc. H_2O and charcoal, boiled 40 min., filtered, and evapd. to dryness, gave 98% *4-hydroxypyridine*, m. 146°. This (12.6 g.) and 50 g. $POCl_3$ were heated on a water bath 3 hrs., after which the excess $POCl_3$ was removed *in vacuo*, and the residue was mixed with 100 cc. 50% NaOH and steam-distd.; the distillate, satd. with NaOH and extd. with Et_2O, yielded 61% *4-chloropyridine*, b$_{760}$ 85.7°; *HCl salt* (1) m. 225° (sealed tube). 1 (9.2 g.) and 50 g. $H_2NCHMeCH_2NEt_2$ were refluxed 5 hrs., then treated with a little H_2O and 13 g. 40% NaOH, and the excess diamine was removed with steam; the residue, treated with 30 cc. 40% NaOH and extd. with Et_2O, gave about 1.5 g. 4-aminopyridine, b$_{760}$ 180–200°, m. 158°, and 5 g. crude (2.5 g. pure) *4-(4-diethylamino-1-methylbutylamino)pyridine*, b$_{10}$ 203–10° (crude), b$_{10}$ 173.5° (pure); *diperiodate* m. 150° (from EtOH). 1 (7 g.) and 28 g. $Et_2NCH_2CH_2OH$ were heated to 175° 5 hrs., cooled, filtered from the OH amine HCl which was washed with Me_2CO, and the mother liquor freed of the excess OH amine by distn. *in vacuo*; the residue was treated with an excess of 40% NaOH and extd. with a 1:2 mixt. of Et_2O-BuOH; the ext. on distn. gave 2 g. *4-(3-diethylamino-2-hydroxypropylamino)pyridine*, b$_5$ 205–8°; *diperiodate* m. 161° (from EtOH). 1 (7 g.) and 28 g. $H_2NCHMeCH_2CH_2NEt_2$ were refluxed 5 hrs.; treatment with 40% NaOH and extn. with Et_2O gave 2.1 g. crude 4-aminopyridine and 3 g. (6 g. crude) *4-(4-diethylamino-1-methylpropylamino)pyridine*, b$_5$ 108–70°; *diperiodate* m. 218° (decompn.; from AcOH).

G. M. Kosolapoff



Derivatives of *p*-sulfamylphenylglycine. V. M. V. Rubtsov and V. T. Klimko (Ministry of Health, Moscow). *J. Gen. Chem.* (U.S.S.R.) 16, 1805–70(1946); cf. *C.A.* 40, 1804ⁱ.—A no. of derivs. of *N*-(*p*-sulfamylphenyl)-glycine (I) were prepd. for medicinal evaluations against gas gangrene and tuberculosis. Esterification or amidation resulted in sharply decreased *biol. activity against gas gangrene; antituberculor action* was weak in all instances. The Me ester, 2'-pyridylamide, and the anilide were equiv. to the free acid in hemolytic streptococcus tests. I (23 g.) and 90 g. MeOH, treated with 98 g. concd. H_2SO_4 and heated to boiling 10 min., yielded, after 4 hrs. standing 82% of the corresponding *Me ester*, m. 183° (from hot water); a 2nd variant was: 23 g. I and 10.6 g. soda ash in 150 cc. H_2O, treated at 60° with 16 g. Me_2SO_4, stirred 3 hrs., and cooled, gave 77.0% Me ester, m. 181°. The *Et ester*, m. 145–6° (from Me_2CO-Et_2O), was prepd. in 73.6% yield according to the 1st variant. *Pr ester*, m. 138° (from H_2O), prepd. in 55% yield by the 1st variant; *Bu ester*, m. 98° (from H_2O), in 54% yield; *phenethyl ester*, m. 175° (from 50% EtOH). The Me ester (12 g.), heated in 100 cc. 20% NH_4OH on a steam bath 6 hrs. in a current of NH_3, gave, on cooling, 53% of the corresponding *amide*, m. 283–4° (from H_2O). The Bu ester (8 g.) and 7 g. benzylamine, heated to 180° 2 hrs., cooled, and treated with H_2O, yielded 65% *benzylamide*, m. 191° (from H_2O). The Me ester (5 g.), heated with 5 g. $PhNH_2$ 2 hrs. at 180°, cooled, and mixed with 5 cc. 17% HCl, gave 50% *anilide*, m. 205° (from 50% EtOH); *p'-methoxyanilide*, prepd. analogously in 58% yield, m. 213° (from EtOH); *2'-pyridylamide* (from the Me ester, after 4 hrs. at 180°), m. 240–1° (from 30% EtOH). $PhCHBrCONH_2$ (13 g.) and 8.6 g. sulfanilamide heated to 170–80° 2 hrs., cooled, and treated with H_2O, gave *α-(p-sulfamylanilino)-α-phenylacetamide*, m. 205° (from EtOH). A suspension of 3 g. $PhCH(NH_2)CO_2H$ in 25 cc. dry pyridine, treated with stirring with 4 g. *p*-$AcNHC_6H_4SO_2Cl$, stirred for 1 hr., heated to 70°, and poured into water, yielded cryst. *α-(p-acetamidophenyl-sulfonamido)-α-phenylacetic acid* (4 g.), which, after washing with water and drying, was hydrolyzed by 20 cc. 20% NaOH at gentle reflux for 3 hrs.; acidification with AcOH gave *sulfanilamidophenylacetic acid*, $H_2NC_6H_4SO_2NHCHPhCO_2H$, which does not m. up to 350° (purified by soln. in aq. alc. NaOH and pptn. by AcOH). G. M. K.

Mechanism of the sulfonation of aromatic amines. II. **Sulfonation at elevated temperatures with sulfuric acid.** Elliot R. Alexander (Univ. of Illinois, Urbana). *J. Am. Chem. Soc.* 69, 1289–92(1947); cf. *C.A.* 40, 4093⁸.—A study of the influence of H_2SO_4 on the sulfonation of $PhNH_2$ and $PhNMe_2$ at 140° and 185° has shown that, in spite of the similarity of the starting materials, the conditions for reaction, and the isomers obtained, the mechanisms of the reactions are different. At 185°, when the reaction is carried out *in vacuo*, the rate of reaction is increased in the case of $PhNH_2$ and decreased in the case of $PhNMe_2$ by the addn. of excess H_2SO_4. At 140°, when the reaction is carried out in a closed system, the rate of

sulfonation of $PhNH_2$ appears to follow the equation [illegible] → [illegible] Reaction mechanisms are proposed which are compatible with these [illegible]

C. J. W.

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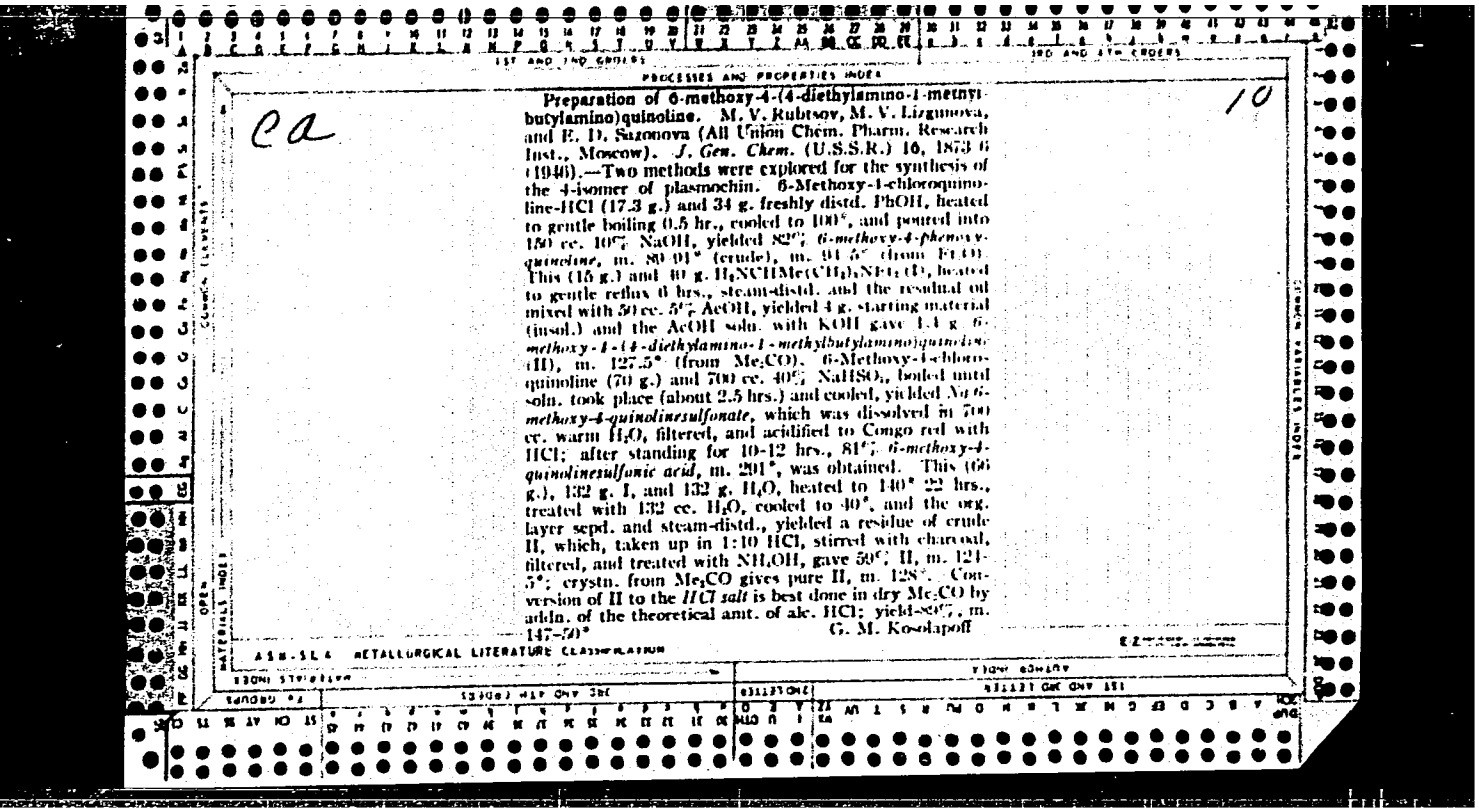

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Preparation of 6-methoxy-4-(4-diethylamino-1-methylbutylamino)quinoline. M. V. Rubtsov, M. V. Lizgunova, and E. D. Sazonova (All Union Chem. Pharm. Research Inst., Moscow). *J. Gen. Chem.* (U.S.S.R.) 16, 1873-6 (1946).—Two methods were explored for the synthesis of the 4-isomer of plasmochin. 6-Methoxy-4-chloroquinoline-HCl (17.3 g.) and 34 g. freshly distd. PhOH, heated to gentle boiling 0.5 hr., cooled to 100°, and poured into 150 cc. 10% NaOH, yielded 82% *6-methoxy-4-phenoxyquinoline*, m. 80-01° (crude), m. 91.5° (from EtOH). This (15 g.) and 40 g. $H_2NCHMe(CH_2)_3NEt_2$ (I), heated to gentle reflux 6 hrs., steam-distd. and the residual oil mixed with 50 cc. 5% AcOH, yielded 4 g. starting material (insol.) and the AcOH soln. with KOH gave 1.4 g. *6-methoxy-4-(4-diethylamino-1-methylbutylamino)quinoline* (II), m. 127.5° (from Me_2CO). 6-Methoxy-4-chloroquinoline (70 g.) and 700 cc. 40% $NaHSO_3$, boiled until soln. took place (about 2.5 hrs.) and cooled, yielded *Na 6-methoxy-4-quinolinesulfonate*, which was dissolved in 700 cc. warm H_2O, filtered, and acidified to Congo red with HCl; after standing for 10-12 hrs., 81% *6-methoxy-4-quinolinesulfonic acid*, m. 201°, was obtained. This (66 g.), 132 g. I, and 132 g. H_2O, heated to 140° 22 hrs., treated with 132 cc. H_2O, cooled to 40°, and the org. layer sepd. and steam-distd., yielded a residue of crude II, which, taken up in 1:10 HCl, stirred with charcoal, filtered, and treated with NH_4OH, gave 59% II, m. 124-5°; crystn. from Me_2CO gives pure II, m. 128°. Conversion of II to the *HCl salt* is best done in dry Me_2CO by addn. of the theoretical amt. of alc. HCl; yield 89%, m. 147-50°

G. M. Kosolapoff

Rubstov, M. V. Doc Chem Sci

Dissertation: "Investigation in the Field of Compounds of the Quinine Alkaloid Type."

10 June 49

All-Union Sci Res Chemicopharmaceutical Inst imeni Sergo Ordzhonikidze.

SO Vecheryaya Moskva
Sum 71

RUBTSOV, M. V.

USSR/Chemistry - Synthesis Jul 49
Quinuclidine

"Synthesis of Quinuclidine (I)," M. V. Rubtsov, V. A. Volskova, All-Union Sci Res Chemicophar Inst imeni Ordzhonikidze, Moscow, 3 3/4 pp

"Zhur Obshch Khim" Vol XIX, No 7

Describes synthesis of I, starting with beta-(piperidyl-(4))-propionic acid and progressing through intermediate stages over corresponding N-benzoyl derivative and beta-(N-benzoyl-piperidyl-(4))-ethylbromide. Submitted 17 Mar 47.

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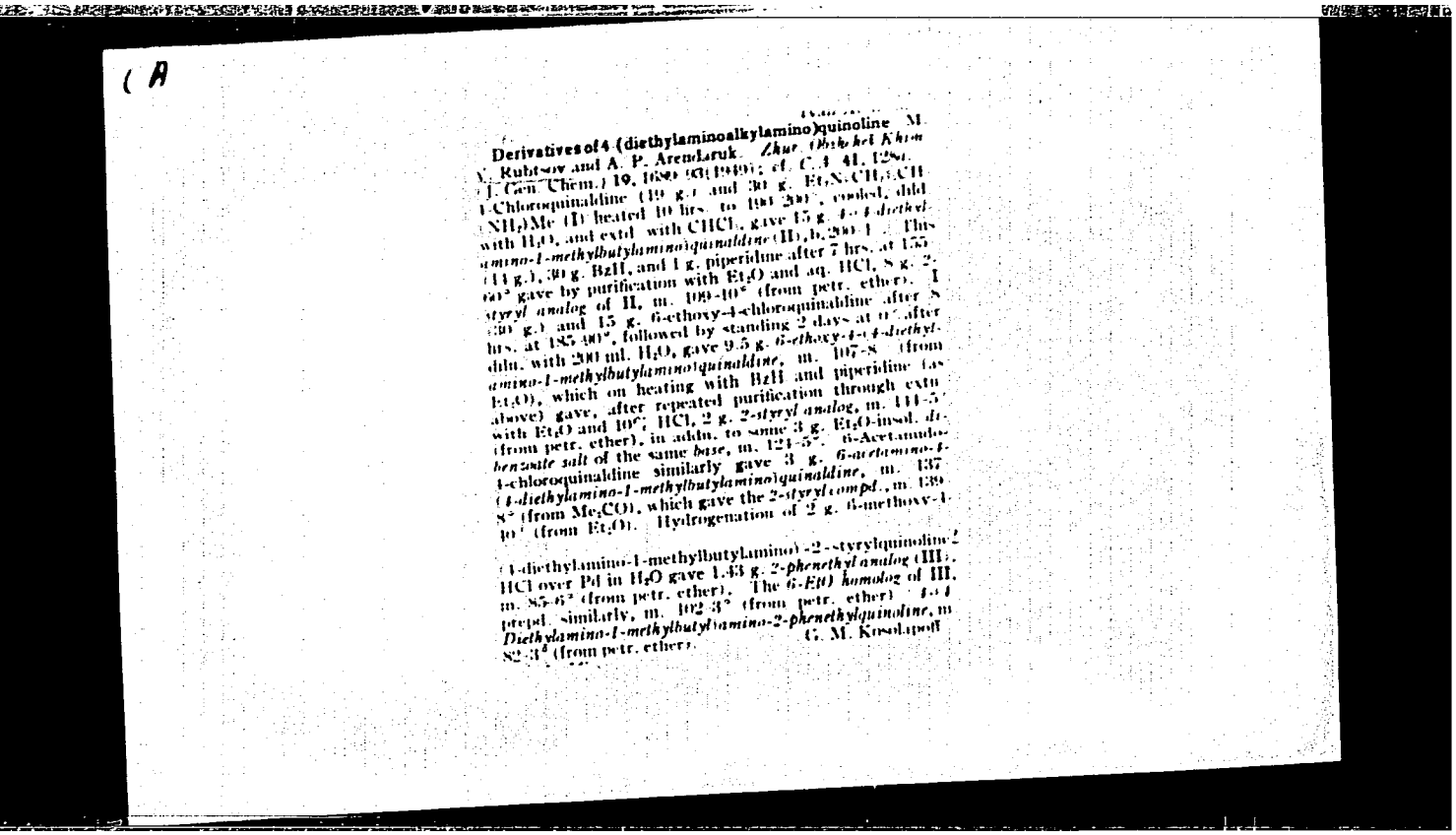
Derivatives of 4-(diethylaminoalkylamino)quinoline. M. V. Rubtsov and A. P. Arendaruk (U.S.S.R. Ministry of Med. Ind., Moscow). *J. Gen. Chem. (U.S.S.R.)* 19, No. 9, 1721-5(1949)(English translation). See *C.A.* 44, 2980e. E. J. C.



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Derivatives of 4-(diethylaminoalkylamino)quinoline. M. V. Rubtsov and A. P. Arendaruk. *Zhur. Obshchei Khim.* J. Gen. Chem.) 19, 1689-93(1949); cf. *C.A.* 41, 1284. 1-Chloroquinaldine (19 g.) and 30 g. $Et_2N.CH_2.CH(NH_2)Me$ (I) heated 10 hrs. to 180-200°, cooled, dild. with H_2O, and extd. with $CHCl_3$, gave 15 g. *4-(4-diethylamino-1-methylbutylamino)quinaldine* (II), b. 200-1°. This (11 g.), 30 g. BzH, and 1 g. piperidine after 7 hrs. at 155-60° gave by purification with Et_2O and aq. HCl, 8 g. *2-styryl analog* of II, m. 109-10° (from petr. ether). I (30 g.) and 15 g. 6-ethoxy-4-chloroquinaldine after 8 hrs. at 185-90°, followed by standing 2 days at 0° after dild. with 200 ml. H_2O, gave 9.5 g. *6-ethoxy-4-(4-diethylamino-1-methylbutylamino)quinaldine*, m. 107-8° (from Et_2O), which on heating with BzH and piperidine (as above) gave, after repeated purification through extn. with Et_2O and 10% HCl, 2 g. *2-styryl analog*, m. 111-5° (from petr. ether), in addn. to same 3 g. Et_2O-insol. *dibenzoate salt* of the same *base*, m. 124-5°. 6-Acetamido-4-chloroquinaldine similarly gave 3 g. *6-acetamino-4-(4-diethylamino-1-methylbutylamino)quinaldine*, m. 137-8° (from Me_2CO), which gave the *2-styryl compd.*, m. 139-40° (from Et_2O). Hydrogenation of 2 g. 6-methoxy-4-(4-diethylamino-1-methylbutylamino)-2-styrylquinoline·2HCl over Pd in H_2O gave 1.43 g. *2-phenethyl analog* (III), m. 85-6° (from petr. ether). The *6-EtO homolog* of III, prepd. similarly, m. 102-3° (from petr. ether). *4-(4-Diethylamino-1-methylbutylamino-2-phenethylquinoline*, m. 82-3° (from petr. ether).

G. M. Kosolapoff

RUBTSOV, M. V.

USSR/Chemistry - Pharmaceuticals 11 Jul 51

"Piperidine-2-Sulfonic Acid," M. V. Rubtsov, All-Union Sci Res Chem Phar Inst imeni S. Ordzhonikidze

"Dok Ak Nauk SSSR" Vol LXXIX, No 2, pp 267, 268

Piperidine-2-sulfonic acid was prepd, using as sulfonatic agents (1) pyridine sulfur trioxide (73.5% yield), and (2) trimethylamine sulfur trioxide (80% yield).

214T8

RUBTSOV, M.V.;MASHKOVSKIY, M.D.

New drugs at the services of public health. Med. promyshl. SSSR no.6:23-26 Nov-Dec 1952. (CLML 23:4)

1. All-Union Scientific-Research of the Pharmaceutic Chemistry Industry.
2. Ethaminal sodium (sodium salt of ethyl-methylbutil barbituric acid), promedol, cardiotrast (contrast medium), pachycarpine, phosphacol (miotic), phthivasid, dicoumarin.

11 Feb 52

RUBTSOV, M.V.

USSR/Chemistry - Pharmaceuticals

"The Synthesis of Quinuclidinecarboxylic Acid-(2)," M.V. Rubtsov, M.I. Dorokhova, All-Union Sci-Res Chemicopharmaceutical Inst im S. Ordzhonikidze

DAN SSSR, Vol 88, No 5, pp 843,844

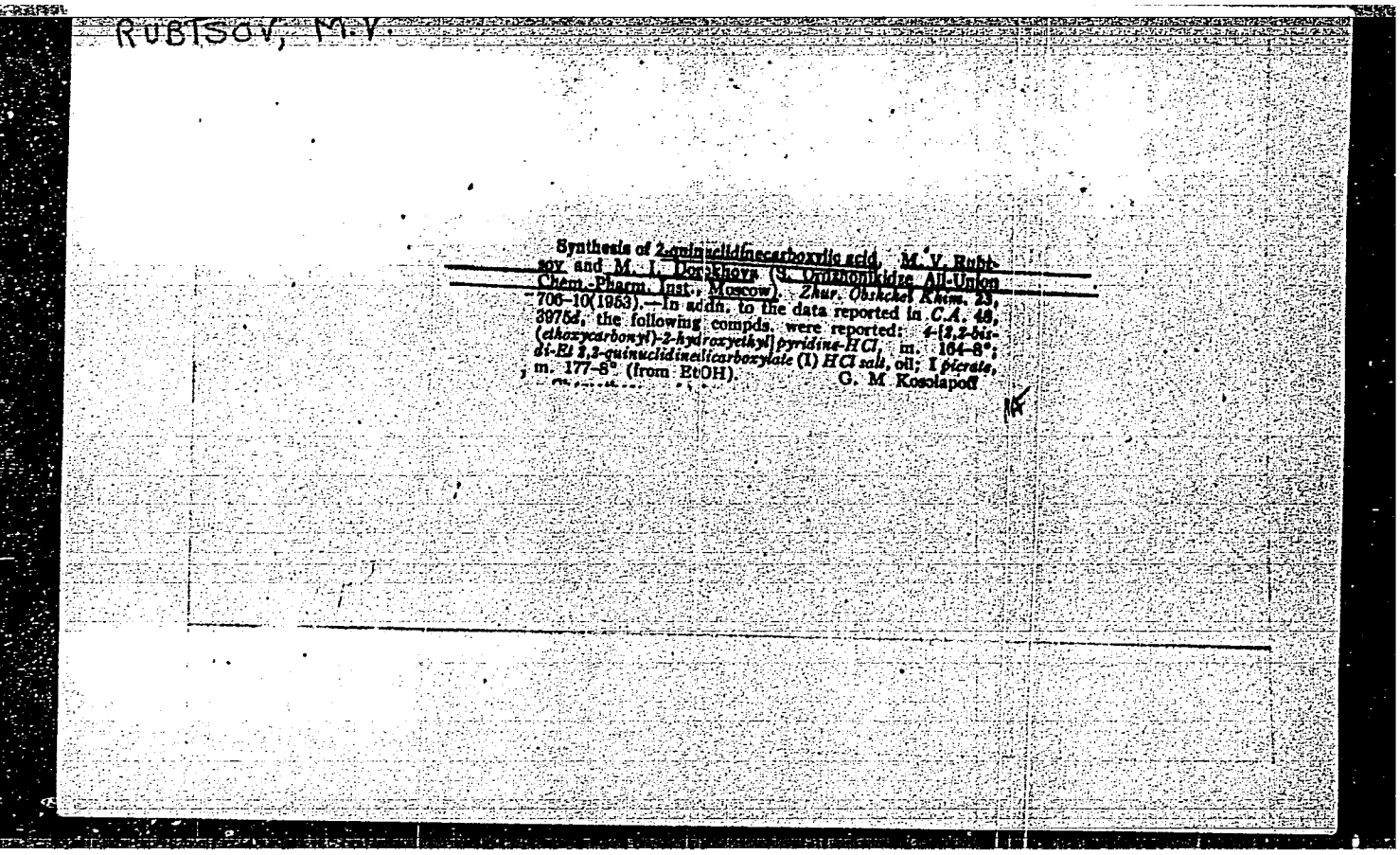
Worked out a simple 5-step synthesis for quinuclidinecarboxylic acid-(2) starting with y-picoline and mesoxalic ester. Presented by Acad V.M. Rodionov 28 Nov 52.

Source #264T26

ABRAMOVA, P.N.; MASHKOVSKIY, M.D., professor, zaveduyushchiy; RUBTSOV, M.V., professor, direktor.

Stability and standard preparations of the adonis herb, digitalis and lily of the valley, used for biological evaluation. Apt.delo 2 no.5:45-48 S-O '53. (MLRA 6:10)

1. Otdel farmakologii Vsesoyuznogo nauchno-issledovatel'skogo khimiko-farmatsevticheskogo instituta im. Sergo Ordzhonikidze Ministerstva zdravookhraneniya SSSR. (Digitalis) (Drugs--Adulteration and analysis)



RUBTSOV, M.V.

Synthesis of 2-quinuclidinecarboxylic acid. M. V. Rubtsov and M. I. Dorokhova (S. Ordzhonikidze All-Union Chem.-Pharm. Inst., Moscow). *Zhur. Obshchei Khim.* 23, 706–10(1953).—In addn. to the data reported in *C.A.* 48, 3975d, the following compds. were reported: *4-[2,2-bis-(ethoxycarbonyl)-2-hydroxyethyl]pyridine-HCl*, m. 164–8°; *di-Et 2,2-quinuclidineilicarboxylate* (I) *HCl salt*, oil; I *picrate*, m. 177–8° (from EtOH). G. M. Kosolapoff

RUBTSOV, M. V.

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Chemical Abst.
Vol. 48
Apr. 10, 1954
Organic Che istry

Synthesis of 2,3-substituted quinuclidines. M. V. Rubtsov and P. P. Mikhlina (S. Ordzhonikidze All-Union Chem.-Pharm. Inst., Moscow). *Zhur. Obshchei Khim.* 23, 823–8(1953).—To 1.25 g. Na in 20 ml. abs. EtOH was added 8.7 g. $CH_2(CO_2Et)_2$ and 9.6 g. Et 4-pyridineacrylate, and the mixt. stirred 1 hr. at 60° and treated with very dil. AcOH and extd. with Et_2O, yielding 94.2% *Et β-[bis(ethoxycarbonyl)methyl]-4-pyridinepropionate*, $b_{0.3}$ 173–5° (some decompn.); *HCl salt* (I), m. 121–2° (from EtOH-Et_2O). This (4.4 g.) refluxed 8 hrs. with 44 ml. concd. HCl gave *3-(4-pyridyl)glutaric acid-HCl*, which, heated 3 hrs. with 35 ml. 5% alc. HCl, concd. *in vacuo*, treated with K_2CO_3, and extd. with Et_2O, yielded 84.4% *di-Et ester*, $b_{0.2}$ 146–8°. I reduced over Pt oxide in EtOH to *Et β-[bis(ethoxycarbonyl)methyl]-4-piperidinepropionate*, isolated as the *HCl salt* (II), a taffy-like mass; the free base is amorphous; treatment with Ac_2O gave the *1-Ac deriv.*, $b_{0.3}$ 200–7°. II (from 47.8 g. pyridine analog) in dry $CHCl_3$ treated over 8 hrs. with 20.4 g. Br in $CHCl_3$, allowed to stand 12–14 hrs., concd., treated with H_2O and K_2CO_3, and extd. with Et_2O yielded crude *Et β-[bis(ethoxycarbonyl)bromomethyl]-4-piperidinepropionate*, which, boiled 2 hrs. with 390 ml. pyridine, concd., and treated with 50% K_2CO_3 gave 72% *Et 2,2-dicarbethoxy-3-quinuclidineacetate*, $b_{0.25}$ 147–8°; *methiodide*, m. 139–41° (from EtOH-Et_2O). The ester refluxed 16 hrs. with concd. HCl gave *2-carboxy-3-quinuclidineacetic acid-HCl* (III), decomp. 253–4° (from aq. Me_2CO); the pure product decomp. 254–5° (from EtOH-Et_2O). This (0.4 g.) 1.1 g. Ag_2O, and 6 ml. H_2O shaken 2 hrs., dild., heated to the b.p., filtered, satd. with H_2S, filtered, and evapd. gave 43.8% *2-carboxy-3-quinuclidineacetic acid*, m. 265–7°; an 87.6% yield is obtained with alc. NH_4. III (7 g.) heated with 100 ml. $SOCl_2$ 10 hrs. at 70°, freed of $SOCl_2$, and the resulting *acyl chloride-HCl* (IV) refluxed 3 hrs. with EtOH gave 82.7% *di-Et 2-carboxy-3-quinuclidineacetate*, $b_{0.2}$ 126°, n_D^{25} 1.4797, (also obtained from III and 5% alc. HCl refluxed 6 hrs.); *methiodide*, m. 140–1° (from EtOH-Et_2O). The ester (8.2 g.) in Et_2O treated with 4.64 g. $LiAlH_4$ suspended in Et_2O, boiled 1 hr., and treated with 9 ml. H_2O gave 88.7% *2-hydroxymethyl-3-(2-hydroxyethyl)quinuclidine*, $b_{0.4}$ 156–7°; *HCl salt*, hygroscopic solid. The latter (5.22 g.) in dry

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$CHCl_3$ treated with 18 ml. $SOCl_2$, boiled 0.5 hr., and concd. *in vacuo*, gave 94% *2-chloromethyl-3-(2-chloroethyl)quinuclidine-HCl*, m. 139–40°; with 50% K_2CO_3 it gave the free base, $b_{0.2}$ 120–2°, which forms a *methiodide*, m. 136°. IV (from 3 g. acid HCl salt) and 40 ml. $Et_2NCH_2CH_2OH$ kept 3.5 hrs. at 80–5° gave 63% *bis(2-diethylaminoethyl) ester, b*$_{0.4}$ 187–9°, of *2-carboxy-3-quinuclidineacetic acid; trimethiodide*, decomp. 197–9°.

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Synthesis of 2,3-substituted quinuclidines. M. V. Rubtsov and E. E. Mikhlina. *J. Gen. Chem. U.S.S.R.* 23, 861–6 (1953)(Engl. translation).—See *C.A.* 48, 3978a.
H. L. H.

RUBTSOV, M.V.

Synthesis of 4-substituted pyridines. M. V. Rubtsov, L. N. Yakhontova, and A. D. Yanina (N. Ordzhonikidze All-Union Chem. Pharm. Inst., Moscow). *Zhur. Obshchei Khim.* 23, 865-8 (1953); cf. *C.A.* 48, 4532g.—To 2.42 g. 4-picolyl pyridine (I) (prepd. by oxidation of 4-picoline) in PhMe was added 10 ml. 50% $NaHSO_3$, the mixt. cooled to 0°, stirred until a mush formed, the liquid was decanted off, and the solid mass rubbed with EtOH, yielding 7.3 g. *Na 1-pyridylhydroxymethanesulfonate* (II) mixed with Na_2SO_3. Crystn. from H_2O gave needles of $^+HN{:}CH{-}CH{:}C[CH(OH)SO_3^-]CH{:}CH$ (A), sol. in hot H_2O, insol. in org. solvents, does not melt. A (0.58 g.) treated with 2.25 ml. *N* NaOH followed by 60 ml. abs. EtOH gave 95% regenerated II, which with $NaHSO_3$ again gave A. Prolonged stirring in PhMe of 3.1 g. II with 2.6 g. $H_2NNHCSNH_2$ in H_2O at 70–5° gave a green ppt., m. 213–14° (crude), m. 215–17° (from EtOH), identified as I *thiosemicarbazone*, which with 10% HCl formed a yellow *HCl salt*, m. 265–6° (from 50% EtOH). Crude II (3 g.) heated 5 min. with 15 ml. H_2O and 30 ml. 50% K_2CO_3, cooled, and extd. with $CHCl_3$, the ext. gave 1.56 g. I, b. 185–7°, rapidly forming on air a *hydrate*, m. 58–60°; I forms a *HCl salt hemihydrate*, m. 133–4°, which sublimes *in vacuo* after loss of H_2O; the *dry salt*, m. 159.5–61.5°, is again rapidly converted to the hemihydrate. Heating 3.1 g. I.HCl with 2.2 g. $CH_2(CO_2H)_2$ and 7.5 ml. AcOH 45 min. at 85–90° gave 3.3 g. *1-(2,2-dicarboxyvinyl)pyridine-HCl* (III), m. 210–20°, which with an equiv. of NaOAc yielded the free *base*, decomp. 253–6° (*sesquihydrate*, losing H_2O *in vacuo* at 100°). III (4 g.) hydrogenated in 4% HCl over PtO at slight pressure gave 91% *1-(2,2-dicarboxyethyl)piperidine-HCl*, m. 237–9°, yielding with AcONa the free *base*, decomp. 255.5–6.0°. The HCl salt refluxed 4 hrs. with 4% alc. HCl gave, after the usual treatment, 79.5% *di-Et ester-HCl*, m. 128–9°. Letting 3.3 g. I.HCl stand 4 days with 3.53 g. $CH_2(CO_2Et)_2$, 8.6 ml. pyridine, and 3.3 ml. piperidine gave, after filtration of the piperidine HCl, evapn. of the filtrate at 50° *in vacuo*, dilu. with Et_2O, filtration, washing the soln. with 15% Na_2CO_3, and distn., 62% *2,1-(2,2-dicarbethoxyvinyl)pyridine*, b. 170–8°; alc. HCl gave the *HCl salt*, m. 180–2° (from EtOH). Hydrogenation gave the Et analog described previously. G. M. K.

RUBTSOV, M. V.

USSR

Synthesis of γ-substituted pyridines. M. V. Rubtsov, E. S. Nikitskaya, and A. D. Yanina. J. Gen. Chem. U.S.S.R. 23, 1001–5(1953)(Engl. translation).—See C.A. 48, 878i.
H. L. H.

RUBTSOV, M. V.

USSR/Chemistry - Pharmaceuticals, Bactericides — Jul 53

"Synthesis of Substituted Hydroxy- and Dihydroxydiphenylmethanes," M. V. Rubtsov, Ye. Ye. Mikhlina and L. A. Pelenitsina, All-Union Sci-Res Chem-Pharm Inst im Ordzhonikidze

Zhur Obshch Khim, Vol 23, No 7, pp 1209-1214

Simplified the methods found in the literature for the prepn of 4,4'- and 2,4'-dioxydiphenylmethanes. Synthesized a series of derivs of hydroxy- and dihydroxydiphenylmethanes and tested their chemotherapeutic activity.

272T20

RUBTSOV, M. V.

USSR/Chemistry - Drugs Sep 53

"Aminoalkyl Derivatives of Quinuclidine," M.V. Rubtsov, Ye.S. Nikitskaya, Ye.Ye. Mikhlina, A.D. Yanina, and V.Ya. Furshtatova, All-Union Sci-Research Chemico-Pharmaceut Inst im Ordzhonikidze

Zhur Obshch Khim, Vol 23, No 9, pp 1555-1559

A number of substituted 2-aminomethyl quinuclidines and 2-aminomethyl-3-(β-aminoethyl)-quinuclidines were synthesized.

268T33

RUBTSOV M.V.

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Synthesis of (5-ethyl-2-quinuclidinyl)(2-pyridyl)carbinol. V. M. V. Rubtsov and V. A. Volskova (S. Ordzhonikidze All-Union Sci. Research Chem.-Pharm. Inst., Moscow). *Zhur. Obshchei Khim.* 23, 1085–8(1953); cf. *C.A.* 41, 7628f.—To 2.4 g. Na in 4.8 g. abs. EtOH in Et_2O was added 15 g. Et picolinate and 17 g. Et *N*-benzoylhomocinchoicinate, the Et_2O removed by heating to 80°, the mixt. stirred 4 hrs. at 80°, cooled, quenched in H_2O, extd. with Et_2O, and the aq. layer neutralized with H_2SO_4 and again extd. with Et_2O, yielding 55.1% red oily *2-(3-ethyl-1-benzoyl-4-piperidyl)-1-carbethoxyethyl 2-pyridyl ketone*, which without purification was refluxed 4 hrs. with 10 parts 17% HCl, the product washed with Et_2O, made alk. with 50% KOH, and extd. with Et_2O, yielding 5.88 g. crude *2-(3-ethyl-4-piperidyl)ethyl 2-pyridyl ketone*; this treated in 10 ml. abs. EtOH with 1.05 g. $(CO_2H)_2$ in 5 ml. abs. EtOH and dild. with 125 ml. dry Me_2CO yielded a ppt. of the pure *ketone oxalate*, $(C_{15}H_{23}ON_2)_2C_2H_2O_4$, m. 175.5–7.0° (from EtOH), in 44.6% yield. The oily free *base* (2.69 g.) in 19 ml. 48% HBr treated at 60° with 1.74 g. Br in 9 ml. 48% HBr, the mixt. stirred 20 min. at 80°, evapd. *in vacuo*, the residue treated with 13.2 g. $NaHCO_3$ in 60 ml. H_2O and 60 ml. $CHCl_3$, shaken 2 hrs., the aq. layer extd. with $CHCl_3$, and the combined $CHCl_3$ soln. evapd. gave 65% *5-ethyl-2-quinuclidinyl 2-pyridyl ketone*, $b_{0.5}$ 155–6°, $[\alpha]_D^{25}$ 75.2° (EtOH) immediately, $[\alpha]_D^{25}$ 76.7° (EtOH) after 24 hrs. The ketone (2.47 g.) in 20.2 ml. *N* HCl shaken with 10 ml. 2% $PdCl_2$ soln. until the orange ppt. dissolved and the mixt. hydrogenated at a slight H pressure and room temp. yielded 2.38 g. corresponding *carbinol*, $b_{0.5}$ 130–43°, $[\alpha]_D^{25}$ 70.3° (in EtOH). Attempts to sep. the expected 4 stereoisomers through the tartrates or camphorsulfonates were unsuccessful. Boiling with dil. AcOH cleaved the quinuclidinyl ring, yielding 2-(3-ethyl-4-piperidyl)ethyl 2-pyridyl ketone. The carbinol was inactive against avian malaria. Synthesis of (2-quinuclidinyl) 2-pyridylcarbinol. VI. *Ibid.* 1088–91.—To EtONa from 1.25 g. Na and 2.5 g. EtOH suspended in Et_2O was added 7.5 g. Et picolinate and 8.5 g. Et 3-(1-benzoyl-4-piperidyl)propionate, the Et_2O distd., the mixt. heated 4 hrs. at 80°, dild. with C_6H_6, cooled, shaken with cold H_2O, the aq. layer washed with Et_2O, and treated with 10% H_2SO_4 until neutral; extn. with Et_2O gave 57.6% crude *3-(1-benzoyl-4-piperidyl)-3-carbethoxyethyl 2-pyridyl ketone*, which, refluxed 4 hrs. with 10 parts 17% HCl, was cleaved to 75.6% *2-(4-piperidyl)-ethyl 2-pyridyl ketone*, an oil; *mono-HCl salt*, m. 183.5–4.5° (crude), m. 189.5–90.0° (from EtOH-Me_2CO). The HCl salt (2 g.) in 7.5 ml. 48% HBr treated at 50° with 1.25 g. Br in 9 ml. 48% HBr, the mixt. heated 15 min. to 80°, evapd. *in vacuo*, and the residue rubbed with abs. EtOH and dild. with dry Me_2CO gave 84.6% yellow *2-(4-piperidyl)-1-bromoethyl 2-pyridyl ketone*; 2.85 g. *di-HBr salt*, decomp. 170–1°, treated in $CHCl_3$ with 3.1 g. $NaHCO_3$ in 45 ml. H_2O and shaken 2.5 hrs. gave 53.7% *2-quinuclidinyl 2-pyridyl ketone*, m. 71.5–3.0° (from petr. ether), hydrogenated over Pd in *N* HCl to mixed *diastereoisomeric racemates* of *(2-quinuclidinyl) (2-pyridyl)carbinol*, m. 60–89°. After conversion to the mono-HCl salts in alc. HCl, a sepn. was accomplished by fractional crystn. from EtOH. The *less sol. isomer* of the *HCl salt*, m. 232–3° (from abs. EtOH), gave the *free carbinol*, m. 118–19° (from petr. ether), which yielded a very hygroscopic *di-HCl salt*. The mother liquor after sepn. of this isomer gave the *HCl salt*, m. 175–7°, of the *2nd racemate*, whose *free base carbinol*, m. 80–2°. Both

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isomers suffer cleavage of the quinuclidinyl ring in hot aq. AcOH; both were inactive against *Plasmodium relictum*. (2-Quinuclidinyl)(1-naphthyl)carbinol. VII. *Ibid*. 1893–6.—To 1.23 g. Na in 2.46 g. EtOH, suspended in Et_2O, was added 10 g. Et 1-naphthoate, the mixt. heated to 100° with distn. of Et_2O, 8.5 g. Et *β-(N-benzoyl-4-piperidyl)*propionate added, the mixt. heated 19 hrs. at 100°, cooled to 70°, dild. with 50 ml. C_6H_6, and allowed to cool with stirring. The cooled mixt. was treated with 200 ml. ice H_2O, the aq. layer washed with Et_2O, neutralized with H_2SO_4, and extd. with $CHCl_3$, to yield 3.2 g. *β-(N-benzoyl-4-piperidyl)-α-carbethoxyethyl 1-naphthyl ketone*, which was refluxed 3 hrs. with 20 parts 1:1 EtOH-concd. HCl, yielding 73.3% *β-(4-piperidyl)ethyl 1-naphthyl ketone*, a yellow oil; *HCl salt*, m. 173.5–5.0° (from abs. EtOH). This (1.97 g.) in 12 ml. 48% HBr at 70° was treated over 10 min. with 1.03 g. Br in 10 ml. 48% HBr and heated 25 min. at 80°. On cooling there was obtained 88.4% *β-(4-piperidyl)-α-bromoethyl 1-naphthyl ketone-HBr*, m. 189–90°. This (2.3 g.) in $CHCl_3$ was shaken 2.5 hrs. with 2.5 g. $NaHCO_3$ in 30 ml. H_2O, yielding 60% *2-quinuclidinyl 1-naphthyl ketone*, m. 98.5–100° (from petr. ether); *HCl salt*, m. 246–7° (from H_2O). This (1.82 g.) hydrogenated over Pd in dil. aq. HCl gave 0.37 g. *2-quinuclidinyl-1-naphthylcarbinol*, m. 200–1°; *HCl salt*, m. 201.5–6.5°; the less sol. material, *racemate A*, is sparingly sol. in Et_2O. The ethereal mother liquor on further evapn. gave 1.08 g. oil, which treated with HCl, gave 0.92 g. *HCl salt*, m. 267.5–9° (from EtOH-Me_2CO), of the other racemate, *racemate B*, the *free base* of which m. 63–5°. The diastereoisomeric racemates *A* and *B* are unchanged after refluxing in AcOH (50%), in which respect they differ from the quinine alkaloids. Both racemates are inactive against avian malaria. G. M. Kosolapoff.

RUBTSOV, M.V.; VOLSKOVA, V.A.

Synthesis of [quinuclidyl-(2)]-[pyridyl-(2)]-carbinol; part 6. Zhur.ob.khim. 23 no.10:1688-1691 O '53. (MLRA 6:11)

1. Vsesoyuznyy Nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut im. S.Ordzhonikidze, Moscow. (Carbinols)

RUBTSOV, M.V.; VOLSKOVA, V.A.

[Quinuclidyl-(2)]-[naphthyl-(1)]-carbinol; part 7. Zhur.ob.khim. 23 no.11: 1893-1896 N '53. (MLRA 6:11)

1. Vsesoyuznyy Nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut im. S.Ordzhonikidze. (Carbinol)

1. RUBTSOV, M. V.; DOROKHOVA, M. I.

2. USSR (600)

4. Quinuclidinecarboxylic Acid

7. Synthesis of quimuclidinecarboxylic acid-(2). Dokl. AN SSSR 88, No. 5, 1953.

9. Monthly List of Russian Accessions, Library of Congress, May 1953. Unclassified.

RUBTSOV, M.V.

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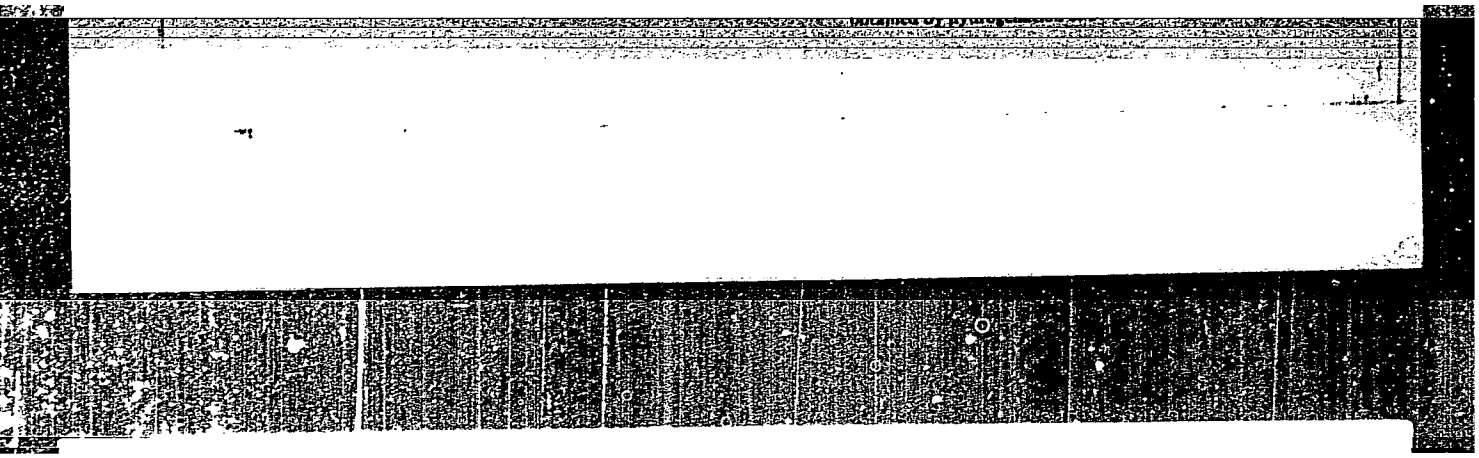
Synthesis of 2,3-disubstituted quinuclidines. M. V. Rubtsov and E. E. Mikhlina (S. Ordzhonikidze All-Union Chem.-Pharm. Inst., Moscow). *Doklady Akad. Nauk S.S.S.R.* 88, 1003–6 (1953); cf. *C.A.* 48, 3978a.—Condensation of an equimolar mixt. of $CH_2(CO_2Et)_2$ and Et 3-(4-pyridyl)acrylate in EtOH with EtONa catalyst 5–6 hrs. at room temp. or 1 hr. at 60° gave 94% *Et 3-dicarbethoxymethyl-3-(4-pyridyl)propionate* (I), $b_{0.5}$ 173–5° (some decompn.). This boiled with concd. HCl gave *3-(4-pyridyl)-glutaric acid*, identified as the *di-Et ester*, $b_{0.5}$ 146–8°. I.HCl was hydrogenated over PtO_2 at room temp. in EtOH to the *piperidine analog* (II), noncryst. mass decompg. on attempted distn.; heated with Ac_2O it gave *Et 3-dicarbethoxymethyl-3-(1-acetyl-4-piperidyl)propionate*, $b_{0.5}$ 206–7°. II with Br gave *Et 3-dicarbethoxybromomethyl-3-(4-piperidyl)-propionate*, which with hot pyridine gave 72% *Et (2,2-dicarbethoxy-3-quinuclidyl)acetate*, $b_{0.5}$ 147–8°, $n^{25}D$ 1.4793; *methiodide*, m. 139–41° (from EtOH-Et_2O). Refluxed 16 hrs. with concd. HCl the ester gave 91.5% *(2-carboxy-3-quinuclidyl)acetic acid-HCl*, decomp. 254–5°. The calcd. amt. of alc. NH_3 gave 87% free *acid* (III), m. 273°, sol. in H_2O, nearly insol. in abs. EtOH; isolation of the acid through the *Ag salt* gave but 43.8% yield owing to the insoly. of the Ag salt. The acid with EtOH-HCl or the acyl chloride with EtOH gave the *di-Et ester*, $b_{0.5}$ 126°, $n^{25}D$ 1.4797. This with $LiAlH_4$ gave 88.7% *2-hydroxymethyl-3-(2-hydroxyethyl)quinuclidine*, $b_{0.5}$ 156–7°, yielding with $SOCl_2$ the *2-chloromethyl-3-(2-chloroethyl)quinuclidine*, $b_{0.5}$ 120–2°, which on standing forms a spongy solid, probably a *polymer*; this process is accelerated by heat (distn.). Heating the acyl dichloride of III.HCl with $Et_2NCH_2CH_2OH$ yields *bis(diethylaminoethyl)* ester of III, $b_{0.5}$ 187–9° (*methiodide*, decomp. 197–9°).

G. M. Kosolapoff



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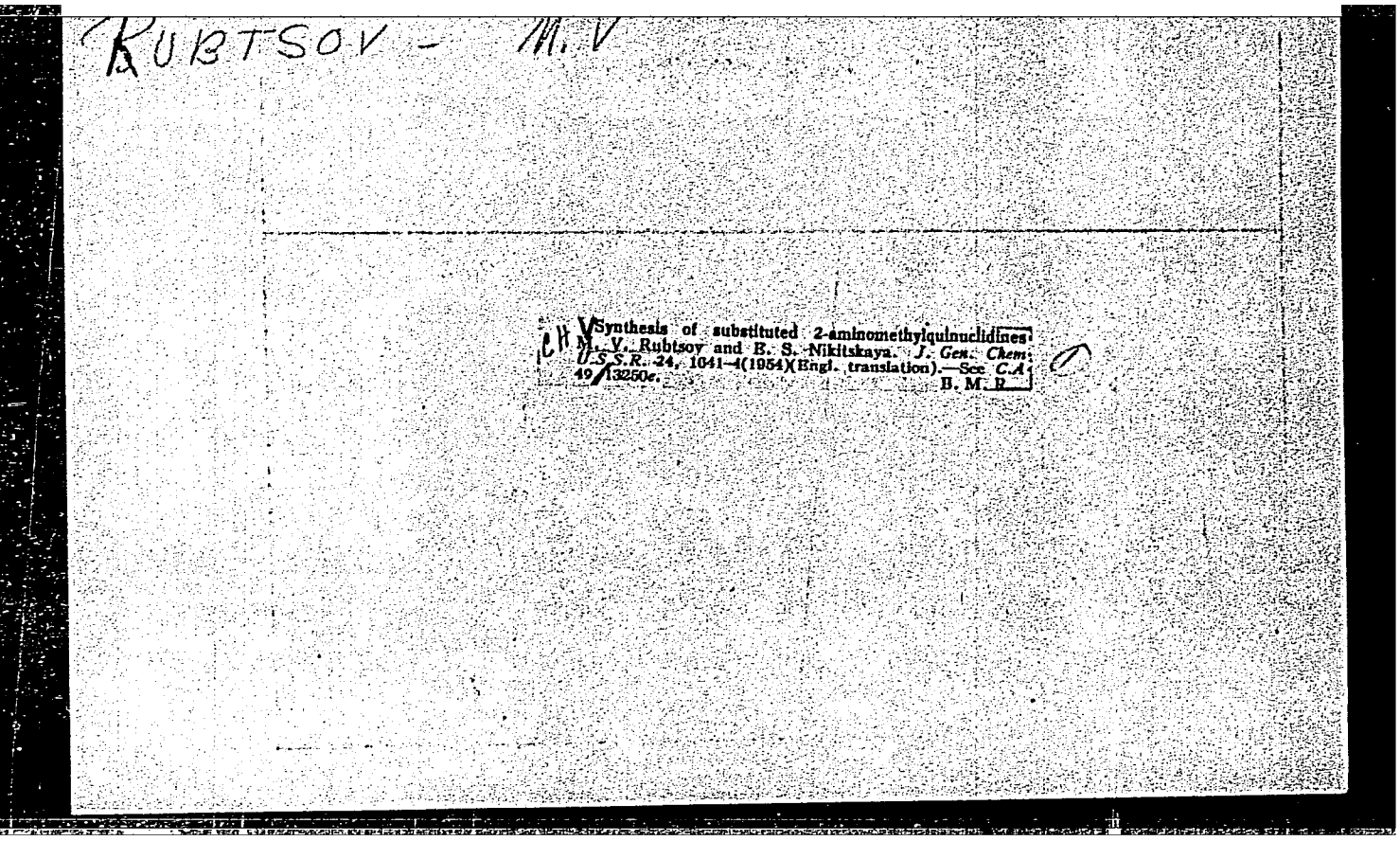

RUBTSOV - M.V

CH V Synthesis of substituted 2-aminomethylquinuclidines. M. V. Rubtsov and B. S. Nikitskaya. *J. Gen. Chem. U.S.S.R.* 24, 1041–4(1954)(Engl. translation).—See *C.A.* 49, 13250e. B. M. R.

RUBTSOV, M.V.

USSR/Chemistry - Synthesis

Card 1/1 : Pub. 151 - 34/42

Authors : Rubtsov, M. V.; Nikitskaya, E. S.; and Yanina, A. D.

Title : Synthesis of gamma-formylpyridine and isonicotinic acid

Periodical : Zhur. ob. khim. 24/9, 1648-1651, Sep 1954

Abstract : The conditions favorable for the synthesis of gamma-formylpyridine by selective oxidation of gamma-picoline, with selenium dioxide in the presence of beta-picoline, are described. Two variants for the derivation of isonicotinic acid, with a yield of 75-80% of the initial gamma-picoline, were developed. The effect of selenium dioxide, on the selective oxidation of gamma-picoline, is explained. Five references: 2-USSR; 1-Swiss; 2-German and USA (1934-1953).

Institution : The S. Ordzhonikidze All-Union Scientific Research Chemical Pharmaceutical Institute

Submitted : April 14, 1954

RUBTSOV, M. V.

USSR/Chemistry - Synthesis

Card 1/1 : Pub. 151 - 36/42

Authors : Rubtsov, M. V., and Nikitskaya, E. S.

Title : Synthesis of substituted 2-aminomethylquinuclidine

Periodical : Zhur. ob. khim. 24/9, 1659-1664, Sep 1954

Abstract : The synthesis of numerous 2-alkyl(aryl)aminomethylquinuclinidines, from 2-quinuclinidine carboxylic acid, is described. The derivation of 2-aminomethylquinuclidine containing the quinoline and acridine cycles through the reaction of 2-aminomethylquinuclidine with 6-methoxy-4-sulfoquinoline and 9-phenoxyacridine is reported. One USSR reference (1953).

Institution : The S. Ordzhonikidze All-Union Scientific Research Chemical Pharmaceutical Institute

Submitted : January 13, 1954

RUBTSOV, M. V.

Synthesis of diastereoisomeric 2-phenyl-3-(4-piperidyl)-glutaric acids. M. V. Rubtsov, I. E. Mikhlina, and V. Ya. Furshtatova (S. Ordzhonikidze All-Union Sci. Research Chem.-Pharm. Inst., Moscow). *Zhur. Obshchei Khim.* 24, 2059–62(1954); cf. *C.A.* 48, 3978a.—A mixt. of EtONa (from 2.6 g. Na and 40 ml. EtOH), 18.56 g. $PhCH_2CO_2Et$, and 20 g. Et 3-(4-pyridyl)acrylate heated 2 hrs. at 60°, and treated with very dil. AcOH gave 90% *di-Et 2-phenyl-3-(4-pyridyl)glutarate*, m. 100° (from petr. ether); hydrolysis with boiling 1:1 HCl 4 hrs. gave the *free acid*, decomp. 231–3°, insol. in org. solvents. Hydrogenation of the *di-Et ester* over a Pt oxide catalyst in EtOH contg. dry HCl required 1.40 hrs., yielding the corresponding *3-(4-piperidyl) analog* (I), m. 79–80°, as a *monohydrate*; distn. results in loss of H_2O, yielding the anhyd. *free ester*, $b_{4.5}$ 173°, which readily picks up 1 H_2O. The product heated with Ac_2O 1 hr. gave *di-Et 2-phenyl-3-(1-acetyl-4-piperidyl)glutarate*, $b_{4.5}$ 215–18°, m. 85°. Hydrolysis of I refluxed 15 hrs. in concd. HCl gave a less-sol. isomer of the *free acid HCl salt* (II), decomp. 230–1°, and a more-sol. *isomer* (III), decomp. 178° (from EtOH–Et_2O). The former isomer with alc. NH_3 gave a free acid decomp. 210–12°, while the latter gave a free acid isomer decomp. 272°. Heating II *in vacuo* 15 min. at 230° converts it to III, isolated as the HCl salt. The di-Et ester with Br in $CHCl_3$ at 21° gave *di-Et 2-phenyl-3-(4-piperidyl)-glutarate perbromide HBr salt*, $C_{18}H_{26}O_4NBr_3$, decomp. 145–7°.

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Rubtsov M.V.

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Synthesis of substituted derivatives of 2-aminomethyl-3-(2-hydroxyethyl)quinuclidine. M. V. Rubtsov, E. E. Mikhlina, and V. Ya. Furshtatova (S. Ordzhonikidze All-Union Sci. Research Chem.-Pharm. Inst., Moscow). *Zhur. Obshchei Khim.* 24, 2217–22(1954); cf. *C.A.* 48, 3978a, 12114e.—Hydrolysis of 13.4 g. di-Et 2-carboxy-3-quinuclidylacetate in H_2O 7 days at room temp. gave 11.35 g. crude *3-carbethoxymethylquinuclidine-2-carboxylic acid* (I) (from abs. EtOH-Et_2O) contg. some *2-carboxy-3-quinuclidineacetic acid*, sepd. through its insoly. in $CHCl_3$, m. 180–2°. The $CHCl_3$ ext. from the above treated with EtOH-HCl gave 85.8% *3-carbethoxymethylquinuclidine-2-carboxylic acid.HCl*, m. 228–9° (decompn.). This (4.7 g.) heated with 47 ml. $SOCl_2$ 4 hrs. at 60–5°, concd. *in vacuo* and treated with dry NH_3 in Et_2O suspension gave 89.0% *3-carbethoxymethylquinuclidine-2-carboxamide* (II), m. 102–3° (from Et_2O); similarly was prepd. the *β-diethylaminoethylamide*, viscous liquid, $b_{0.4}$ 185–6°, and the *diethylaminoisopentylamide*, 76.1%, $b_{0.3}$ 190–1° (structure not given), as well as the *2-pyridylamide*, 70.2%, $b_{0.3}$ 210–12°, m. 56–8°, and 50.8% corresponding *piperidide*, $b_{0.4}$ 160–2°, m. 45–7°. II (3.65 g.) reduced with 2.4 g. $LiAlH_4$ in Et_2O-C_6H_6 gave 78.7% *2-aminomethyl-3-(2-hydroxyethyl)quinuclidine* (III), $b_{0.3}$ 157–60°; *dipicrate*, m. 202–4°. Similar reduction of the other amides gave: 65% *2-(β-diethylaminoethylaminomethyl)-3-(2-hydroxyethyl)quinuclidine*, $b_{0.35}$ 170–2°; 86.5% *2-(diethylaminoisopentylaminomethyl)-3-(2-hydroxyethyl)quinuclidine*, $b_{0.4}$ 185–6°, and 69.8% *2-(2-pyridylaminomethyl)-3-(2-hydroxyethyl)quinuclidine*, m. 137–9° (from $CHCl_3$), as well as 67.6% *N-[3-(2-hydroxyethyl)quinuclidylaminomethyl]piperidine*, m. 116–17°. III (1.25 g.) and 1.31 g. 6-methoxy-4-chloroquinoline heated in PhOH 3 hrs. at 100° gave 46.6% *2-(6-methoxy-4-quinolyl)aminomethyl-3-(2-hydroxyethyl)quinuclidine*, m. 207–9° (from Et_2O-$CHCl_3$). Similar reaction with 2-methoxy-6-chloro-9-phenoxyacridine in BuOH gave 78.3% *2-[2-methoxy-9-phenoxy-6-acridylaminomethyl]-3-(2-hydroxyethyl)quinuclidine*, m. 165–6.5°; *di-HCl salt*, decomp. 258–60°. G. M. Kosolapoff

(2)

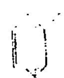
RUBTSOV - M. V.

2. Synthesis of 3-(2-hydroxyethyl)-4-(2-carbethoxyethyl)-*N*-acetylpiperidine. / M. V. Rubtsov/ (S. Ordzhonikidze All-Union Chem. Pharm. Sci. Research Inst., Moscow). *Zhur. Obshchei Khim.* 25, 1021–35(1955); cf. Woodward and Doering, *C.A.* 39, 3002².—Refluxing 196 g. KOAc, 180 ml. AcOH, and 224.5 g. 2,6-dichloro-3-(2-chloroethyl)-4-methylpyridine 10 hrs., the mixt. filtered, the filtrate concd. until the b.p. rose to 175°, and the mixt. again refluxed 10 hrs. yielded 81% *2,6-dichloro-3-(2-acetoxyethyl)-4-methylpyridine*, b_{11} 181–4°. Hydrogenation of this over Pd in aq. MeOH-HCl at room temp. gave a mixt. of *3-(2-hydroxyethyl)-4-methylpyridine* (I) and *2,6-dichloro-3-(2-hydroxyethyl)-4-methylpyridine* (II); extn. with Et_2O and treatment of the aq. soln. with KOH gave 59.3% I, b_{11} 159–61°, m. 65.5–7°; the org. layer gave 35.7% II, b_{11} 182–4°, m. 73.5–5°, which on catalytic hydrogenation yields I. Heating 3-(2-chloroethyl)-4-methylpyridine-HCl with H_2O to 140–50° 3 hrs. in sealed tube gave 70% I. I heated with Ac_2O gave 94.3% *acetate ester*, b_{11} 137–9°; *HCl salt*, m. 101–3°. This (55.5 g.), 63 g. CCl_3CHO, 3.5 ml. piperidine, and 2.2 ml. AcOH heated 17 hrs. at 82–6° and the product (IIa) boiled briefly with 2*N* HCl, chilled, and treated with much 15% Na_2CO_3 gave 54.2% *3-(2-hydroxyethyl)-4-(3,3,3-trichloro-2-hydroxypropyl)pyridine*, m. 166.5–8°; this heated to 70° with alc. KOH 2 hrs. gave a compd. (III) which is either *3,4-(3',4'-pyridino)-2-methyldihydropyran-6-carboxylic acid* (IIIa), or *3,4-(4',3'-pyridino)-dihydropyran-2-acetic acid* (IIIb), decomp. 274–5°, whose *Et ester* (from the acid and EtOH in the presence of HCl), $b_{0.3}$ 130–1°, d_{20} 1.1535, n_D^{20} 1.5230, gave an *HCl salt*, m. 175–7°. In addn. to III the reaction yielded a small amt. of $C_{18}H_{19}O_3N$, m. 172–84°, purified by way of its *Et ester*, $b_{0.3}$ 126–8° (HCl salt, m. 141–3°). Hydrolysis of the pure ester gave the pure free *acid*, decomp. 188–92°, which is the alternative (i.e. IIIa or b) of III. If the hydrolysis of IIa is run 3 hrs. at 40° and 1 hr. at reflux and the evapd. mixt. is neutralized with CO_2, there is obtained 74.6% *3-(2-hydroxyethyl)-4-(2-carboxyvinyl)pyridine*, m. 202–2.5° (from H_2O), sol. in dil. acids and bases; heating this with dry HCl in EtOH gave 85.8% *Et ester* (IV), m. 100–1° (from Me_2CO) (*HCl salt*, m. 174–5°). IV with Ac_2O gave 90% *3-(2-acetoxyethyl)-4-(2-carbethoxyvinyl)pyridine*, $b_{0.3}$ 145–7°, m. 39–41°; *HCl salt*, m. 140.5–1.5° (from Me_2CO). Hydrogenation of IV over PtO_2 in EtOH gave, among other products, *3-(2-hydroxyethyl)-4-(2-carbethoxyethyl)piperidine* (V), $b_{0.3}$ 169–71°; this gave oils with picric, picrolonic, and hydrochloric acids; with chloroplatinic acid it gave an oil which slowly yielded a solid, decomp. 200–9°. V treated with Ac_2O and heated 2 hrs. on a steam bath gave 71.2% *3-(2-acetoxyethyl)-4-(2-carbethoxyethyl)-N-acetylpiperidine* (VI), $b_{0.3}$ 181–4°, d_{20} 1.1117, n_D^{20} 1.4883. Hydrogenation of 3-(2-acetoxyethyl)-4-(2-carbethoxyvinyl)pyridine-HCl in EtOH over Pt gave *3-(2-acetoxyethyl)-4-(2-carbethoxyethyl)piperidine* (VII), $b_{0.3}$ 138–41°, d_{20} 1.0583, n_D^{20} 1.4718, whose HCl salt is a glassy mass. With Ac_2O it gave VI. VI refluxed 5 hrs. with 99.6% EtOH in the presence of a little dry HCl gave on distn. EtOAc while the residue, after drying *in vacuo* at 80° gave a mixt. of products which was taken up in Et_2O, and sepd. from the residue, yielding 79% *N-Ac deriv.* of V, $b_{0.3}$ 199–202°, d_{20} 1.1170, n_D^{20} 1.4982. Treatment of VII with BzCl in $CHCl_3$ in the presence of powd. K_2CO_3 gave 85.3% *N-Bz deriv.* of VII, $b_{0.3}$ 207–10°, d_{20} 1.1335, n_D^{20} 1.5190, which refluxed 5 hrs. with dry EtOH-HCl in 2 stages gave 65.3% *N-Bz deriv.* of V, $b_{0.3}$ 231–6°, d_{20} 1.1486, n_D^{20} 1.5378.

G. M. Kosolapoff

Rubtsov, M.V.

Synthesis of 5-(2-hydroxyethyl)quinuclidine-2-carboxylic ... Khentov ... S. Ordzhoni- CH



II

... IIa b... 180–200°. The mixt. ... HCl and the oil ...

formed by hydrolysis of 3-(2-acetoxyethyl)-4-(3,3,3-trichloro-2-hydroxypropyl)pyridine (cf. preceding abstr.). ... in dry EtOH over PtO_2 at room ...

... after treatment with K_2CO_3 45.2% ... *dicarbethoxyquinuclidine*, b... 110–70°, n_D^{20} 1.4809, d_{20} 1.133, mixt. of 2 stereoisomers; all salts were oils. Refluxing 10 hrs. with concd. HCl gave 89.2% *5-(2-hydroxyethyl)quinuclidine-2-carboxylic acid-HCl*, amorphous powder; treatment with NaOH and evapn. gave the free acid, the same being obtained by treatment of the HCl salt with Ag_2O, followed by decompn. of the Ag salt with H_2S. The *free acid* is a very hygroscopic powder. Treatment with alc. HCl at ... followed by base gave 10.2% *Et 5-(2-hydroxy-*

CO_2H) m.p. decomp. 102°, identical with that gave the *free acid*, decomp. 102°, identical

RUBTSOV, M. V.

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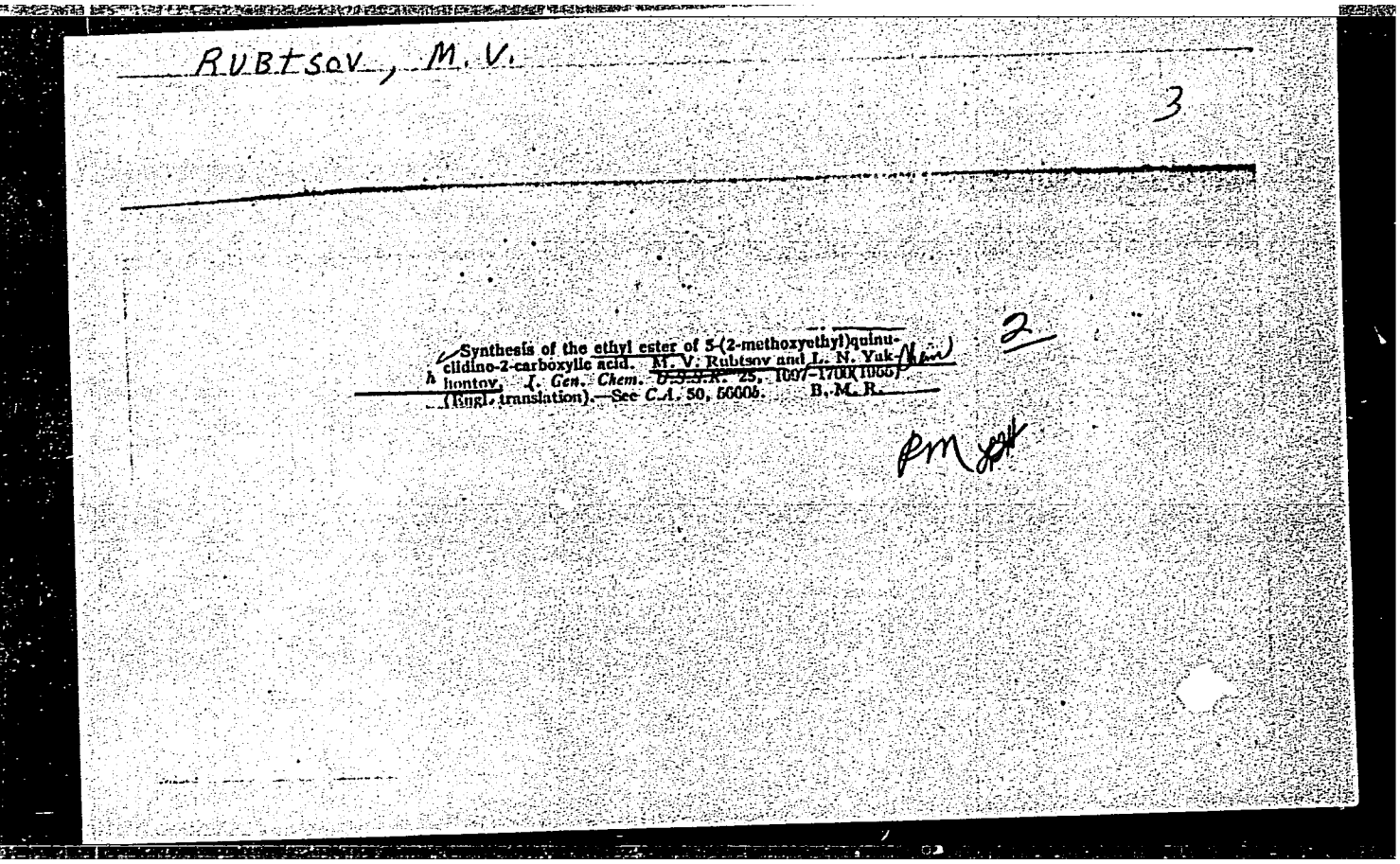
Intermediate product in the synthesis of trichlorocollidine. M. V. Rubtsov and L. N. Yakhontov (S. Ordzhonikidze All-Union Sci. Research Chem.-Pharm. Inst., Moscow). *Zhur. Obshchei Khim.* 25, 1358-60(1955).—Heating 150 g. 6-hydroxy-4-methyl-2,3-(4,5-dihydro-2,3-furano)pyridine (I) and 450 ml. $POCl_3$ in a bomb 5 hrs. at below 160°, followed by ice-treatment, gave 98.5% crude product, which was purified by soln. in hot concd. HCl, cooling, sepn. of the pptd. HCl salt, soln. in Me_2CO, dilu. with H_2O, sepn. of the pptd. monohydrate and vacuum drying, yielding 20.5 g. *2,6-dihydroxy-3-(2-chloroethyl)-4-methylpyridine* (II) *monohydrate*, m. 133.5-4° (this is different than the constitution assigned by Stevens, *et al.*, *C.A.* 36, 4121⁹). This (10 g.) and 20 ml. $POCl_3$ heated in sealed ampul 5 hrs. at 180-90° and then quenched in ice gave the crude product, which after soln. in hot ligroine and distn. gave 92.8% *2,6-dichloro-3-(2-chloroethyl)-4-methylpyridine* (III), bis 159-61°, m. 69-70°, identical with the product prepd. according to S. (*loc. cit.*). I does not lose its Cl with Pd catalyst while heating with KOAc-AcOH cleaves 1 mole of KCl. II heated with EtOH gives I. The high temp. reaction of $POCl_3$ with I probably goes in stages: under 160° the furan ring is opened yielding a dichlorophosphate deriv. at the nuclear HO group, which intermediate in further reaction with $POCl_3$ at 180° yields III. Also in *J. Gen. Chem. U.S.S.R.* 25, 1304-7(1955)(Engl. translation).

G. M. Kosolapoff



RUBTSOV, M. V.

3

Synthesis of the ethyl ester of 5-(2-methoxyethyl)quinuclidino-2-carboxylic acid. M. V. Rubtsov and L. N. Yakhontov. *J. Gen. Chem. U.S.S.R.* 25, 1697–1700(1955) (Engl. translation).—See *C.A.* 50, 5600h. B.M.R.

2

RUBTSOV, M.V.; YAKHONTOV, L.N.

Synthesis of the ethyl ester of 5-(β-methoxyethyl)quinuclidine-carboxylic acid-2. Zhur.ob.khim. 25 no.9:1743-1747 S '55(MIRA 9:2)

1.Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S.Ordzhonikidze.
(Quinuclidinecarboxylic acid)

Rubtsov, M. V.

CH

Synthesis of 3-(2-methoxyethyl)-4-methylpyridine. M. V. Rubtsov and L. N. Yakhontov (S. Ordzhonikidze All-Union Chem. Pharm. Sci. Research Inst., Moscow). *Zhur. Obshchei Khim.* 25, 1820–7(1955).—Refluxing 11.2 g. 2,6-dichloro-3-(2-chloroethyl)-4-methylpyridine (I) with 2 g. KOH in 200 ml. dry EtOH 8 hrs. and acidification with HCl gave 8.8 g. *3-vinyl analog* (II), b_{16} 142–3°, which does not form HCl salt, picrate or methiodide, and which yields by reduction over Pd β-collidine. Refluxing 4.2 g. fresh Ag_2O with 5.6 g. I and 50 ml. dry pyridine 6 hrs. gave 2.7 g. II, b_{16} 136–40°, and 2.3 g. recovered I, b_{16} 182–5°. II (1.88 g.) treated with 2.4 g. Br_2 in $CHCl_3$ readily gave *the dibromide*, b_{15} 177–8°, which does not form salts. Refluxing 360.9 g. 3-(2-acetoxyethyl) analog of I in 1.5 l. 2% alc. HCl 3 hrs. gave 98.9% *3-(2-hydroxyethyl) analog* (III) of I, b_{16} 186–7°, m. 73–5°, which refluxed 2 hrs. with BzCl in C_6H_6 gave 86.1% *benzoyloxyethyl analog*, b_6 234–5°, m. 110°. A mixt. of 8 g. *tert*-AmOH, 3 g. K, and 60 ml. MePh was refluxed 1 hr. and treated with 10.3 g. III in MePh; after 2 hrs. at room temp. and treatment with 4.5 ml. MeI, the mixt. was kept 12 hrs. yielding 90.7% *6-chloro-4-methyl-2,3-(2',3'-dihydrofurano)pyridine* (IV), b_{16} 167–9°, m. 45.5–6°; *HCl salt*, m. 98–8.5°, hydrolyzed by H_2O. Hydrogenation of IV over Pd in 17% HCl gave 88.5% *4-methyl-2,3-(2',3'-dihydrofurano)pyridine-HCl* (V), m. 141–2°; *free base*, b_1 110.5–11°, m. 63–4°; *picrolonate*, decomp. 160–1°. V (4.3 g.) heated with 20 ml. $POCl_3$ in sealed tube 5 hrs. at 180–90° gave 77% *2-chloro-3-(2-chloroethyl)-4-methylpyridine*, b_1 113–14°, n_D^{19} 1.5533; *HCl salt*, m. 106.5–8°. To 5.1 g. powd. Na in Et_2O was added 40.3 g. II and the mixt. refluxed 90 hrs., treated with 10 ml. MeI, and refluxed 10 hrs., yielding a mixt., b_{16} 154°–b_6 270°. The 1st fraction, b_{16} 154–80°, was chilled, yielding 7.4 g. III, and the residual liquid was refluxed with BzCl in C_6H_6, yielding 22.5 g. mixed *Me ether* (VI) of III and IV; the Bz deriv. of III was left in the distn. residue. The mixed distillate was then treated with dry HCl in Et_2O, yielding 2.74 g. IV.*HCl* while the mother liquor gave 40.7% VI, b_{16} 154–6°, n_D^{19} 1.5392, d_{20} 1.255. When *tert*-AmOH (85 ml.) was refluxed with 10.1 g. Na in MePh and the cooled mixt. treated with 70 g. II and stirred 9 hrs., then treated with 35 ml. MeI and stirred 12 hrs. longer, there was obtained 8.1 g. III, b_6 166–8°; and a mixed fraction, b_6 136–66°, which was treated with dry HCl in Et_2O, yielding 45.9% IV.HCl, while the residual liquid gave 28% VI, b_{16} 153–5°. A similar reaction run with iso-PrONa gave 71.6% VI and a low yield of IV. Hydrogenation of VI over Pd in 17% HCl gave 91.3% *3-(2-methoxyethyl)-4-methylpyridine*, b_{12} 112–14°; *HCl salt*, m. 118–19°; *methiodide*, m. 129.5–31°, which sublimes on further heating.

G. M. Kosolapoff

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Synthesis of 2-formylquinuclidine. M. V. Rubtsov and L. N. Yakhontov (S. Ordzhonikidze All-Union Sci. Research Chem. Pharm. Inst., Moscow). *Zhur. Obshchei Khim.* 25, 2143–5(1955).—Heating 4.44 g. 2-quinuclidinecarboxylic acid HCl salt and 45 ml. $SOCl_2$ 14 hrs. at 60–5°, followed by removal of excess $SOCl_2$ *in vacuo* and addn. of the product to 8.1 g. PhNHMe in Et_2O at −2°, followed by stirring 2 hrs. and treatment with 50% K_2CO_3 gave *N-methylanilide of 2-quinuclidinecarboxylic acid*, $b_{0.5}$ 161–2°, m. 95–6°. This (2.7 g.) treated with 0.21 g. $LiAlH_4$ in Et_2O at −5°, followed by aq. treatment and shaking out with $NaHSO_3$ soln., sepn. of the bisulfite adduct and its decompn. with satd. Na_2CO_3 gave 0.6 g. *2-formylquinuclidine*, $b_{0.4}$ 80–2°, n_D^{20} 1.5296; *HCl salt*, decomp. 228°; *picrate*, decomp. 218–19°; *phenylhydrazone*, m. 147–8°; *semicarbasone*, decomp. 244°. 2-Formylquinuclidine gives a red color with fuchsine-SO_2 and forms a Ag mirror with Tollens reagent.

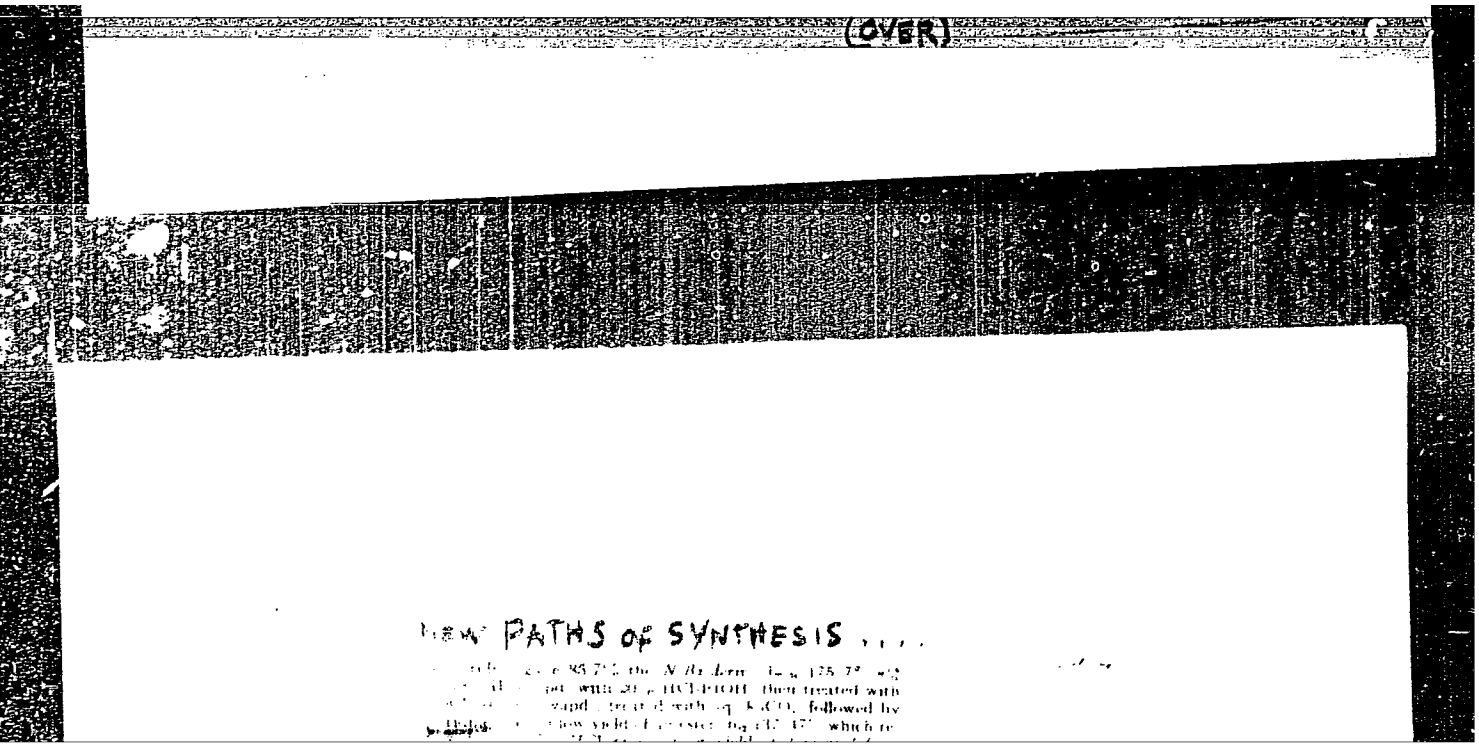
G. M. Kosolapoff

New paths of synthesis of 2-quinuclidinecarboxylic acid

M. V. Rubtsov and E. E. Mikhlina [illegible]
[illegible] Pharm. Research Inst. [illegible]

[illegible] in alc. HCl gave 94.8% corresponding piperazine [illegible] decomp. [illegible] HBr salt decomp. 188-9 [illegible]

[illegible] piperazine [illegible] and 20 ml. $CHCl_3$ and [illegible] chloromethylquinuclidine [illegible]



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New PATHS of SYNTHESIS . . . .

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6000

Synthesis of β-(2-quinuclidinyl)propionic acid. M. V. Rubtsov, L. N. Yakhontov, and E. S. Nikitskaya (S. Ordzhonikidze All-Union Chem. Pharm. Research Inst., Moscow). *Zhur. Obshchei Khim.* 25, 2311–13(1955).—Keeping 0.7 g. 2-formylquinuclidine, 3 ml. dry pyridine, and 5 drops piperidine with 0.8 g. $CH_2(CO_2Et)_2$ 4 days gave after extn. with Et_2O, 66% *di-Et 2-quinuclidinylmethylenemalonate*, $C_{18}H_{29}O_4N$, b_4 142–3°, n_D^{20} 1.4821. Refluxed with concd. HCl 6 hrs. it gave 90% *β-(2-quinuclidinyl)acrylic acid-HCl*, m. 197–8°, which hydrogenated over Raney Ni gave *β-(2-quinuclidinyl)propionic acid-HCl*, decomp. 215–16°, also formed from upon hydrolysis of the ester, b_4 149–50°, obtained by condensation of 2-bromoethylquinuclidine-HBr with $NaCH(CO_2Et)_2$. Treatment of the acid HCl salt with $SOCl_2$, followed by refluxing the crude acyl chloride with EtOH gave *Et β-(2-quinuclidinyl)propionate*, isolated as the *methiodide*, m. 87.9°, in 37% yield.

G. M. Kosolapoff

RUBTSOV, M. V.

USSR/Organic Chemistry - Synthetic Organic Chemistry, E-2

Abst Journal: Referat Zhur - Khimiya, No 19, 1956, 61543

Author: Rubtsov, M. V., Nikitskaya, Ye. S., Usovskaya, V. S.

Institution: None

Title: Alkamino Esters of Some Heterocyclic Acids as Possible Hypotensive Remedies

Original Periodical: Zh. obshch. khimii, 1956, 26, No 1, 130-134

Abstract: There have been synthesized the diethylaminoethyl esters of dipicolinic (I), dipipecolinic (II), N-methyl dipipecolinic (III), 6-methyl picolinic (IV), 6-methyl pipecolinic (V), 1,6-cimethyl pipecolinic (VI), and quinuclidine carboxylic-2 acid (VII). On pharmacological investigation it was found that the di-methyl iodides of VI and VII have high ganglion-blocking activity. A mixture of 3 g dipicolinic acid (VIII) and 30 ml $SOCl_2$ is boiled until completely dissolved (6-8 hours) heat the thus formed di-acid chloride (IX) with 30 ml diethylaminoethanol (X) for 6 hours at

USSR/Organic Chemistry - Synthetic Organic Chemistry, E-2

Abst Journal: Referat Zhur - Khimiya, No 19, 1956, 61543

Abstract: 110-115°; I is obtained with a yield 55.4%, BP 214-215°/0.5 mm; dihydrochloride MP 190-191°; dimethyl iodide MP 200-202°. Analogously from 6-methyl picolinic acid (XI) is obtained IV (yield 77%, BP 128-131°/0.25 mm; hydrochloride, MP 147-149°; methyl iodide, MP 115-117°) and [redacted] quinuc[redacted]dine carboxylic-2 acid, there is obtained VII; yield 73%, BP 160-164°/9 mm, di[redacted]ethyl iodide MP 222-223° (from acetone). 10.7 g of I are hydrogenated in 165 ml of 2.5% solution of HCl in alcohol (0.63 g PtO_2 ~20°, 40-60 cm of water column, 9-10 hours); water is ad[redacted]ed, the mixture is filtered, evaporated to dryness, treated with 50% solution of K_2CO_3 and extracted with ether; II is obtained with a yield 86%, BP 182-184°/0.2 mm; trihydrochloride MP 232-233°. Analogously is prepared V, yield 52.3%, BP 98-100°/0.2 mm; dihydrochloride MP 220°. By boiling of IX with absolute alcohol is synthesized the diethyl ester of I (XII), yield 84.7%, BP 127-128°/0.2 mm MP 44-46°. Analogously is prepared the ethyl ester of XI (XIII), yield 87.3%, BP 79-81°/0.25 mm; hydrochloride MP 74-75°. By hydrogenation of XII and XIII over Pt (from PtO_2) under the above-described conditions are obtained respectively the diethyl ester of dipipecolinic acid (XIV), yield

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USSR/Organic Chemistry - Synthetic Organic Chemistry, E-2

Abst Journal: Referat Zhur - Khimiya, No 19, 1956, 61543

Abstract: 90%, BP 103-105°/0.25 mm, and the ethyl ester of 6-methyl pipecolinic acid (XV), yield 92%, BP 99-100°/13 mm; hydrochloride MP 213-215°. Mixture of 4.27 g XIV, 1.32 g CH_3J and 23 ml absolute alcohol heated for 6 hours at 40-45°, evaporated in vacuum, residue extracted with dry C_6H_6, the insoluble hydroiodide of XIV is filtered off and from the benzene extract is recovered the diethyl ester of N-methyl dipipecolinic acid (XVI), yield 52.7%, BP 107-108°/0.2 mm. Analogously is prepared the ethyl ester of 1,6-dimethyl pipecolinic acid, yield 43.7%, BP 53-54°/0.2 mm; hydrochloride MP 198-200°. In 7 ml of X are dissolved 0.01 g Na, added with stirring 1.32 g XVI, heated 3 hours at 150° (distilling off the alcohol) excess of X is distilled off, the residue is treated with 50% solution K_2CO_3 and extracted with ether; III is thus obtained, yield 51.2%, BP 176-178°/0.2 mm; methyl iodide and hydrochloride are oily subs[redacted] Analogously is synthesized VI, yield 44.7%, BP 106-108°/0.25 mm; dimethyl iodide MP 201-202°.

Card 3/3

RUBTSOV, M. V

USSR/Organic Chemistry - Synthetic Organic Chemistry, E-2

Abst Journal: Referat Zhur - Khimiya, No 19, 1956, 61542

Author: Rubtsov, M. V., Mikhlina, Ye. Ye.

Institution: None

Title: Preparation and Properties of Ethyl-N-(quinuclidyl-2)-urethane

Original Periodical: Zh. obshch. khimii, 1956, 26, No 1, 135-138

Abstract: Described is an attempt to synthesize 2-aminoquinuclidine from quinuclidine carboxylic acid-2 (I) over its hydrozide (II) according to Curtius. On interaction of II with iso-C_5H_{11}-ONO (III) in alcoholic solution of HCl there is obtained ethyl-(IV) and in the solution of HCl in iso-$C_5H_{11}OH$ respectively the isoamyl (V)-N-(quinuclidyl-2)-urethane; together with IV as a by-product were isolated ethyl-(VI) and with V the isoamyl (VII) ester of I. On saponification of IV by action of dilute HCl was obtained NH_4Cl and amorphous polymer of dehydroquinuclidine (VIII). On heating of IV with $C_6H_5CH_2NH_2$ (IX) to 100° evidently takes place

Card 1/3