(including hydrogen) have a positive value. It is rather surprising that 4-methylbenzhydrol gave a better yield of ketone than did benzhydrol. Interestingly, Arnett[3] found that both of these compounds gave a nearly quantitative yield of corresponding ketone when treated with a solution of bromine in acetic acid to which sodium bromide had been added.[3] The effect of the nitro group can be seen by the difference in reactivity of benzyl alcohol *vs.* 4-nitrobenzyl alcohol which gave a much better yield of corresponding aldehyde. Triphenylcarbinol as well as phenyl-*p*-tolyl-α-naphthylcarbinol gave excellent yields of corresponding methyl ethers as expected.

Experimental Section

All melting points are uncorrected. Analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

All of the benzhydrols (except diphenylcarbinol which was obtained from commercial sources) were prepared from reduction of the corresponding benzophenones. Lithium aluminum hydride was used as the reducing agent in all cases with the exception of benzophenones which were substituted with the nitro group. Sodium borohydride was used in these latter cases and the nitro group remained unaffected with this reagent.

The substituted benzophenones were prepared in good yields with the use of the Friedel–Crafts reaction of appropriate acyl halide and benzenoid moiety. With the exception of 4-nitro-4′-*t*-butylbenzophenone, 4-nitro-4′-bromobenzhydrol, and 4-nitro-4′-*t*-butylbenzhydrol, all ketones and alcohols are well characterized in the literature. Phenyl-*p*-tolyl-α-naphthylcarbinol was prepared according to the method of Schlenk and Meyer.[4] Benzyl alcohol and 4-nitrobenzyl alcohol were obtained from commercial sources.

Bromine Oxidations.—The benzhydrols were dissolved in a liberal amount of absolute methanol. Bromine (0.5 *M* excess) was added to the cold solution. The mixture was allowed to stir at room temperature overnight although it was found that in the case of nitro-substituted benzhydrols, the oxidation was complete in approximately 2 hr. The mixture was poured into ice–water which contained sodium thiosulfate to destroy any unreacted bromine. The ketonic fragment usually crystallized without difficulty and was recovered by filtration. Benzaldehyde was recovered by distillation. The oxidation of 4-nitrobenzhydrol and 4-nitrobenzyl alcohol is described below as illustrative of the procedure.

Ether Formation.—The procedure described above for oxidation was followed. The triaryl-substituted carbinols, however, were converted to corresponding methyl ethers. Only a catalytic amount of bromine was needed for this conversion although the reaction proceeded best when approximately equimolar amounts of bromine were used. The methyl ether of triphenylcarbinol has previously been characterized. A mixture melting point determination of the methyl ether prepared by the above described method and by the reaction of triphenylmethyl chloride and methanol in the presence of pyridine was not depressed. The methyl ether of phenyl-*p*-tolyl-α-naphthylcarbinol has been recorded by Dilthey[5] as melting at 120–121°. We found the ether to melt at 50–52°. The infrared spectrum showed aromatic skeletal vibrations at 1605 and 1495 cm^{-1} and C=O stretching at 1076 and 1072 cm^{-1}. No OH stretching band was observed.

Anal. Calcd: C, 88.73; H, 6.54. Found: C, 88.70; H, 6.61.

4-Nitro-4′-*t*-butylbenzophenone.—*t*-Butylbenzene (150 g, 1.1 moles), 4-nitrobenzoyl chloride (230 g, 1.25 moles), and aluminum chloride (200 g, 1.5 moles) were placed in a 2-l. resin kettle. After 3 hr of stirring at room temperature, the reaction mixture, which had set to a black solid was chipped from the kettle and hydrolyzed in ice–water. The resultant solid was isolated by filtration and air dried. Recrystallization from a chloroform–petroleum ether (bp 30–60°) solvent pair yielded 125 g (40%) of pure ketone, mp 112–113°. Strong bands appeared in the infrared spectrum at 1670, 1530, 1360, and 850 cm^{-1} indicating C=O stretching, NO_2 asymmetric and symmetric stretching, and CN stretching.

Anal. Calcd: C, 72.2; H, 6.05. Found: C, 72.6; H, 6.13.

4-Nitro-4′-*t*-butylbenzhydrol.—A solution of 94 g (0.33 mole) of 4-nitro-4′-*t*-butylbenzophenone and 500 ml tetrahydrofuran was cooled to ice-bath temperature and stirred mechanically. To this solution was added 5 g (0.132 mole) of sodium borohydride in 0.5-g portions each dissolved in 2 ml of ice–water. The rate of addition was adjusted to maintain the temperature of the mixture below 15°. After an additional 15-min period of stirring, the dark green solution was poured slowly with stirring on a mixture of cracked ice and hydrochloric acid. The mixture was stirred overnight under a current of air. A yellow precipitate was obtained which was recovered by filtration and weighed (93 g, 99% crude). The product was recrystallized from an acetone–water solvent pair (mp 110–111°). A weak band at 3580 and strong bands at 1525 and 1350 cm^{-1} in the infrared spectrum appeared indicating OH stretching and asymmetric and symmetric NO_2 stretching, respectively.

Anal. Calcd: C, 71.7; H, 6.72. Found: C, 72.3; H, 6.91.

4-Nitro-4′-bromobenzhydrol.—This compound was prepared according to the above procedure. 4-Nitro-4′-bromobenzophenone (260 g, 0.85 mole) was reduced with 12 g (0.315 mole) of sodium borohydride to yield 255 g (92%) of product, mp 160–161°. A weak band at 3580 and strong bands at 1525 and 1352 cm^{-1} appeared in the infrared spectrum indicating OH stretching and asymmetric and symmetric NO_2 stretching, respectively.

Anal. Calcd: C, 50.7; H, 3.28; Br, 25.9. Found: C, 50.9; H, 3.38; Br, 26.1.

4-Nitrobenzophenone.—A solution of 5 g (0.0219 mole) 4-nitrobenzhydrol, 15 g (0.094 mole) bromine, and 50 ml of absolute methanol was stirred at room temperature for 2 hr. The reaction mixture was poured slowly into an ice-cold solution of sodium thiosulfate. Elementary sulfur was liberated as well as an oil that crystallized on standing (mp 134–136°). The yield was 5.0 g (100%). A mixture melting point determination with an authentic sample was not depressed.

4-Nitrobenzaldehyde.—In a manner similar to that described above a yield of 8.1 g (80%), mp 105–106°, of 4-nitrobenzaldehyde was obtained from the reaction of 10 g (0.064 mole) of 4-nitrobenzyl alcohol and 0.15 g (0.094 mole) of bromine in 100 ml of absolute methanol.

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[3] E. M. Arnett and G. B. Klingensmith, *J. Am. Chem. Soc.*, **87**, 1023 (1965). Indeed E. M. A. suggested that less activated benzhydrols would undergo oxidation rather than cleavage with bromine. Benzhydrols which were substituted by methoxy groups were cleaved by the action of bromine in aqueous acetic acid.

[4] W. Schlenk and E. Meyer, *Ber.*, **52B**, 17 (1919).

[5] W. Dilthey, E. Haussler, E. Hausdorfer, and O. Reek, *J. Prakt. Chem.*, **109**, 313 (1925).

A New Synthesis of 2-Pyridine Aldoximes

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The use of 2-pyridine aldoxime methiodide (2-PAM) as an antidote for organophosphorus poisons has stimulated interest to find new convenient routes for the synthesis of the precursor 2-pyridine aldoximes.[3]

The classical method for the syntheses of these compounds involves acetic anhydride rearrangement[4] of the corresponding 2-picoline N-oxide to the acetate of 2-pyridinemethanol, hydrolysis of the acetate to the alcohol, oxidation of the carbinol to the aldehyde, and then conversion of the aldehyde to the oxime. The over-all yield for this multistep sequence for a series of

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[1] Ash Stevens, Inc.

[2] U. S. Army Edgewood Arsenal.

[3] See D. F. Heath, "Organo Phosphorus Poisons," Pergamon Press Inc., New York, N. Y., 1961.

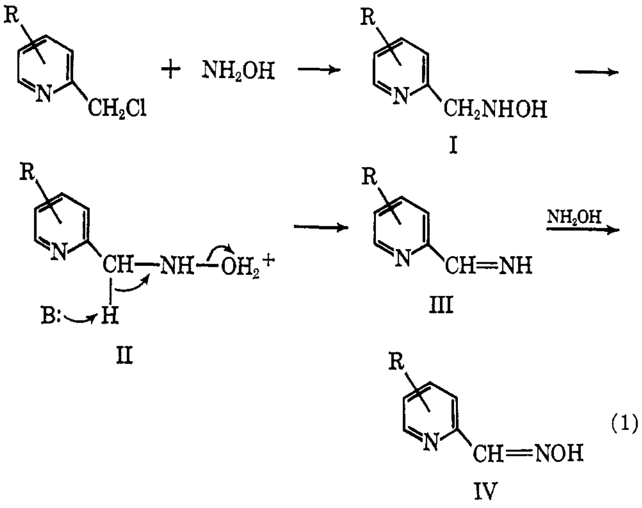
[4] V. Boeckleheide and W. Linn, *J. Am. Chem. Soc.*, **76**, 1286 (1954); V. J. Traynelis and P. L. Pacini, *ibid.*, **86**, 4917 (1964).

substituted 2-picoline N-oxides is 23–30%.[5] Recently Forman[6] has reported the direct high yield oximation of 2-picoline using sodium amide and *n*-butyl nitrite. The applicability of the procedure to substituted 2-picolines is not presently known.

We have found that the reaction of 2-chloromethyl pyridines with buffered solutions of aqueous hydroxylamine gives good yields of the corresponding 2-pyridine aldoximes. The procedure consists of heating the 2-chloromethylpyridine in an aqueous ethanolic solution of hydroxylamine hydrochloride buffered to pH 7–8 on a steam bath for 2 to 3 hr. Upon cooling the reaction to room temperature, the product usually crystallized from the solution.

The reaction is significant in view of the fact that treatment of *p*-chlorobenzyl chloride under identical conditions gave the dialkyl hydroxylamine as the only product. The acidity of the hydrogens α to the halo group seems to be important since 2-bromocyclohexanone on treatment with buffered hydroxylamine solution affords a 34% yield[7] of 1,2-cyclohexanedione dioxime.

In view of this acidity requirement, the mechanism shown (1) may be postulated: nucleophilic displacement of the chloro group yields the alkylhydroxylamine (I); subsequent protonation of the hydroxyl group of I followed by the elimination yields the aldimine III;[8] the aldimine in the presence of excess hydroxylamine yields the product oxime IV.



(1)

Experimental Section

Melting points were determined using a Thomas-Hoover melting point apparatus and are uncorrected. Elemental analyses were performed by Midwest Microlabs, Inc., Indianapolis, Ind.

The 2-chloromethylpyridines were prepared by a modification and extension of previously reported procedures.[9,10] Substituted pyridine N-oxides were treated with a twofold excess of methanesulfonyl chloride or *p*-toluenesulfonyl chloride in refluxing dioxane for 6 to 12 hr. Best results were obtained with *p*-toluenesulfonyl chloride in the case of 6-methyl, 5-methyl, and 5-ethyl derivatives.

New 2-chloromethylpyridines prepared by this procedure were as follows: 4-chloro, 51%, bp 51° (0.9 mm), $n^{25}\text{D}$ 1.5225, picrate mp 123–125°; 4-carboethoxy, 62%, 75° (0.12 mm), $n^{25}\text{D}$ 1.5208, picrate mp 110–111°; 5-carboethoxy, 59%, 64° (0.05 mm), $n^{25}\text{D}$ 1.5252, picrate mp 123–125°; 5-chloro, 40%, 48° (0.5 mm), $n^{25}\text{D}$ 1.5293, picrate mp 96–98°. All compounds had acceptable elemental analyses in carbon, hydrogen, and nitrogen (chlorine).

The appropriate 2-chloromethyl pyridine (0.02 mole) was added to a solution of hydroxylamine hydrochloride (0.1 mole) in 40 ml of 50% aqueous ethanol (v/v) which had been buffered to pH 7 to 8 with 10 *N* sodium hydroxide solution. The solution was heated on a steam bath for 2 to 3 hr; ethanol was added from time to time so as to maintain a homogeneous solution. Upon cooling the solution, the product crystallized and was recrystallized from either benzene or aqueous ethanol. The data are summarized in Table I.

TABLE I

CONVERSION OF MONOSUBSTITUTED (R) 2-CHLOROMETHYL PYRIDINES TO 2-PYRIDINE ALDOXIMES

R	Yield, %	Mp, °C
H	50	112–114[a]
4-Cl	18	151–153[b]
5-Cl	63	194–195[c]
4-$COOC_2H_5$	52	157–158[d]
5-$COOC_2H_5$	72	128–129[e]
5-C_2H_5	78	149–150[f]
6-CH_3	91	170–172[g]

[a] S. Ginsberg and I. Wilson [*J. Am. Chem. Soc.*, **79**, 481 (1957)] report mp 114°; mixture melting point with an authentic sample was undepressed. [b] S. Furukawa[5] reports 154–155°; mixture melting point with an authentic sample was undepressed. [c] Calcd for $C_6H_5ClN_2O$: C, 46.04; H, 3.22; N, 17.90. Found: C, 45.74; H, 3.40; N, 17.63. [d] Calcd for $C_9H_{10}N_2O_3$: C, 55.66; H, 5.19; N, 14.42. Found: C, 55.39; H, 5.29; N, 14.32. [e] Found: C, 55.86; H, 5.42; N, 14.07. [f] Calcd for $C_9H_{10}N_2O$: C, 64.00; H, 6.70; N, 18.65. Found: C, 64.17; H, 6.95; N, 18.53. [g] S. Ginsberg and I. Wilson [*J. Am. Chem. Soc.*, **79**, 481 (1957)] report mp 170–171°.

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A New Self-Condensation Product of Biacetyl[1a]

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The self-condensation products of biacetyl have been of interest to organic chemists since 1889. Three dimers[2-4] and two trimers[5,6] have been isolated in crystalline form from reactions in which biacetyl was treated with either strongly alkaline or acidic catalysts. While studying the reaction of biacetyl with certain heterocyclic amines, we came upon considerable quan-

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