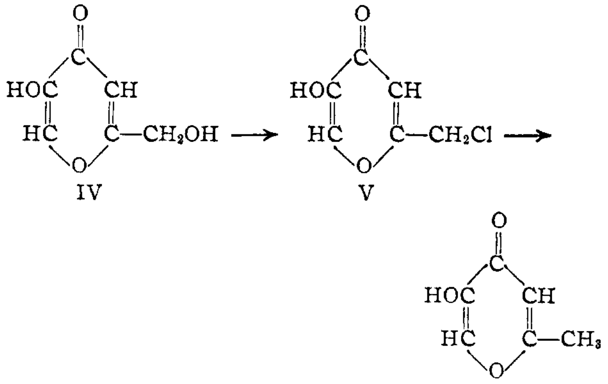

IV

V

VI

the grouping $HO—[\overset{|}{C}=\overset{|}{C}]—CH_2Cl$ might be expected to show some of the behavior of $HOCH_2Cl$.

Experimental

2-Chloromethyl-3-hydroxy-1,4-pyrone (II).—The pyrone from hydroxystreptomycin (289 mg.) was refluxed with 1.5 ml. of dry chloroform and 0.5 ml. of purified thionyl chloride. After 10 minutes, 0.4 ml. of thionyl chloride and 1 ml. of chloroform were added and the refluxing continued for 30 minutes more. The dark brown solution was concentrated *in vacuo* to almost black crystals. Crystallization from benzene gave 140 mg. of dark brown crystals melting at 120–140°. Sublimation followed by crystallization from benzene yielded 40 mg. of pure chloro compound in the form of white needles.

Anal. Calcd. for $C_6H_5O_3Cl$: C, 44.9; H, 3.14; Cl, 21.6. Found: C, 44.6; H, 3.49; Cl, 21.9.

The chloro compound started to sinter and darken at 137° and melted at 145–146° to a red melt. It gave a violet color with ferric chloride and was decomposed by hot water with the liberation of hydrochloric acid.

Reduction of the Chloro Compound.—The chloro compound (58 mg.) was dissolved in 1.5 ml. of acetic acid and 350 mg. of zinc dust added. The reaction mixture was worked with a glass rod for 10 minutes. After removal of the excess zinc, the acetic acid solution was treated with hydrogen sulfide, diluted with water and the zinc sulfide removed by filtration. The filtrate was neutralized and then made slightly acid with hydrochloric acid. Extraction with ether gave 25 mg. of crystals which were purified by sublimation and crystallization from benzene. The 20 mg. of colorless product analyzed correctly for maltol.

Anal. Calcd. for $C_6H_6O_3$: C, 57.1; H, 4.80. Found: C, 57.6; H, 4.88.

The material had the characteristic odor of maltol and gave a violet color with ferric chloride. It melted at 147.5–148.5° (uncor.) and showed no depression in melting point with carefully purified maltol (m.p. 148.5–149.5°).

Further confirmation was obtained by conversion to the benzoate. For this purpose 5.5 mg. of the product was benzoylated with 6 mg. of benzoyl chloride in pyridine. Crystallization from dilute alcohol and then acetone–petroleum ether gave 6.8 mg. of maltol benzoate (m.p. 113–114°, cor.) which showed no depression on admixture with an authentic sample (m.p. 114–115°, cor.).

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[5] One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture. Article not copyrighted.

A Modified Method for the Meerwein-Ponndorf-Verley Reduction

BY W. L. TRUETT AND W. N. MOULTON

Although it is generally assumed in the reduction of carbonyl compounds by aluminum isopropoxide that the acetone formed must be removed in order to obtain good yields,[1] several α-haloketones[2,3] and one β-aminoketone[4] have been successfully reduced without removal of acetone.

TABLE I

Compound reduced	Product	Yield,[a] %	n_D or m.p.[b] °C.	Method
Benzophenone	Benzhydrol	96	64–66	A_1
		98	63–65	A_2
		98	60–62	A_3
Benzosuberone[c]	Benzosuberol[d]	94	102.5–104.5	A_1
		99	90–95	A_2
		99	98–100	A_3
dl-Camphor	*dl*-Isoborneol *dl*-Borneol	92[e]	167–172	A_1
Cinnamylideneacetone[f]	1-Phenylhexa-1,3-diene-5-ol[g]	76[h]	60–62	A_1
Cyclopentanone	Cyclopentanol	60	1.4387[i]	B
β-Piperidylpropiophenone[j]	1-Phenyl-3-piperidylpropanol-1-hydrochloride[k,l]	40[h]	134–135.5	A_1
Benzaldehyde	Benzyl alcohol	85	1.5321[i]	B
Phenyl-2-methoxy-1-naphthyl ketone[m]	Phenyl-2-methoxy-1-naphthylcarbinol	0[n]	80–90	A_1
		95	98–100	C
Benzoin	*meso*-Hydrobenzoin	94	131–134	A_1
α-Benzylaminodesoxybenzoin[o]	1,2-Diphenyl-2-benzylaminoethanol hydrochloride[o,l]	72[h]	225–229	A_1
Benzalacetophenone	1,3-Diphenyl-2-propene-1-ol[p]	76[h]	57–59	A_1
Pinacolone	Pinacolyl alcohol	36	1.3980[i]	B

[a] Yield refers to the crude product unless otherwise noted. [b] Melting points (uncorrected) are listed for solid products, refractive indices (at 25°) for liquid products. [c] This compound was prepared by the method of Pl. A. Plattner [*Helv. Chim. Acta*, **27**, 801 (1944)]. [d] This compound was reported by G. Baddeley and J. Chadwick [*J. Chem. Soc.*, 368 (1951)], m.p. 100–101°. [e] The yield stated represents a mixture of isomers. Isoborneol was isolated from the mixture by preparation of its *p*-nitrobenzoate in 30% yield, m.p. 125.5–126.5°. [f] This compound was prepared by the method of J. T. Plati, W. H. Strain and S. L. Warren [THIS JOURNAL, 65, 1273 (1943)]. [g] This compound has been reported by A. K. Macbeth and J. A. Mills [*J. Chem. Soc.*, 2646 (1949)], m.p. 65–66°. [h] Yield stated is that of the purified compound crystallized from the appropriate solvent. [i] The low value of the refractive index is believed due to the difficulties inherent in the purification of small quantities of liquids. The material gave a negative 2,4 DNPH test by the method reported in R. L. Shriner and R. C. Fuson ["Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N.Y., 1948, p. 171]. [j] This compound was prepared by the method of F. F. Blicke ["Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N.Y., 1942, p. 329]. [k] This compound has been reported by C. Mannich and D. Lammerling [*Ber.*, **55**, 3510 (1922)], m.p. 138°. [l] The compound was isolated by the addition of ethereal hydrogen chloride to the dried ether extract of the crude product. [m] The ketone was prepared by the method of F. E. Ray and W. A. Moomaw [THIS JOURNAL, **55**, 3833 (1933)]; Dr. C. F. Koelsch furnished us with a generous sample. The carbinol was also reported by the above investigators, m.p. 98°. [n] Although the melting point of the crude product prepared by method A_1 suggests the presence of the carbinol, crystallization of the material yielded only unreduced ketone, m.p. 123–123.5°, 80% recovery. [o] The ketone was prepared by the method of R. E. Lutz, J. A. Freek and R. S. Murphy [THIS JOURNAL, **70**, 2015 (1948)]. The carbinol was also reported by these investigators, m.p. 228–229°. [p] This compound was reported by H. Meerwein and R. Schmidt [*Ann.*, **444**, 221 (1925)], m.p. 57–58°.

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[1] A. L. Wilds, "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 178.

[2] (a) S. Winstein, *et al.*, *J. Org. Chem.*, **11**, 150 (1946); (b) S. Winstein, *et al.*, THIS JOURNAL, **68**, 1831 (1946).

[3] R. E. Lutz, J. F. Codington and N. H. Leake, *ibid.*, **69**, 1260 (1947).

[4] R. E. Lutz, R. H. Jordan and W. L. Truett, *ibid.*, **72**, 4085 (1950).

We have been able to show that in the Meerwein–Ponndorf–Verley reduction in a majority of cases removal of acetone is unnecessary. Compounds reduced are listed in Table I. It will be noted that in the cases of benzophenone and benzosuberone, which were reduced using varying mole ratios of aluminum isopropoxide, the quality of the product, as judged by melting point, is better with the higher mole ratios of aluminum isopropoxide.

Of particular interest is the successful reduction of benzalacetophenone, cinnamylideneacetone and cyclopentanone. As has been pointed out by Macbeth and Mills,[5] compounds of this type cannot be reduced in good yields by the normal procedure, but by the modification introduced by Macbeth and Mills of slowly adding the carbonyl compound to an excess of aluminum isopropoxide, excellent yields are realized. Apparently in our method the rate of reduction is more rapid than the rates of the competing aldol and Tischtschenko condensations.

The one failure of our method noted is in the reduction of phenyl 2-methoxy-1-naphthyl ketone, which was reduced in 95% yield by the normal method.

Experimental

Method A_1.—To 51 g. (0.25 mole) of aluminum isopropoxide in 200 ml. of boiling isopropyl alcohol was added 0.05 mole of the appropriate carbonyl compound in 50 ml. of boiling isopropyl alcohol over a period of 5 minutes. The solution was heated under reflux for one hour, poured into approximately 1.5 liters of water and sodium hydroxide solution was added until a clear solution resulted. The product was extracted with ether and the ether extract dried over magnesium sulfate. Evaporation of the dried ether extract gave the crude product.

Method A_2.—Method A_2 differs from method A_1 in that only 0.15 mole of aluminum isopropoxide and 150 ml. total volume of isopropyl alcohol was employed.

Method A_3.—Method A_3 differs from method A_1 in that only 0.05 mole of aluminum isopropoxide and 50 ml. total volume of isopropyl alcohol was employed.

Method B.—Method B differs from method A_1 only in the manner in which the product was isolated. After one hour reflux the isopropyl alcohol was evaporated to a low volume and sodium hydroxide solution was added. The liquid was filtered from the gelatinous mixture which was then washed twice with ether. The combined filtrates were dried over magnesium sulfate, decanted and distilled through a small Vigreux column.

Method C.—The normal procedure as outlined by Wilds[1] was followed.

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[5] A. K. Macbeth and J. A. Mills, *J. Chem. Soc.*, 2646 (1949).

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The Preparation of Alpha C^{14}-Labeled Pyruvic Acid and a Study of the Hydrolysis of Pyruvonitrile[1]

BY R. C. THOMAS, JR., C. H. WANG AND BERT E. CHRISTENSEN

The importance of alpha C^{14}-labeled pyruvic acid as an intermediate metabolite has made the synthesis of this acid in good yield increasingly important in tracer work. The older procedures employing aqueous hydrolysis of pyruvonitrile either give low over-all yields 20–25%[2] (based on acetate), or a product which is unsatisfactory[3] due to the incomplete removal of an acid contaminant in the pyruvic acid, probably acetic acid. For these reasons the hydrolysis of pyruvonitrile in an ethereal medium as recently described by Anker[4] has been modified and adapted to a larger scale operation for the preparation of pyruvic acid from sodium acetate. This procedure gives an over-all yield of 40% of a 98% pyruvic acid based both on radioactivity measurements and the quantity of sodium acetate used.

Experimental[5]

Hydrolysis of Pyruvonitrile in Aqueous Concentrated Hydrochloric Acid Media.—The hydrolysis of 7.12 g. (103 millimoles) of C^{14}-carbonyl labeled pyruvonitrile (specific activity of 2.1×10^4 c.p.m./millimole or a total count of 2.2×10^6 c.p.m.) at 0° with 7.4 ml. (309 millimoles based on water) of 12 *N* hydrochloric acid yielded 2.12 g. (53 millimoles) of non-radioactive formic acid, 4.08 g. (68 millimoles) of acetic acid (specific activity 2.1×10^4 c.p.m./millimole or a total count of 1.4×10^6 c.p.m.), 2.9 g. of a mixture composed of 10.5 millimoles of pyruvamide and 22.3 millimoles of pyruvic acid (specific activity of the mixture 2.1×10^4 c.p.m./millimole or a total count 0.70×10^6 c.p.m.).

Hydrolysis of Pyruvonitrile in an Ethereal Medium.—Hydrolysis of 6.6 g. of C^{14}-carbonyl labeled pyruvonitrile in an ethereal medium using dry hydrogen chloride gave 6.6 g. of pyruvamide (79% based on pyruvonitrile or 62% based on sodium acetate) m.p. 123–124° (corrected). The starting material, 14.5 mg. of sodium acetate gave 6.6×10^7 c.p.m. and the product 6.6 g. of pyruvamide gave 4.2×10^7 c.p.m. which is equivalent to a radioactivity recovery of 63%.

Conversion of the pyruvamide to pyruvic acid by hydrolysis in concentrated hydrochloric acid gave a 64% yield of pyruvic acid which was found by analysis to be 98% pure. The pyruvic acid thus obtained had a radioactivity of 2.7×10^7 c.p.m., equivalent to a radioactivity recovery of 65% based on the radioactivity of pyruvamide or 41% based on the radioactivity of the sodium acetate.

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[1] This research was conducted under a contract No. N8 onr 73501, between the Office of Naval Research and Oregon State College and supported in part by U.S.A.E.C.

[2] Claisen and Shadwell, *Ber.*, **11**, 620 1503 (1878); Claisen and Marasse, *ibid.*, **20**, 2196 (1887); Gould and co-workers, *J. Biol. Chem.*, **177**, 722 (1949).

[3] Hughes and Reid, Atomic Energy Commission Document number 2370.

[4] Anker, *J. Biol. Chem.*, **176**, 133 (1949).

[5] For complete details order Document 3354 from American Documentation Institute, 1719 N Street, Washington 6, D. C., remitting $1.00 for microfilm (images 1 inch high on standard 35 mm. motion picture film) or $1.20 for photocopies (6 × 8 inches) readable without optical aid.

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RECEIVED JULY 16, 1951

Preparation and Identification of N-Formylbenzamide and its Condensation Product with Phenylhydrazine

BY QUENTIN E. THOMPSON

In connection with studies on the diacylation of amides, we have prepared N-formyldibenzamide hydrate (I).[1] This compound was observed to cleave during attempted recrystallization from nonpolar solvents giving benzoic acid and a compound, m.p. 112–113°. On the basis of analytical data, molecular weight determinations and oxidation to benzamide and carbon dioxide, this material was identified as the expected product, N-formylbenza-

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[1] Q. E. Thompson, THIS JOURNAL, **73**, 5841 (1951).