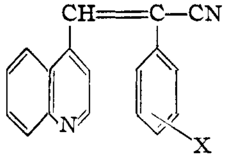
TABLE I

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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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

TABLE I

TRANSFORMATIONS OF IODIDE AND BROMIDE SALTS TO CHLORIDES USING METHANOLIC HYDROGEN CHLORIDE

Reactant	Product[a]	M.p., °C.[b]	Chlorine, % Calcd.	Chlorine, % Found
1-Methyl-4-(4′-dimethylamino)-stilbazoline hydroiodide[c]	Dihydrochloride	212–213	22.2	22.2
N,N′-Dibenzylpiperazine methiodide[d]	Chloride hydrochloride	207–210	20.1	20.2
2-Stilbazole methiodide[e]	Chloride	255–256	15.3	15.3
2-Picoline methiodide[f]	Chloride[f]	*ca.* 70,[f] very hygroscopic		
Nicotinic acid methyl ester methiodide[g]	Chloride[g]	100–101		
Homoveratryltrimethylammonium bromide[h]	Chloride[i]	204–205		

[a] Under product is described just the nature of the anionic portions associated with the reactant molecule. [b] All melting points are uncorrected. [c] A. P. Phillips, THIS JOURNAL, **72**, 1850 (1950). [d] W. van Rijn, *Nederland. Tijdschr. Pharm.*, **10**, 5 (1898); through *Chem. Centr.*, **79**, I, 381 (1898). [e] A. P. Phillips, *J. Org. Chem.*, **12**, 333 (1947). [f] P. Murrill, THIS JOURNAL, **21**, 841, 842 (1899). [g] A. Hantzsch, *Ber.*, 19, 31 (1886). [h] White crystals from alcohol–ether; m.p. 232–233°. *Anal.* Calcd. for $C_{13}H_{22}BrNO_2$: C, 51.3; H, 7.3; N, 4.6. Found: C, 51.3; H, 7.6; N, 4.6. [i] J. S. Buck, R. Baltzly and W. S. Ide, THIS JOURNAL, **60**, 1789 (1938).

of between one and two hours were commonly used. The desired chloride is obtained pure simply by crystallization from the methanol solution, either by cooling or by the addition of appropriate precipitating solvents.

The process is believed to go by the scheme

$$R_4N^+I^- + H^+Cl^- + MeOH \rightleftarrows MeO^+H_2 + I^- \longrightarrow MeI + H_2O + R_4N^+Cl^-$$

This depends upon the greater nucleophilic reactivity of iodide or bromide over that of chloride in combining with the alcohol solvent. Methanol is believed to represent a more favorable reactant than ethanol because of the greater susceptibility of methyl to nucleophilic attack than ethyl and because of the greater volatility of the lower alkyl halides allowing easier removal from the reaction mixture during the evaporation. In several experiments methyl iodide was collected from the evaporating mixture through a distilling condenser. It was identified by combination with dimethylaniline to form phenyltrimethylammonium iodide.

Experimental

Transformations of Iodide and Bromide Salts to Chlorides.—In general a solution of 0.02 mole of iodide or bromide salt in about 30–40 cc. of methanol containing 0.1 to 0.2 mole of hydrogen chloride was allowed to evaporate freely on a steam-bath. After one hour the product was crystallized from the methanol solution by cooling or by the addition of a second solvent such as ethyl acetate, acetone, or ether. The absence of any iodide in the product was determined by treating an aliquot in aqueous hydrochloric acid in the presence of carbon tetrachloride with a few drops of dilute sodium nitrite solution.

The transformation works well for quaternary ammonium iodides or bromides as well as for the hydrogen iodides or bromides of primary, secondary or tertiary amines.

The reaction is very rapid. In cases where the rate of disappearance of iodide was followed, using the test method given above, the test for iodide, strongly positive initially, was very faint after 15 minutes, and was negative after 20 minutes.

In several cases evaporation was accomplished through a distillation condenser collecting methanol and methyl iodide. After addition of an excess of dimethylaniline, evaporation of solvent, and recrystallization, a 50% yield of phenyltrimethylammonium iodide was obtained; melting point 215–216°. This gave a strong test for iodide.

Pertinent details for a number of specific compounds transformed by this procedure are shown in Table I.

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Anodic Polarography: Catechol[1]

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In a recent paper, Doskocil[2] reported polarographic data for the system catechol–*o*-quinone in the *p*H range 6.20 to 7.89. Vlcek[3] and coworkers obtained polarographic data for catechol in the *p*H range 3.70 to 8.32. Each of the investigators uses phosphate buffers which give ill-defined diffusion currents for catechol in the low *p*H ranges. This is due to a sudden reversal of current at the dropping mercury electrode, occurring in phosphate buffer solutions at potentials corresponding to the oxidation potential of catechol in the *p*H range 5 to 6. The sharp discontinuity in the anodic wave prevents one from obtaining a complete polarographic wave for catechol in this *p*H range.

Vlcek considered the discontinuity observed to be the anodic oxidation wave of catechol. The present authors feel that the reversal of current is caused only by the anodic dissolution mercury and the formation of a film of mercurous phosphate at the electrode–solution interface. Work in progress in this Laboratory indicates that the potential at which the discontinuity is observed is dependent upon the concentration of the phosphate buffer.

Müller[4] has calculated the usable potential ranges for solutions containing the $HPO_4^{=}$ ion and we have found that actual values obtained from polarograms of solutions of phosphate buffers agree in general with his calculations. Polarograms of catechol in acetate buffer solutions obtained by Doskocil[2] and in this research indicate that the discontinuity observed by Vlcek in phosphate buffer solutions is due only to the buffer components, since no reversal of current occurs in acetate buffer solutions and a well-defined oxidation wave for catechol is obtained.

Because of the indefinite waves obtained for catechol due to the peculiar effect of phosphate

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(1) Taken in part from the M. S. thesis of R. P. Vigneault.

(2) J. Doskocil, *Collection Czechoslov. Chem. Communs.*, **15**, 599 (1950).

(3) A. K. Vlcek, V. Mansfeld and D. Krkoskova, *Collegium*, No. 874, 245 (1943).

(4) O. H. Müller, "The Polarographic Method of Analysis," 2nd edition, Chemical Education Publishing Co., Easton, Pa., 1951, p. 152.