

A solution of 1.8 g. (0.01 mole) of the carbinol base (IV) in 10 cc. of absolute ether and a similar solution of 1.4 g. (0.01 mole) of freshly distilled benzoyl chloride were poured together in a large Pyrex test-tube. An insoluble white addition compound was immediately formed, the heat of reaction causing the ether to boil. The test-tube was placed in a steam-bath and the ether boiled off. The residue darkened slightly and melted to a viscous liquid. Heating in the steam-bath was continued for one hour under reduced pressure, for three hours under atmospheric pressure. Moisture was excluded by means of a calcium chloride tube. The contents of the tube, now a solid crystalline mass, were dissolved in boiling hexone containing a little absolute alcohol. On cooling the solution a mass of white crystals slowly formed. The crystals were filtered off and recrystallized twice from pure hexone, the gummy insoluble portion being discarded. One gram of the pure benzoate hydrochloride was thus obtained. It melted at 162.5–163°. An additional 0.25 g. was obtained by concentrating and cooling the mother liquors and recrystallizing the product that separated. The yield of pure benzoate hydrochloride, calculated from carbinol base used, was 39% of the theoretical.

This hydrochloride is very soluble in water, ethyl alcohol, and *n*-butyl alcohol but only slightly soluble in acetone.

It may be recrystallized from pure acetone or acetone containing a little ethyl alcohol, but is best purified by recrystallizing from hexone. It is not hygroscopic.

An apparently polymorphic form of this hydrochloride melting at 151.5–152.5° was obtained the first time it was prepared. The presence of a trace of the high melting form raised the melting point to 163°. The low-melting form was converted into the high melting form by recrystallization from hexone and seeding with a trace of the high melting form. Calcd. for $C_{17}H_{21}N_2O_2Cl$: C, 63.63; H, 6.60; Cl, 11.08. Found: C, 63.77; H, 6.66; Cl, 10.99.

Summary

The preparation and properties of β -pyridyl- β -dimethylaminoethylcarbinyl benzoate hydrochloride and certain incidental compounds are described.

This benzoate is an effective local anesthetic and its pharmacological properties are compared to those of procaine, cocaine and the previously described β -pyridylmethylcarbinyl benzoate hydrochloride.

MADISON, WISCONSIN

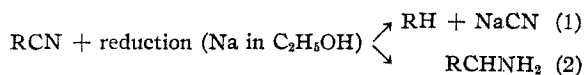
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[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

The Reduction of Cyanides

By L. A. WALTER AND S. M. McELVAIN

In an attempt to reduce α -phenyl- β -phenoxy-butyl cyanide to the corresponding amine with sodium and alcohol¹ an excellent yield of β -phenylbutyl phenyl ether with only a trace of the expected primary amine was obtained. This halogen-like behavior of the cyanide group suggested a further study of the reduction of cyanides in order to ascertain the effect of structure on the extent of the two competing reactions



The present paper reports the results obtained from the reduction of nine cyanides of varying structure. The amount of reaction (1) was determined by a Volhard titration of an aliquot of the water-soluble portion of the reaction mixture; in a few cases the cleavage product (RH) was isolated and found to correspond in amount to the cyanide ion found by titration. The extent of reaction (2) was determined by isolating and weighing the primary amine. In each reduction the ratio of cyanide to sodium was 0.25 mole to 1.5 atoms.

(1) Adams and Marvel, *THIS JOURNAL*, **42**, 315 (1920).

The results obtained are summarized in Table I.

TABLE I
PRODUCTS FROM THE REDUCTION OF CYANIDES

Run	RCN, R is	Yield of NaCN, %	Yield of RH, %	Yield of RCH ₂ NH ₂ , %
1	<i>n</i> -C ₄ H ₉	16	..	76
2	(CH ₃) ₂ CH	24	..	63
3	(CH ₃) ₃ C	33	..	60
4	<i>n</i> -C ₃ H ₇ \begin{matrix} \nearrow \text{CH} \\ \searrow \text{CH} \end{matrix}	6	..	64 ^a
5	<i>n</i> -C ₄ H ₉ \begin{matrix} \nearrow \text{C} \\ \searrow \text{C} \end{matrix}	10	7	54 ^a
6	(<i>n</i> -C ₄ H ₉) ₂	84	..	7
7	C ₆ H ₅ CH ₂	88	..	10
8	C ₆ H ₅ \begin{matrix} \nearrow \text{CH} \\ \searrow \text{CH} \end{matrix}	91	89 ^b	5
9	C ₆ H ₅ O(CH ₂) ₃ \begin{matrix} \nearrow \text{C} \\ \searrow \text{C} \end{matrix}	61	33 ^d	23 ^a

^a This amine is described in Table II. ^b β -Phenylbutyl phenyl ether, see Table II. ^c In addition to the products shown in the table a 21% yield of piperidine and an 11% yield of isobutylamine were obtained. Considering the yield of the latter compound it is apparent that 95% (61 + 23 + 11) of the original cyanide was accounted for. ^d Isopropylpiperidine, *cf.* Drake and McElvain, *THIS JOURNAL*, **55**, 1155 (1933), Ref. 5.

In the cases of the unsubstituted alkyl cyanides (runs 1-5) it is seen that the yield of primary amine decreases as R changes from a primary to a secondary and to a tertiary radical. With the lower molecular weight compounds (runs 1-3) the rise in the yield of sodium cyanide parallels the decrease in the yield of primary amine. With the higher molecular weight secondary and tertiary cyanides (runs 4 and 5) the yield of amine corresponds quite well to those obtained from the lower secondary and tertiary cyanides, but the yields of sodium cyanide are decidedly lower. The low yields of this latter product (and possibly the primary amines also) in these cases are due to incomplete reduction of the cyanide, for in both runs 4 and 5 sufficient unreacted cyanide was recovered to allow for as much of the original material to be accounted for as was possible in runs 1-3.

When the cyanide group is attached to a carbon which carries a phenyl group (runs 7 and 8), its halogen-like behavior is very pronounced. In this connection it should be noted that in the formation of the sodium salts of benzyl cyanide and α -phenylpropyl cyanide considerable amounts of toluene and *n*-propylbenzene are formed.² In these cases the hydrocarbon formation was explained as a reduction of the sodium salt of the cyanide by the hydrogen produced in its formation. It does not seem that intermediate salt formation is involved in the reductions described

would indicate that no intermediate salt formation is involved.

Velghe³ has reported the formation of *t*-butyl-piperidine from the reaction of methylmagnesium bromide with α -piperidinoisobutyronitrile. The halogen-like behavior of this particular cyanide group is demonstrated also by the high yield of sodium cyanide obtained from its reduction by sodium and alcohol (run 9). In this reduction there was also a small amount of cleavage of the α -piperidino grouping (see footnote *c*, Table I).

Finally, it should be noted that the readiness with which the cyanide group may be cleaved from a substituted benzyl cyanide offers a practical and convenient method of attaching a normal side chain to the benzene nucleus.

Experimental

The Nitriles.—4-Cyanoctane was prepared in 61% yields by the alkylation of butyl cyanide with butyl bromide and sodamide and 5-cyano-5-*n*-propylnonane was prepared in 69% yields by the alkylation of 4-cyanoctane with butyl bromide and sodamide according to the method of Ziegler and Ohlinger.⁴ The properties of these cyanides are described in Table II. α -Phenyl- θ -phenoxybutyl cyanide has been previously described.⁵ α -Piperidinoisobutyronitrile was prepared in 65% yields from piperidine hydrochloride, acetone and potassium cyanide.³ Isopropyl cyanide, phenyl cyanide and *t*-butyl cyanide were prepared in 51, 74 and 70% yields, respectively, by distillation of the corresponding amide with an equal weight of phosphorus pentoxide. Butyl and benzyl cyanides were prepared by the usual procedure from the corresponding halides and sodium cyanide.

TABLE II
COMPOUNDS NOT PREVIOUSLY LISTED IN THE LITERATURE

Compound	Formula	B. p., °C. (mm.)	d_4^{25}	n_D^{25}	Analyses, %			
					Calcd.		Found	
					C	H	C	H
4-Cyanoctane	C ₉ H ₁₇ N	72-73 (9)	0.8086	1.4188	77.62	12.31	78.00	12.65
5-Cyano-5- <i>n</i> -propylnonane	C ₁₃ H ₂₅ N	115-116 (9)	.8259	1.4356	79.91	12.91	80.53	12.92
5- <i>n</i> -Propylnonane	C ₁₂ H ₂₆	195-196 (740)	.5706	1.4217	84.60	15.40	84.88	15.35
2- <i>n</i> -Propylhexylamine	C ₉ H ₂₁ N	183-184 (740)	.7892	1.4324	75.43	14.78	75.36	14.90
2- <i>n</i> -Propyl-2- <i>n</i> -butylhexylamine	C ₁₈ H ₃₉ N ^a	113-114 (10)	.8169	1.4479	78.30	14.66	78.04	14.57
2-Methyl-2-piperidinopropylamine	C ₉ H ₂₀ N ₂ ^b	215-216 (740)	.9043	1.4746	69.20	12.91	69.29	12.86
θ -Phenylbutyl phenyl ether	C ₁₆ H ₁₈ O	144-146 (1)	1.0201	1.5504	84.90	8.02	85.16	8.16

^a Hydrochloride, C₁₃H₃₀NCl, m. p. 139-141. Calcd.: Cl, 15.04. Found: Cl, 15.27.

^b Dihydrochloride, C₉H₂₂N₂Cl₂, m. p. 260-265 (decomp.). Calcd.: Cl, 30.94. Found: Cl, 30.86.

in the present paper because under the conditions used cyanoacetic ester and malononitrile gave no sodium cyanide or primary amine but formed salts which appeared to be unaffected by the reducing agent. Also the high yield of sodium cyanide and low yield of amine from the reduction of both phenyl and benzyl cyanides (runs 6 and 7)

General Procedure.—In a one-liter three-necked flask equipped with a mechanical stirrer, reflux condenser and a dropping funnel was placed 150 cc. of toluene and 35 g. of sodium. The toluene was heated to boiling and the mixture stirred vigorously until the sodium was finely divided. To this was added, just rapidly enough to keep

(3) Velghe, *Bull. Sci. Acad. Roy. Belg.*, [5] **11**, 301 (1925).

(4) Ziegler and Ohlinger, *Ann.*, **485**, 84 (1932).

(5) Walter and McElvain, *This Journal*, **55**, 4627 (1933).

(2) Rising and co-workers, *This Journal*, **52**, 1069, 2524 (1930).

the mixture refluxing vigorously, 0.25 mole of the cyanide dissolved in 35 g. of absolute alcohol. After this addition, another 35 g. of absolute alcohol was added at the same rate. The mixture was allowed to cool and 95% alcohol slowly added until any unreacted sodium had disappeared. Then 500 cc. of water was added, the toluene layer separated and washed several times with 150-cc. portions of water and these washings together with the first aqueous layer diluted to exactly one liter. An aliquot portion of the solution was titrated for cyanide ion with standard silver nitrate solution according to the method of Volhard.

The amine was removed from the toluene by extracting with 15% hydrochloric acid and any amine in the aqueous washings steam distilled and added to this acid extract.

Those amines which were very insoluble in water were isolated by fractionation of the toluene layer. The cleavage product resulting from the replacement of the cyanide group by hydrogen was isolated in a few instances and found to correspond to the amount of cyanide ion found by titration.

Summary

A study of the reduction of a variety of cyanides by sodium and alcohol has been made and the extent of the two competing reactions, $\text{RCN} \rightarrow \text{RCH}_2\text{NH}_2$ and $\text{RCN} \rightarrow \text{RH} + \text{NaCN}$, determined in each case.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

The Oxidation of the Benzene Ring of Arylboric Acids by Potassium Permanganate

BY BERNARD BETTMAN AND G. E. K. BRANCH

When *m*- and *p*-tolylboric acids, $\text{CH}_3\text{C}_6\text{H}_4\text{B}(\text{OH})_2$, are dissolved in 0.3 *N* alkali and oxidized with a saturated solution of potassium permanganate, good yields of *m*- and *p*-carboxylphenylboric acids, $\text{HO}_2\text{CC}_6\text{H}_4\text{B}(\text{OH})_2$, are obtained.¹

These preparations can be carried out at room temperatures, though heating near the end of the reaction is advisable. Koenig and Scharrnbeck report a similar preparation of *o*-carboxylphenylboric acid. The product melted at 152° and gave percentages of carbon and hydrogen corresponding to the formula $\text{C}_7\text{H}_7\text{O}_4\text{B}$. We have found the method very suitable for the preparation of *m*- and *p*-carboxylphenylboric acids, but we have not succeeded in preparing the *o*-isomer.

Oxidation of *o*-Tolylboric Acid.—When we added the theoretical amount of potassium permanganate (six oxidizing equivalents per mole of tolylboric acid) to an alkaline solution of *o*-tolylboric acid at room temperatures, the permanganate ion was rapidly and completely reduced to manganese dioxide. From the reaction product we obtained an acid melting at 150–154°. When this acid was titrated with alkali using phenolphthalein as the indicator, an equivalent weight greater than a thousand was obtained. In the presence of mannitol an equivalent weight of 130 was obtained. These results show that the acidic group in the reaction product is $\text{B}(\text{OH})_2$ and not carboxyl. When the substance was purified the melting point rose to 170°. The product was

unchanged *o*-tolylboric acid, m. p. 171° (Koenig and Scharrnbeck give 168°), equivalent weight 136. We varied the *P_H* of the solution from that of 1 *N* acid to that of 1.5 *N* alkali, and the temperature from 20 to 0°, and tried the substitution of manganate for permanganate ion. In every case the theoretical amount of oxidizing agent was reduced, but the only arylboric acid obtained was *o*-tolylboric acid. Our results seemed to indicate that oxidation of the benzene ring in *o*-tolylboric acid or in *o*-carboxylphenylboric acid is faster than the oxidation of the methyl group in *o*-tolylboric acid to a carboxyl group.

If our failure to obtain *o*-carboxylphenylboric acid is to be attributed to the oxidation of the benzene ring, *o*-tolylboric acid can rapidly reduce much more than six oxidizing equivalents of permanganate ion per mole of tolylboric acid. We tested this deduction in the following experiment.

A saturated solution of potassium permanganate was added in small portions to a 2% solution of *o*-tolylboric acid in 0.3 *N* alkali. The portions of permanganate solutions contained about a quarter of an oxidizing equivalent per mole of tolylboric acid. Fresh portions of the permanganate solutions were added when the previously added portions had been reduced completely to manganese dioxide. This process was continued until the permanganate was no longer reduced. The experiment was done at room temperatures. In this way we were able to reduce twenty-four equivalents of potassium permanganate per mole of *o*-tolylboric acid. The reduction was quite fast. The individual portions of permanganate were reduced in less than a minute, and this rate was maintained nearly up to the last one or two equivalents.

The large quantities of potassium permanganate reduced

(1) Michaelis, *Ann.*, **315**, 19 (1901), and Koenig and Scharrnbeck, *J. prakt. Chem.*, **128**, 153 (1930).