with aqueous sodium hydroxide. *m*-Hydroxyacetophenone similarly gave *m,m'*-diacetyl-1,3-diphenoxypropane which underwent the Willgerodt reaction with sulfur and morpholine[4] giving 1,3-diphenoxypropane-*m,m'*-diacetic acid.

Experimental[5,6]

***p,p'*-Dinitro-1,3-diphenoxypropane.**—A mixture of potassium *p*-nitrophenoxide (35.4 g., 0.20 mole), trimethylene bromide (20.2 g., 0.10 mole) and ethylene glycol (60 ml.) was stirred and heated at 130° for one hour. The cooled mixture was poured into cold water (600 ml.) giving 19.5 g. (61%) of product melting at 122–125°; after two crystallizations from ethanol it melted at 129.5–130.5°.

***p,p'*-Diamino-1,3-diphenoxypropane.**—When the above dinitro compound (120 g., 0.375 mole), dissolved in ethyl acetate (1 liter), was shaken with Raney nickel and hydrogen at 60° and 500 p.s.i., the theoretical amount of hydrogen was taken up in two hours. The residue, after removal of catalyst and solvent, weighed 97 g. (100%) and melted at 102–105°. An analytical sample, after two crystallizations from Skellysolve C, melted at 104.5–105.5°.

Anal. Calcd. for $C_{15}H_{18}N_2O_2$: N, 10.93. Found: N, 10.89 (by titration with acetous perchloric acid).

***p,p'*-Dibenzalamino-1,3-diphenoxypropane.**—*p,p'*-Diamino-1,3-diphenoxypropane (12.9 g., 0.05 mole) and benzaldehyde (10.6 g., 0.10 mole) were mixed and heated until a uniform melt was obtained (internal temperature about 130°). The cooled mixture was crystallized from ethanol giving 17.5 g. (80%) of product melting at 120–125°. An analytical sample, after two more crystallizations from ethanol, melted at 125–126.5°.

Anal. Calcd. for $C_{29}H_{26}N_2O_2$: N, 6.45. Found: N, 6.40 (Kjeldahl).

***p,p'*-Dibenzylamino-1,3-diphenoxypropane.**—The above dibenzal compound was hydrogenated over Raney nickel in ethyl acetate at 60°. After one crystallization from ethanol the diamine was obtained in 70% yield melting at 88–89°. An analytical sample, after an additional crystallization from ethanol, melted at 88.5–89.5°.

Anal. Calcd. for $C_{29}H_{30}N_2O_2$: N, 6.38. Found: N, 6.25 (by acetous perchloric acid titration).

This compound was also obtained in 82% yield melting at 83–87° by direct hydrogenation of a solution of *p,p'*-diamino-1,3-diphenoxypropane and benzaldehyde in ethyl acetate.

1,3-Diphenoxypropane *p,p'*-Diisocyanate.—*p,p'*-Diamino-1,3-diphenoxypropane (25.0 g., 0.10 mole) was suspended in dry toluene (100 ml.). This mixture was heated to reflux with stirring and then saturated with hydrogen chloride. Phosgene was then bubbled into the mixture with continued refluxing and stirring for three hours at which time there was no further evidence of clearing of the mixture. The hot mixture was filtered through Filter-cel and the toluene was removed from the filtrate by distillation *in vacuo*. The residue on cooling crystallized; it weighed 21.7 g. (70%) and melted at 100–105°. An analytical sample, after crystallization from Skellysolve C, melted at 103–105°.

Anal. Calcd. for $C_{17}H_{14}N_2O_4$: N, 9.03. Found: N, 8.71 (micro-Dumas).

***p,p'*-Dicarbethoxy-1,3-diphenoxypropane.**—A mixture of ethyl *p*-hydroxybenzoate (83 g., 0.50 mole), trimethylene bromide (50.5 g., 0.25 mole) and 85% potassium hydroxide (33 g., 0.50 mole) was heated at 130° with stirring for three hours. The cooled mixture was poured into water (1500 ml.) giving a solid which after crystallization from ethanol (500 ml.) weighed 58 g. (63%) and melted at 93–100°. An analytical sample, after two more crystallizations from ethanol, melted at 102–105°.

Anal. Calcd. for $C_{21}H_{24}O_6$: C, 67.74; H, 6.45. Found: C, 67.70; H, 6.39.

1,3-Diphenoxypropane-*p,p'*-dicarboxylic Acid.—The above diester (7.4 g., 0.02 mole) was refluxed with 20% sodium hydroxide solution (175 ml.) for three hours. Chilling gave 6.5 g. (90%) of the disodium salt of 1,3-diphenoxypropane-*p,p'*-dicarboxylic acid. This solid was boiled with ethanol (250 ml.) to remove any unhydrolyzed ester, then taken up in water (30 ml.) and reprecipitated by pouring into ethanol (250 ml.). The product weighed 5.9 g. (82%).

Anal. Calcd. for $C_{17}H_{14}O_6Na_2$: Na, 12.78. Found: Na, 12.90.

This disodium salt was taken up in water (50 ml.) and the solution was acidified by slow addition of dilute hydrochloric acid. The 1,3-diphenoxypropane-*p,p'*-dicarboxylic acid which separated weighed 4.9 g. (77% based on ester used) and melted at 305–309°. The compound is extremely insoluble in water and no suitable recrystallization solvent could be found.

Anal. Calcd. for $C_{17}H_{16}O_6$: neut. equiv., 158. Found: neut. equiv., 163.

***m,m'*-Diacetyl-1,3-diphenoxypropane.**—A mixture of *m*-hydroxyacetophenone (272 g., 2.0 mole), trimethylene bromide (202 g., 1.0 mole) and 85% potassium hydroxide (132 g., 2.0 mole) in ethanol (1.0 liter) was refluxed with stirring for 14 hours. The solid which formed when the cooled mixture was poured into water was so fine it filtered with great difficulty; consequently it was filtered with the aid of Filter-Cel from which it was subsequently removed by extraction with chloroform. The residue, after removal of the chloroform by distillatin *in vacuo*, rapidly crystallized, weighed 221 g. (71%) and melted at 71–80°. An analytical sample, after two crystallizations from ethanol, melted at 91–93°.

Anal. Calcd. for $C_{19}H_{20}O_4$: C, 73.00; H, 6.41. Found: C, 72.97; H, 6.66.

1,3-Diphenoxypropane-*m,m'*-diacetic Acid.—A mixture of *m,m'*-diacetyl-1,3-diphenoxypropane (15.6 g., 0.05 mole), sulfur (8.0 g., 0.25 mole) and morpholine (17.4 g., 0.20 mole) was heated at reflux for one hour. The reaction mixture was taken up in chloroform (250 ml.) and the chloroform solution was washed with dilute hydrochloric acid. The chloroform was removed under vacuum and the residue was hydrolyzed by refluxing with 50% (by weight) sulfuric acid (200 ml.). The crude diacid was removed from the cooled hydrolysis mixture by filtration and after crystallization from water (4 l.) it weighed 4.8 g. (28%) and melted at 168–170°. An analytical sample, after crystallization from methanol, melted at 171–172.5°.

Anal. Calcd. for $C_{19}H_{20}O_6$: C, 66.28; H, 5.81. Found: C, 66.15; H, 5.72.

STERLING-WINTHROP RESEARCH INSTITUTE
RENSSELAER, NEW YORK

Condensations of Cinchoninaldehyde. V.[1] With Phenylacetonitriles

BY ARTHUR P. PHILLIPS

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Cinchoninaldehyde reacted rapidly with a variety of substituted phenylacetonitriles to produce the α-(substituted phenyl)-β-(4-quinolyl)-acrylonitriles (see Table I).

When an alcohol solution of the reactants was treated with alkali the mixture turned first yellow, then orange, and finally deep red and the colorless product separated, all within less than a minute. The intense color changes may be associated with anionic intermediates.

The condensation of the *p*-nitrophenylacetonitrile, expected to be more reactive because of activation by the *p*-nitro, gave a poor yield of IV (Table I) in the usual procedure with alkali catalyst. When a more weakly basic catalyst, such as diethylamine or piperidine, was used the reaction gave good yields of IV. Apparently with the more reactive nitrile the stronger base catalyst is detrimental.

In the condensation with *o*-methoxyphenyl-

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[4] E. Schwenk and E. Bloch, THIS JOURNAL, **64**, 3051 (1942); J. A. King and F. H. McMillan, *ibid.*, **68**, 2335 (1946).

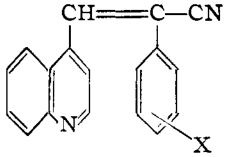
[5] Melting points are uncorrected.

[6] Analyses were performed in the analytical laboratories of this Institute under the direction of Mr. Morris E. Auerbach.

[1] Paper IV, THIS JOURNAL, **70**, 452 (1948).

TABLE I

CONDENSATION PRODUCTS FROM CINCHONINALDEHYDE AND PHENYLACETONITRILES



Compound number	X	M.p., °C.[a]	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
I	H	134–135	$C_{18}H_{12}N_2$	84.4	84.4	4.7	4.7
II	4-CH_3	168–169	$C_{19}H_{14}N_2$	84.4	84.5	5.2	5.3
III	4-Cl	165–166	$C_{18}H_{11}ClN_2$	74.3	74.4	3.8	4.0
IV	4-NO_2[b]	199–200	$C_{18}H_{11}N_3O_2$	71.7	71.9	3.7	3.9
V	2-CH_3O[c]	149–150	$C_{19}H_{14}N_2O$	79.7	80.0	4.9	4.9
VI	4-CH_3O	180–181	$C_{19}H_{14}N_2O$	79.7	79.7	4.9	4.9
VII	4-C_2H_5O	155–156	$C_{20}H_{16}N_2O$	80.0	80.0	5.4	5.4
VIII	3-CH_3O-4-C_2H_5O	160–161	$C_{21}H_{18}N_2O_2$	76.3	76.3	5.5	5.7
IX	H[d]	184–185	$C_{18}H_{14}N_2O$	78.8	78.7	5.2	5.2

[a] All melting points are uncorrected. [b] Several variations of the usual conditions were used in this case: (1) the reaction mixture was left 24 hours at 25° (1 cc. of KOH) and gave 20% of IV; (2) the reaction mixture was heated 2 hours at 100° (5 drops of Et_2NH) and gave 60% of IV; (3) the reaction mixture was left 24 hours at 25° (5 drops of piperidine) and gave 95% of IV. [c] No color developed here. The mixture was heated 3 hours at 100° and a second 1 cc. of 20% aqueous KOH was added. The final yield was 70%. [d] This compound is the aldol related to I. The usual reaction mixture, using 5 drops of Et_2NH as the catalyst, was heated 2 hours at 100°; yield of IX was 60%.

acetonitrile to give V (Table I), no color appeared in the solution and the reaction seemed to go more slowly. Both of these deviations might possibly be relatable to the increased steric hindrance of the *o*-methoxy superimposed on the already partially hindered cinchoninaldehyde.

When the condensation with phenylacetonitrile, itself, was carried out as usual but using diethylamine as the catalyst, the unsaturated product I (Table I) was not obtained. Instead the corresponding intermediate aldol IX (Table I) was isolated in good yield. In the case of phenylacetonitrile, which is of lesser reactivity or acidity than its *p*-nitro derivative, the more weakly basic catalyst appears to be inadequate to accomplish the dehydration of the intermediate aldol. The aldol, IX, was also obtained when a dilute suspension of the reactants in water was treated with a little diethylamine.

Experimental

Condensation of Cinchoninaldehyde with Phenylacetonitriles.—In the usual conditions a solution of 0.01 *M* of cinchoninaldehyde and 0.01 *M* of the phenylacetonitrile in 30 cc. of 95% alcohol was treated with 1 cc. of 20% aqueous potassium hydroxide. The reaction mixture underwent several rapid color changes, from yellow to orange to deep red, and in some cases a little heat was evolved. The product precipitated out, usually in less than a minute, as white or pale yellow crystals.

The products were purified by recrystallization from alcohol or from mixtures of benzene with Skellysolve B. Yields ordinarily were 80% or greater. Details for all compounds appear in Table I.

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THE WELLCOME RESEARCH LABORATORIES
TUCKAHOE 7, NEW YORK

Transformations of Organic Nitrogen Base Iodide and Bromide Salts to Chlorides

BY ARTHUR P. PHILLIPS AND RICHARD BALTZLY

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In many preparative reactions organic bases are first obtained as iodide or bromide salts, due to the common use of alkyl iodides and bromides which are more available and more reactive toward nucleophilic reagents than the corresponding chlorides. For certain purposes, such as for drugs which are to be taken internally in moderate quantities and in various catalytic hydrogenation procedures, the chlorides are preferred to avoid toxic properties associated with iodides or bromides. When conversion to chlorides is desired this is frequently accomplished by liberation and separation of the base, with subsequent addition of hydrogen chloride. Iodides can also be converted to chlorides by short warming with silver chloride in aqueous or, as found in these laboratories, methanol solution. This latter method is less suitable for conversion of bromides to chlorides, and the former procedure is not applicable to quaternary ammonium salts or to amines which are unstable as the free bases, such as primary α-aminoketones.

In preparing amines from organic bromides and hexamethylenetetramine it was observed that after hydrolysis of the intermediate quaternary salts with ethanolic hydrogen chloride the products were obtained as hydrochlorides containing no appreciable amount of bromide ion. The absence of bromides in the products suggests that bromide might have been lost as ethyl bromide.

This led to the concept of a simple, rapid method for preparing chlorides from bromides and iodides which avoids the use of expensive silver chloride, which eliminates the necessity for liberating the free base, and which no longer requires the time-consuming process of evaporation of large quantities of water, usually used in the silver chloride method, to obtain the dry salt. When a solution of the amine salt, iodide or bromide, either quaternary ammonium or hydrohalide of primary, secondary or tertiary amine, in excess of methanolic hydrogen chloride was evaporated on a steam-bath it was rapidly and completely transformed into the corresponding chloride. The yields were nearly quantitative and reaction was usually complete in less than one-half hour, although heating times