TABLE I

3-PYRIDYL ARYL KETONES

3-Pyridyl ketones	Yields, g.	Yields, %	M.p., °C.	B.p.,[g] °C.	Analyses, % Calcd. C	Analyses, % Calcd. H	Analyses, % Found C	Analyses, % Found H
Phenyl	22.3	60.9	32–34[a,b]	139–142				
m-Tolyl	4.1	41.9	37–38[c]	148–150	79.17	5.62	79.01	5.77
p-Tolyl	5.1	52.4	78.0–78.5[c,d]	175–176				
p-Chlorophenyl	1.7	15.6	88–89[e]	150–153	66.12	3.71	66.19	3.95
2-Naphthyl	3.8	32.5	77.8[e,f]	197–200	82.40	4.72	82.91	4.85

[a] Unrecrystallized. [b] The m.p. of 3-pyridyl phenyl ketone has been given as 39°.[14] [c] From benzene–petroleum ether "A." [d] This agrees with the literature value.[15] [e] From alcohol. [f] "3-Pyridyl naphthyl ketone" has been described as a brown tar.[14] [g] The boiling points were determined at 2 mm. pressure except for 3-pyridyl *p*-tolyl ketone which was determined at 6 mm.

1,3-Diphenyl-3-(3-pyridyl)-propanone-1.—Benzalacetophenone (10.4 g.) was treated with 3-pyridyllithium in the usual way, and the mixture decomposed with dilute hydrochloric acid, which produced a brown tar. The tar and the acid layer were both made basic with ammonium hydroxide and extracted quickly with ether. The ether extract started depositing a light yellow solid at once (2 g., 10%). The solid was white when crystallized from alcohol and melted at 190.5–191.5°. Analysis in the Grignard machine seemed to indicate one carbonyl per mole of compound, so tentatively it is assumed that 1,4-addition had occurred.

Anal. Calcd. for $C_{20}H_{17}NO$: carbonyl, 9.76. Found: carbonyl, 9.76.

The compound crystallized from benzene with one molecule of benzene of crystallization; m.p. (in a preheated block) 220–221°.

Anal. Calcd. for $C_{20}H_{17}NO \cdot C_6H_6$: C, 85.43; H, 6.38. Found: C, 85.50, 85.53; H, 6.23, 6.35.

No picrate nor chloroplatinate could be prepared from the above compound.

1,3-Diphenyl-1-(3-pyridyl)-propanol-1.—Benzylacetophenone (10.5 g.) was added as a solid to an equivalent of 3-pyridyllithium. The product was worked up as for diphenylpyridylcarbinol except that the hydrochloride could not be recrystallized. The free base crystallized easily from benzene; m.p. 118.5–119°. There was an indefinite second m.p. at about 100° which was observed in a preheated block. The yield was 7.6 g. (52.4%).

Anal. Calcd. for $C_{20}H_{19}NO$: C, 82.96; H, 6.63. Found: C, 83.43, 83.45, 83.49; H, 6.85, 6.72, 6.77.

The chloroplatinate was prepared in and recrystallized from a mixture of two parts alcohol and one part 6 *N* hydrochloric acid. The salt formed light orange needles; m.p. 211–212° (dec.).

Anal. Calcd. for $C_{40}H_{40}Cl_6N_2O_2Pt$: C, 48.57; H, 4.09; Pt, 19.74. Found: C, 48.92; H, 4.32; Pt, 19.76.

1-(3-Pyridyl)-cyclohexanol.—Cyclohexanone (19.6, 0.2 mole) in 50 ml. of ether was added to an equivalent of pyridyllithium at −40° in the usual way. The mixture was decomposed with 10% hydrochloric acid. The acid layer was removed and made basic with ammonium hydroxide and the product extracted with ether. A tan solid (24.5 g., 69.2%) was left after evaporation of the ether. This was decolorized in alcohol with Norite but was recrystallized from a benzene–petroleum ether "A" mixture with about 50% loss. The compound formed pure white plates melting at 89–90°.

Anal. Calcd. for $C_{11}H_{15}NO$: C, 74.55; H, 8.63. Found: C, 74.61, 74.54; H, 8.64, 8.67.

The picrate was prepared in benzene and recrystallized from alcohol. It formed fine dark yellow needles melting at 166–167°.

3-Pyridyl Ketones.—The ketones containing the pyridyl radical were prepared by the following procedure. The aromatic nitrile (0.05 mole, except for benzonitrile which was used in runs four times as large) dissolved in dry ether (20 ml., or more when the solubility of the nitrile was low) was cooled to −35°, when crystallization could be avoided, and was added rapidly to an equivalent of 3-pyridyllithium at −35 to −50°. The orange reaction mixture was treated with 10% hydrochloric acid (30 ml.) and the two layers separated. The ether layer was extracted with 25% hydrochloric acid (25 ml.). The combined acid layers were boiled, cooled and made basic with 40% sodium hydroxide. The product was extracted with ether, dried and distilled. The physical constants and analyses of the ketones are listed in Table I.

3-Pyridylmagnesium Bromide.—3-Bromopyridine (5 ml.) was converted to the Grignard reagent by the entrainment method using 4 ml. of ethyl bromide as an auxiliary halide. After spontaneous refluxing had stopped, the mixture was warmed, allowed to stand, and treated with benzophenone (15 g.). The product was worked up by the usual procedure and yielded a small amount of diphenyl-3-pyridylcarbinol, identical in m.p. and mixed m.p. with the same carbinol prepared above.

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(14) Wolfenstein and Hartwich, *Ber.*, **48**, 2043 (1915).

(15) Just, *Monatsh.*, **18**, 452 (1897).

Aromatic Reductive Debromination with a Glycol-alkali Mixture

BY HENRY GILMAN, DONALD L. ESMAY AND ROBERT K. INGHAM

Hydroxy-substituted dibenzofurans have been prepared from the corresponding bromo- derivatives by oxidation of the Grignard compounds[1] and by alkali fusion in the presence of a catalyst in an autoclave.[2,3] The first method gives low yields, and the second procedure, although it gives improved yields, is inconvenient. An experiment was conducted to determine if high temperatures and a catalyst were sufficient to bring about the latter reaction through the use of a high boiling solvent such as triethylene glycol, thus obviating the necessity of a bomb. A related procedure was carried out by Thirtle[4] in a reaction between 2-bromopyridine and potassium hydrosulfide. It was found, however, that the bromine atom was replaced by a hydrogen atom rather than by an hydroxyl group. The reductive debromination was found to take place with 2-bromodibenzofuran, 2,8-dibromodibenzofuran, and 2,8-dibromodibenzothiophene. The isolation of 2-bromodibenzofuran when diethylene glycol was used as the reaction medium for 2,8-dibromodibenzofuran indicates that the reaction proceeds stepwise. When ethanol was employed as the solvent, no reductive debromination occurred un-

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(1) Gilman, Bywater and Parker, THIS JOURNAL, **57**, 885 (1935).

(2) Gilman and Van Ess, *ibid.*, **61**, 1365 (1939).

(3) I. G. Farbenind. A.-G., German Patent 606,350 [*C. A.*, **29**, 1434 (1935)].

(4) Thirtle, THIS JOURNAL, **68**, 342 (1946).

TABLE I

Halogen compound	Solvent	B. p., °C.	Catalyst	Product	Yield, %
2-Bromodibenzofuran	Triethylene glycol[a]	290	Cu–CuSO$_4$	Dibenzofuran	55
2,8-Dibromodibenzofuran	Triethylene glycol[a]	290	None	Dibenzofuran	50
2,8-Dibromodibenzothiophene	Triethylene glycol[a]	290	Cu–CuSO$_4$	Dibenzothiophene	54
2,8-Dibromodibenzofuran	Diethylene glycol[b]	244	None	Dibenzofuran and 2-Bromodibenzofuran	22 10
2,8-Dibromodibenzofuran	Ethanol	78	None	Starting material	. .

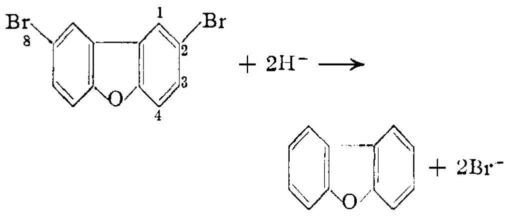
[a] Eastman Kodak Company, Technical grade. [b] Eastman Kodak Company, Practical grade.

der our experimental conditions.[5] Omitting the copper–copper sulfate catalyst had little effect on the results. The results of these reactions are given in Table I.

It has been shown by Nef[6] and by Fry and coworkers[7] that alcohols and glycols react with alkali at elevated temperatures to yield hydrogen. While an explanation of the reductive debromination achieved in the present instance might be based on the direct action of the hydrogen produced, a more likely mechanism (reactions 2-5) would appear to be one similar to those recently proposed for the Meerwein–Ponndorf–Verley reduction[8,9,10] and the reduction of ketones by primary alcohols.[11] The authors consider reactions (3) and (4) to represent parts of a concerted process which occurs without the liberation of hydride ions as such. It is possible that an unidentified tarry residue, which was obtained whenever reductive debromination occurred, was formed by resinification of the aldehyde produced in accordance with reaction (5).

$$\mathrm{HOCH_2(CH_2OCH_2)_2CH_2OH + 2NaOH \longrightarrow NaOCH_2(CH_2OCH_2)_2CH_2ONa + 2H_2O} \quad (2)$$

$$\mathrm{NaOCH_2(CH_2OCH_2)_2CH_2ONa \longrightarrow NaO\overset{+}{C}H(CH_2OCH_2)_2\overset{+}{C}HONa + 2H^-} \quad (3)$$



(4)

$$\mathrm{2Br^- + NaO\overset{+}{C}H(CH_2OCH_2)_2\overset{+}{C}HONa \longrightarrow 2NaBr + CHO(CH_2OCH_2)_2CHO} \quad (5)$$

The ease with which the bromine atoms were replaced by hydrogen atoms suggests that the procedure described may be of use for the replacement of halogen by hydrogen in other aromatic compounds.

The authors are grateful to William Meikle for assistance.

Experimental

General Procedure.—In a typical reaction, 10 g. (0.0405 mole) of 2-bromodibenzofuran, 8.5 g. of sodium hydroxide, 3.0 g. of cupric sulfate, 10 g. of copper turnings, 1 g. of copper-bronze, and 75 ml. of triethylene glycol were placed in a 250-ml. two-necked flask equipped with air condenser and motor stirrer. The reaction mixture was slowly heated, with stirring, to reflux and maintained at this temperature for twelve hours. Vacuum distillation and addition of water to the distillate yielded 3.7 g. (55%) of product melting at 75–78°. Crystallization from dilute ethanol gave 3.1 g. (45%) of dibenzofuran; m. p. and mixed m. p. with an authentic sample was 83–84°.

In a further attempt to replace the halogen atom by an hydroxyl group, kerosene[12] was employed as the reaction medium, thus diminishing the probability of hydrogen formation. Only starting material was isolated.

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(5) Replacement of halogen by hydrogen in 1- and 2-haloanthraquinones using an ethanol–sodium hydroxide solution was reported by Goldstein and Gardner, *ibid.*, **56**, 2130 (1934).

(6) Nef, *Ann.*, **335**, 310 (1904).

(7) (a) Fry, Schutze and Weitkamp, THIS JOURNAL, **46**, 2268 (1924); (b) Fry and Schutze, *ibid.*, **50**, 1131 (1928).

(8) Jackman and Mills, *Nature*, **164**, 789 (1949).

(9) Lutz and Gillespie, THIS JOURNAL, **72**, 344 (1950).

(10) Doering and Young, *ibid.*, **72**, 631 (1950).

(11) Hargreaves and Owen, *J. Chem. Soc.*, 750 (1947).

(12) National Aniline and Chemical Company, British Patent 181,673, Dec. 14, 1921 [*C. A.*, **16**, 3762 (1922)].

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The Use of Double Dilution for the Simultaneous Determination of Yield and Activity of Radioactive Compounds[1]

BY ROWLAND H. MAYOR[2] AND CLAIR J. COLLINS

Isotope dilution methods have been used extensively to determine yields in chemical and biological processes when the yield or purity is so low that it is impossible to isolate quantitatively the pure product.[3,4,5] When these methods are applied to the determination of the yield of a radioactive compound, an aliquot of the reaction mixture is diluted with a known amount of the inactive product, and a sample of the diluted compound is isolated and assayed for radioactivity. The measured specific activity, A_1, is related to the yield, X, in mg. by the equation

$$A_1(D_1 + X) = A_0X \quad (1)$$

In the usual case, where D_1 is very large with respect to X, the equation becomes

$$X = (A_1D_1)/A_0 \quad (2)$$

where A_0 is the specific activity of the undiluted compound, and D_1 is the weight of diluent added.

Using either equation (1) or (2) the amount of the product, X, may be calculated using the known D_1 and the determined A_1, if the specific activity, A_0, of the undiluted product is known either by an independent determination or by calculation from the known specific activity of the previous radioactive reactant.

When the quantity A_0 is not known and cannot

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(1) This paper is based upon work performed for the Atomic Energy Commission at the Oak Ridge National Laboratory.

(2) Rhode Island State College, Kingston, Rhode Island.

(3) D. Rittenberg and G. L. Foster, *J. Biol. Chem.*, **133**, **737** (1940).

(4) A. S. Keston, S. Udenfriend and R. K. Cannan, THIS JOURNAL, **68**, 1390 (1946); **71**, 249 (1949).

(5) G. A. Ropp, *ibid.*, **73**, 4459 (1951).