aluminum hydride. We wish now to report an even simpler and less expensive method based on the direct dehydration of D-mannitol.

Montgomery and Wiggins[4] investigated the complex mixture which results when D-mannitol is heated with concentrated hydrochloric acid and were able to demonstrate, through the isolation of dibenzylidenestyracitol, that 1,5-anhydro-D-mannitol was present. More recently Foster and Overend[5] have found that when D-mannitol is boiled with concentrated hydrochloric acid for 24 hours the chief product isolated (other than unchanged D-mannitol) is 1,4(=3,6)-anhydro-D-mannitol. We have confirmed Foster and Overend's observation but wish now to add that extension of the reaction time to 48 hours results in the isolation of 1,5- rather than 1,4-anhydro-D-mannitol. While the yield, 10.9%, is low, the starting material is cheap and the styracitol obtained is readily purified. The identity of the styracitol was confirmed through comparison with authentic material and through the preparation of its tetraacetate.

Experimental

In each experiment 50.0 g. of pure D-mannitol was dissolved in 200 ml. of concentrated hydrochloric acid and the solution boiled gently under reflux for the specified time (Table I). The reaction mixture was then concentrated *in vacuo* to a sirup, dissolved in 150 ml. of water, treated with decolorizing carbon and reconcentrated *in vacuo*. After the evaporation (*in vacuo*) of two successive 50-ml. batches of absolute alcohol from the residual sirup it was dissolved in 50 ml. of absolute alcohol. The properties of the various crops of crystalline products obtained thus are listed in Table I.

TABLE I

Run	Hr. reflux	No.	Wt., g.	Fractions M.p.,[a] °C.	Fractions $[\alpha]^{20}$D (H_2O)[b]
I	24	1	4.4	120–130	−24.8°
		2	2.5	132–137	−35.8
		3	0.9	140–150	−43.6
II	36	1	4.4	146–154	−45.7
		2	0.7	118–122	−31.6
III	48	1	4.9	139–150	−45.6
IV	60	1	4.1	145–152	−46.5
V	72	1	4.2	145–150	−45.6
VI	96	1	3.6	145–151	−45.0

[a] Melting points are corrected. 1,4-Anhydro-D-mannitol melts at 147–148°; 1,5-anhydro-D-mannitol at 156–157°. [b] 1,4-Anhydro-D-mannitol shows $[\alpha]^{20}$D −23.8° in water; 1,5-anhydro-D-mannitol shows $[\alpha]^{20}$D −50.9° (H_2O).

A number of crops of crude 1,5-anhydro-D-mannitol (20.4 g., $[\alpha]^{20}$D *ca.* −45°) were combined and recrystallized from seven parts of ethanol to give 16.3 g. of pure styracitol showing $[\alpha]^{20}$D −50.3° in water (*c*, 1.06) and melting at 156–157° either alone or in admixture with authentic styracitol.

Three grams of styracitol, made as described above, was acetylated with acetic anhydride in pyridine solution to give 1.5 g. (25%) of its tetraacetate melting at 66–67° and showing in chloroform −42.4° (*c*, 0.826); a mixed melting point with authentic styracitol tetraacetate was undepressed. Fletcher and Hudson[6] reported a value of $[\alpha]^{20}$D −42.0° for the rotation of 1,5-anhydro-D-mannitol tetraacetate in chloroform.

NATIONAL INSTITUTE OF ARTHRITIS AND
METABOLIC DISEASES
NATIONAL INSTITUTES OF HEALTH, PUBLIC HEALTH SERVICE
FEDERAL SECURITY AGENCY, BETHESDA 14, MARYLAND

---

(4) R. Montgomery and L. F. Wiggins, *J. Chem. Soc.*, 2204 (1948).

(5) A. B. Foster and W. G. Overend, *ibid.*, 680 (1951).

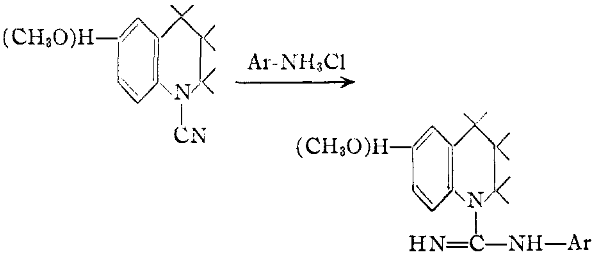
(6) H. G. Fletcher, Jr., and C. S. Hudson, THIS JOURNAL, **71**, 3682 (1949).

Guanidines Derived from N-Cyanotetrahydroquinolines

BY ROBERT D. GANO WITH R. L. MCKEE AND J. W. AGER, JR.

RECEIVED APRIL 14, 1950

N-Cyano-1,2,3,4-tetrahydroquinoline has been prepared by v. Braun[1] through interaction of 1-alkyltetrahydroquinolines with cyanogen bromide. In the present work, this compound and its 6-methoxy and 6-chloro analogs have been prepared in excellent yield from corresponding 1,2,3,4-tetrahydroquinolines. The cyanamides thus prepared were condensed with aromatic amine hydrochlorides to form guanidines.[1]



Under the conditions employed (prolonged reflux in alcohol or hexanol-1 or heating without solvent to temperatures as high as 250°) methylammonium chloride failed to condense with the cyanamides. Other conditions involving heating 1-cyano-6-chlorotetrahydroquinoline with a mixture of molar quantities of diethylamine and its hydrochloride likewise failed to produce isolable amounts of the alkyl derivatives. A low yield of the desired product was obtained from diethylcyanamide and 6-chlorotetrahydroquinoline hydrochloride.

Experimental

The yields here reported are those obtained in a single experiment and are not considered to be the maximum obtainable.

1-Cyano-6-methoxy-1,2,3,4-tetrahydroquinoline.—To a solution of cyanogen bromide (52 g., 0.49 mole) in 240 cc. of benzene was added dropwise with stirring, a solution of 160 g. (0.98 mole) of thalline in 125 cc. of benzene, the temperature being maintained at 25° by external cooling. After standing overnight, the solution was filtered from the precipitated thalline hydrobromide (110 g., 92%), the benzene distilled at atmospheric pressure, and the product distilled *in vacuo* to yield 82 g. of a pale yellow oil boiling at 160–177° (4.0–4.5 mm.). Redistillation gave 73 g. (79% of the theoretical) of material boiling from 177–182° (4.0–4.5 mm.) which solidified to form white crystals melting at 44–47°. Neither recrystallization of this substance from petroleum ether nor redistillation produced any alteration in melting point.

Anal. Calcd. for $C_{11}H_{12}N_2O$: N, 14.89; CH_3O, 16.49. Found: N, 15.18; CH_3O, 16.73.

1-Cyano-1,2,3,4-tetrahydroquinoline.[1]—Cyanogen bromide (63.1 g., 0.595 mole) and tetrahydroquinoline (159.5 g., 1.19 moles) were allowed to react as above to form a 90% yield of the desired product boiling at 153.5–154.5° (7 mm.) and 169–172° (13 mm.).

1-Cyano-6-chloro-1,2,3,4-tetrahydroquinoline.—6-Chloro-1,2,3,4-tetrahydroquinoline was prepared from tetrahydroquinoline by acetylation, chlorination with sulfuryl chloride in carbon tetrachloride, and acid hydrolysis. It boiled at 125–127° at 3 mm., melted at 41°, and formed a hydrochloride which decomposed at 195° and a picrate melting at 151.5–152.5°.[2] The cyanamide was prepared from 21.2

---

(1) J. v. Braun, *Ber.*, **42**, 2219 (1909).

(2) J. v. Braun, A. Grabowski and M. Rawicz, *ibid.*, **46**, 3169 (1913).

g. of cyanogen bromide and 67 g. of 6-chlorotetrahydroquinoline. The yield of purified material boiling at 155° (2 mm.) and melting at 54–55° was 44%.

Anal. Calcd. for $C_{10}H_9ClN_2$: N, 14.53. Found: N, 14.43.

1-(*p*-Nitrophenylguanyl)-1,2,3,4-tetrahydroquinoline.—N-Cyanotetrahydroquinoline (13.0 g., 0.082 mole) and *p*-nitroaniline hydrochloride (14.3 g., 0.082 mole) were heated in the absence of a solvent by means of an oil-bath, the temperature being slowly raised to 200° (bath temperature). The resulting red solid was dissolved in 180 cc. of hot alcohol, poured into 200 cc. of water containing 8 g. of sodium hydroxide, and the solid material (24.9 g., m.p. 155–169°) which separated was removed by filtration. After crystallization once from 800 cc. of alcohol and once from 800 cc. of acetone, the material (9.1 g., m.p. 176.5–179.5°) was extracted with 600 cc. of boiling dioxane leaving a small residue melting from 162° to 275°. The dioxane solution was concentrated to 160 cc. and water was added to a faint turbidity while hot. On chilling 6.3 g. of an orange yellow solid melting at 187.5–188.5° was obtained. An additional 3.6 g. of less pure product (m.p. 183.5–187°) was recovered from the mother liquors.

Anal. Calcd. for $C_{16}H_{16}N_4O_2$: C, 64.83; H, 5.44; N, 18.91. Found: C, 64.78; H, 5.62; N, 18.88.

1-(*p*-Methoxyphenylguanyl)-1,2,3,4-tetrahydroquinoline hydrochloride was prepared similarly from 11.1 g. of N-cyanotetrahydroquinoline and 11.1 g. of *p*-anisidine hydrochloride. The substance was precipitated from an ether solution with hydrogen chloride and recrystallized three times from alcohol–ether to give 3.4 g. (15%) of white crystals melting at 185–186°.

Anal. Calcd. for $C_{17}H_{20}ClN_3O$: C, 64.10; H, 6.34; Cl, 11.16. Found: C, 64.10; H, 6.35; Cl, 11.13.

Bis-(1,2,3,4-tetrahydroquinolyl-1)-ketimine was prepared in 57% yield from 16.5 g. of cyanotetrahydroquinoline and 22.7 g. of tetrahydroquinoline hydrobromide in the absence of a solvent at 160°. Crystallization from alcohol–petroleum ether formed a white microcrystalline powder melting at 146.5–147.5°.

Anal. Calcd. for $C_{19}H_{21}N_3$: C, 78.31; H, 7.27; N, 14.42. Found: C, 78.35; H, 7.40; N, 14.62.

Bis-(6-methoxy-1,2,3,4-tetrahydroquinolyl-1)-ketimine was prepared as in the previous reaction from 9.8 g. of thalline hydrobromide and 7.5 g. of N-cyanothalline. Crystallization from aqueous alcohol gave a 23% yield of a white powder melting at 143.5–143.8°.

Anal. Calcd. for $C_{21}H_{25}N_3O_2$: C, 71.77; H, 7.67; N, 11.96; CH_3O, 17.67. Found: C, 71.62; H, 7.31; N, 12.21; CH_3O, 17.93.

1-(*p*-Nitrophenylguanyl)-6-methoxy-1,2,3,4-tetrahydroquinoline.—Seven grams of *p*-nitroaniline hydrochloride and 7.5 g. of N-cyanothalline treated as in the previous reaction gave a 23% yield of deep red crystals (from alcohol) melting at 132.5–134°.

Anal. Calcd. for $C_{17}H_{18}N_4O_3$: C, 62.62; H, 5.56; N, 17.17; CH_3O, 9.51. Found: C, 62.92; H, 5.68; N, 17.08; CH_3O, 10.08.

1-(1-Chlorophenylguanyl)-6-methoxy-1,2,3,4-tetrahydroquinoline.—Analogously, 13.1 g. of *p*-chloroaniline hydrochloride and 15.0 g. of N-cyanothalline formed 17.5% of white crystals melting (after crystallization from ethyl acetate) at 135.5–136.5°.

Anal. Calcd. for $C_{17}H_{18}ClN_3O$: C, 64.65; H, 5.74; N, 13.31; CH_3O, 10.2. Found: C, 64.81; H, 5.49; N, 13.96; CH_3O, 10.2.

1-Diethylguanyl-6-chlorotetrahydroquinoline Hydrochloride.—Seven grams of 6-chlorotetrahydroquinoline hydrochloride and 3.4 g. of diethylcyanamide were heated in absence of a solvent. At about 100°, an exothermic reaction took place, the temperature rising spontaneously to 165°. The melt was dissolved in water, adjusted to a *p*H of 8.5 and extracted (ether) to remove tetrahydroquinoline. The aqueous layer was made strongly basic and extracted thoroughly with ether after drying, dry hydrogen chloride was pressed through the solution to precipitate the hydrochloride (1 g.) which was crystallized to constant melting point, 207–210°, from ethyl acetate.

Anal. Calcd. for $C_{14}H_{21}Cl_2N_3$: C, 55.6; H, 6.96; N, 13.9. Found: C, 55.8; H, 6.73; N, 13.8.

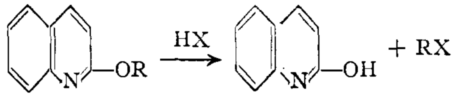
THE VENABLE CHEMICAL LABORATORY
THE UNIVERSITY OF NORTH CAROLINA
CHAPEL HILL, NORTH CAROLINA

Reactions of Some Amines with Heterocyclic Ethers

BY HENRY GILMAN, IRVING ZAREMBER AND JOHN A. BEEL

RECEIVED JANUARY 8, 1952

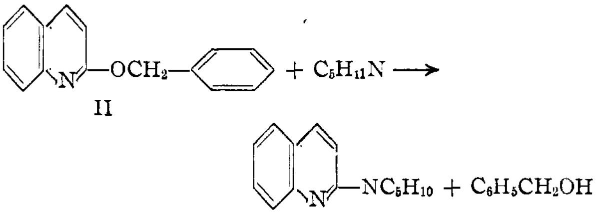
It has been shown that alkoxy groupings in the 2-position of quinoline are labile to reagents like hydrochloric acid,[1] thiophenols[2] and carboxylic acids.[3] The cleavage results in the formation of 2-hydroxyquinoline (I) and the alkylated cleaving reagent.



I X = Cl-, C_6H_5S-, RCOO-

These reactions suggested the possibility that 2-alkoxyquinolines might be cleaved by compounds containing the =NH grouping. Consequently in this work we have investigated the reactions between 2-benzyloxyquinoline (II) and certain aliphatic amines, aromatic amines and amides.

The aromatic amines, aniline, N-methylaniline, diphenylamine, carbazole and phenothiazine, reacted at relatively high temperatures like the acidic reagents to yield I and the alkylated amine. The aliphatic amines, piperidine and morpholine, showed this same cleavage at lower temperatures (boiling points of the amines). In addition, these cyclic aliphatic amines effected cleavage between the quinoline ring and the oxygen atom to yield the 2-aminoquinoline and benzyl alcohol. Dibenzylamine, acetanilide and N-benzylbenzenesulfonamide showed neither type of cleavage.



The reaction was also affected by the alkyl grouping, for experiments with diphenylamine and morpholine indicated that II was more reactive than 2-ethoxyquinoline. 2-Benzyloxybenzothiazole[3] did not react with diphenylamine at 115–125°.

Since phenothiazine reacted with II to form I in 90% yield, the other product which melted at 91–92° was thought to be N-benzylphenothiazine. The melting point corresponded with that reported by Desai[4] for N-benzylphenothiazine, but we were unable to prepare the compound by his method of heating sulfur and N-benzyldiphenylamine.

Finzi[5] reported a melting point of 132–134°

---

(1) P. Friedländer and H. Ostermaier, *Ber.*, **15**, 333 (1882).

(2) G. Illuminati and H. Gilman, THIS JOURNAL, **71**, 3349 (1949).

(3) H. Gilman, K. E. Lentz and J. A. Beel, *ibid.*, **74**, 1081 (1952).

(4) R. D. Desai, *J. Ind. Inst. Sci.*, **7**, 235 (1924).

(5) C. Finzi, *Gazz. chim. ital.*, **62**, 175 (1932).