116.5°. The ortho acid, 1.5 g., was somewhat impure and melted at 47.1–49.3° (recorded value 51°). A small amount of material[3] which was probably a disubstitution product was also present.

A preparation, carried out in the apparatus which was used before the high speed stirrer was developed, consisted of the addition of 250 ml. of isopropylbenzene to the product of the reaction of 42 g. (0.4 mole) of amyl chloride and 37 g. of sodium in 200 ml. of petroleum ether. The mixture was refluxed at 52° for two and one-half hours. Cuminic acid, 3.8 g., was isolated and characterized by the melting point, 154°, of the amide. The recorded value is 155°.[4]

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[3] Persoz, *Ann.*, **44**, 312 (1842).

[4] Gattermann and Schmidt, *ibid.*, **244**, 52 (1888).

CONTRIBUTION NO. 305 FROM THE
RESEARCH LABORATORY OF ORGANIC CHEMISTRY
MASSACHUSETTS INSTITUTE OF TECHNOLOGY
CAMBRIDGE, MASS.

RECEIVED MARCH 15, 1945

An Improved Method for the Preparation of 1-Isobutyryl-2-phenylhydrazine

BY MARTIN JACOBSON AND FRED ACREE, JR.

The preparation of 1-isobutyryl-2-phenylhydrazine has been reported by several investigators in either very low or unspecified yields. Bölsing and Tafel,[1] Brunner,[2] Leighton[3] (25% yield) and van Alphen[4] (38% yield) prepared the hydrazine from phenylhydrazine and isobutyric acid. Ponzio[5] prepared the substance from isobutyryldinitroethane and phenylhydrazine, while Widman[6] and van Alphen[4] treated phenylhydrazine with isobutyryl chloride and isobutyryl bromide, respectively.

In this Laboratory 67% of the theoretical quantity of the hydrazine has been obtained by the following procedure: A mixture of 378 g. (3.5 moles) of phenylhydrazine (technical), 700 g. (7 moles, 100% excess) of isobutyric acid (technical), and 250 ml. of toluene was refluxed under a condenser equipped with a water trap. After forty-eight hours 77 ml. of water had been collected (theory for 3.5 moles, 63 ml.) and the reaction mixture was then cooled in an ice-box overnight. The substance which separated was filtered and washed with ether, and the crude air-dried product (425 g., 68% yield), consisting of colorless, shining plates, melted at 139–141°. After it was recrystallized from ethanol the substance weighed 418 g. (67% yield) and had a constant melting point of 143° (cor.). Reworking of the toluene and ethanol mother liquors caused an additional 12 g. of crude material to separate, from which 2 g. (0.3%) of the pure hydrazine was obtained on recrystallization.

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[1] Bölsing and Tafel, *Ber.*, **25**, 1552 (1892).

[2] Brunner, *Monatsh.*, **18**, 97 (1897).

[3] Leighton, *Am. Chem. J.*, **20**, 678 (1898).

[4] van Alphen, *Rec. trav. chim.*, **43**, 823 (1924).

[5] Ponzio, *Gazz. chim. ital.*, **35**, 395 (1905).

[6] Widman, *Ber.*, **27**, 1967 (1894).

U. S. DEPARTMENT OF AGRICULTURE
AGRICULTURAL RESEARCH ADMINISTRATION
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RECEIVED MAY 12, 1945

Improved Preparation of Isopropylidene Glycerol

BY MELVIN S. NEWMAN AND MARY RENOLL

We have recently modified Fischer's[1] procedure for making isopropylidene glycerol so that this compound may be prepared quite easily in almost quantitative yield. The physical properties of our once-distilled product compare favorably with those for Fischer's thrice-distilled material.

Experimental

A mixture of 100 g. (1.09 moles) of anhydrous distilled glycerol, 300 cc. of acetone, 300 cc. of petroleum ether (b. p. 35–55°, Skellysolve F) and 3.0 g. of *p*-toluenesulfonic acid monohydrate was placed in a one-liter three-necked flask fitted with a stirrer and a helices-packed (18 inches) total-reflux column topped by a total-reflux phase-separating head. The mixture was stirred and refluxed (temperature at head 25–28°) for forty-three hours. The mixture was homogeneous after eighteen hours. After twenty-four hours the reaction was almost complete as judged by the amount of lower aqueous phase being formed in the head. The cooled reaction mixture was neutralized with 1.3 g. of powdered fused sodium acetate. After filtration and evaporation of solvent, the isopropylidene glycerol was obtained in 96.6% yield (139 g.) as a colorless liquid, b. p. 80.5–80.8° (11 mm.), $n^{25}_{\rm D}$ 1.4326, d^{25}_{4} 1.0626, $MR_{\rm D}$ 32.30, calcd. 32.43 (using values in Gilman[2] except for ether oxygen which was calculated as 1.60 by means of the Lorentz–Lorenz formula using $n^{20}_{\rm D}$ 1.42227 and d^{20}_{4} 1.03361 for dioxane[3]). In a similar experiment using 100 g. of about 95% glycerol the yield of isopropylidene glycerol was 125 g.

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[1] E. Fischer and Pfähler, *Ber.*, **53**, 1606 (1920).

[2] Gilman, "Organic Chemistry," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 1751.

[3] Allsopp and Willis, *Proc. Roy. Soc.* (London), **A153**, 392 (1936).

CHEMISTRY LABORATORY
THE OHIO STATE UNIVERSITY
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RECEIVED JUNE 11, 1945

Reaction of Theophylline with Gibbs' Reagent

BY HARRY W. RAYBIN

Recently, the use of Gibbs' reagent (2,6-dichloroquinone-chloro-imide) has been proposed for the detection and determination of uric acid.[1]

The interaction of various compounds including the purines, with Gibbs' reagent have been studied by Scudi,[2] Leahy,[3] and Fearon,[1] and among the purines only uric acid has been noted as reacting. The statement of Fearon[1] that "Less oxidized purines, such as hypoxanthine and xanthine, give no colours with this reagent" needs qualification in view of the readily obtained blue color given by theophylline (1,3-dimethylxanthine) with this reagent. The addition of a few drops of 0.4% alcoholic Gibbs' reagent to a borax or sesquicarbonate solution of theophylline produces a blue color, with the noteworthy property of giving an insoluble red-violet precipitate by the addition of solid sesquicarbonate to saturation. The violet-red precipitate is obtained with 0.2 mg. of theophylline per cc. (aminophylline is not suited

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[1] W. R. Fearon, *Biochem. J.*, **38**, 399 (1944).

[2] J. V. Scudi, *J. Biol. Chem.*, **139**, 715 (1941).

[3] H. W. Leahy, *et al.*, *J. Milk Technology*, **3**, 183 (1940).

to demonstrate the reaction as the ethylenediamine destroys the reagent). The blue solution fades in about fifteen minutes, but may be stabilized by extraction with butyl alcohol. Another glyoxaline (4,5-diphenylglyoxaline) has also been observed to give a blue color with Gibbs' reagent.

CHEMICAL LABORATORY
NEW YORK CITY
DEPARTMENT OF HEALTH
RECEIVED MAY 23, 1945

The Protolytic Activity of Hydrogen Chloride and of Hydrogen Bromide in Ethyl Ether

BY A. WEISSBERGER

Hantzsch and Weissberger[1a,b] found a remarkable difference in the reaction rate of diazoacetic ester with hydrogen chloride and hydrogen bromide in ethyl ether as a solvent. While 0.01 M hydrogen bromide and diazoacetic ester in ether react at a rate similar to that in tetrachloroethane, (2.2[2]), a 0.01 M solution of hydrogen chloride and diazoacetic ester in ether reacts about 10^4 times slower (0.00016[2]). The difference between the two hydrogen halides, which appears to diminish at higher concentrations, is regarded as characteristic for the ethereal solutions of the hydrogen halides and not as specific for their reaction with diazoacetic ester because dimethylaminoazobenzene in ether containing 0.02 mole per liter of hydrogen chloride is less red than a solution containing 0.007 mole per liter of hydrogen bromide.[1a]

In order to test further the difference between ethereal solutions of hydrogen chloride and hydrogen bromide, *l*-menthone was used as a reagent.[3] The optical inversion of this compound was measured as described previously.[4] The data are listed in the table, $k + k' = \frac{1}{t} \log^{10} \frac{\rho_\infty - \rho_0}{\rho_\infty - \rho_t}$, where ρ_0, ρ_∞ and ρ_t are the rotation angles at the time of the first reading, at equilibrium and at a time t after the first reading, respectively.[4a]

MENTHONE 0.5 MOLE/LITER IN ETHYL ETHER, 20.0 ±0.1°

Acid	Concn. in mole/liter	$k + k'$	$(k + k')$/Concn.
HCl	0.05	0.0019 min.$^{-1}$	0.038 liters mole^{-1} min.$^{-1}$
HBr	.0005	.07	140
	.001	.15	150
	.0025	.36	144

In the interval measured, the rate is proportional to the concentration of hydrogen bromide. By means of a linear extrapolation, one calculates for the inversion of 0.5 M menthone with 0.05 M hydrogen bromide in ether a rate $(k + k') = 7.2$, which is 3.8 × 10^3 times higher than that found with 0.05 M hydrogen chloride.[4d] This confirms that the effect of ether on hydrogen chloride is not specific for the diazo ester decomposition. The factor for the menthone inversion (3.8 × 10^3) is smaller than for the diazo ester decomposition (1.4 × 10^4), presumably because the acid is more dilute in the diazo ester decomposition and the effect of the ether increases with greater dilution.

The rate of the menthone inversion with hydrogen bromide in ether is, in the range of the experiments, proportional to the concentration of the acid, while the inversion rate with hydrogen chloride is proportional to the square of the acid concentration.[4d] The latter dependence agrees with the mechanism of the menthone inversion with trichloroacetic acid in benzene,[4a] *viz.*, a transition from *l*-menthone to *d*-iso-menthone and *vice versa* by interaction of a binary acid menthone complex with a further molecule of the acid.

In the *reaction with diazoacetic ester*, 0.1 M hydrogen bromide has about the same rate in ether (2.2[2]) and in tetrachloroethane (2.5[2]), and 0.01 molar hydrogen chloride in tetrachloroethane has roughly the same rate (1.6[2]). The corresponding rates[2] for the 0.02 M hydrogen halides are 3.6, 6 and 3, respectively. With 0.02 and 0.01 M hydrogen chloride in toluene, the rates are 0.28 and 0.022, respectively, *i. e.*, the reactivity of the hydrogen chloride in toluene is lower than in tetrachloroethane and shows a greater drop with the dilution than in the latter solvent. A direct comparison between the rate of the *menthone inversion* with hydrogen bromide in ether and that with hydrogen chloride in benzene is not possible because of the different dependency of the rate on the acid concentration which was mentioned above. However, it is noteworthy that the rate of the menthone inversion with 0.0025 M hydrogen bromide in ether is 0.36, while the rate of the inversion with 0.0048 M hydrogen chloride in benzene is 0.00067. An effect of the excess menthone on the hydrogen chloride may be responsible for the difference between the two hydrogen halides. However, the relatively low rate of both the menthone inversion and the diazo ester decomposition seems to indicate that there is also an interference of the aromatic solvent with hydrogen chloride.

This brings to mind that Kablukoff[5] obtained a crystalline compound from solutions of hydrogen chloride in benzene. The same author found a sinking of the molecular conductivity of hydrogen chloride in ether with increasing dilution. This observation was confirmed by Mounajed[6] and may indicate a peculiarity of solutions of hydrogen chloride in ether which has to do with their low protolytic activity.

No special experiments were made in order to make sure that the difference in the activity of

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(1) (a) Hantzsch and Weissberger, *Z. physik. Chem.*, **125**, 251 (1927); (b) Weissberger, Dissertation, Leipzig, 1924.

(2) Rate constant of 2nd order reaction at 0° in liters mole^{-1} min.$^{-1}$ (natural logarithms).

(3) A. Dörken, Dissertation, Leipzig, 1934.

(4) (a) Weissberger, THIS JOURNAL, **65**, 102 (1943); (b) **65**, 242 (1943); (c) **65**, 245 (1943); (d) Weissberger and Thomas, *ibid.*, **65**, 402 (1943).

(5) Kablukoff, *Z. physik. Chem.*, **4**, 429 (1889).

(6) Mounajed, *Comp. rend.*, **197**, 44 (1933).