652. *Hydrogen Transfer. Part XVI.* Dihydrides of Nitrogenous Heterocycles as Hydrogen Donors.*

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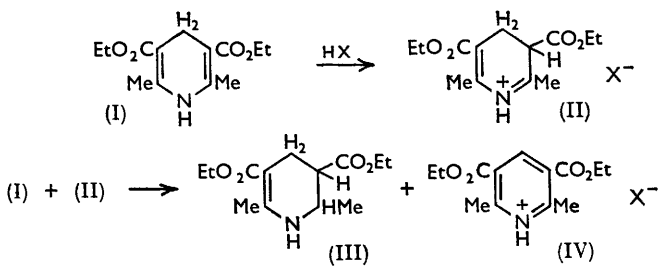
The preparation, purification, and properties of various dihydrides of nitrogenous heterocycles are summarised and their reactions with chloranil described. 1,2-Dihydro-1-methylquinoline with chloranil yields a " phenol salt; " this is a model system for biological enzymic reduction by diphosphopyridine nucleotide ($DPNH_2$).

Previous papers from this College have described the use of dihydro-derivatives of aromatic and of macrocyclic compounds as hydrogen donors. We have now examined various dihydrides of the nitrogenous heterocycles. Compounds of this type are known to play an important part in biological oxidation–reduction systems. The present paper describes various dihydrides and their reactions with chloranil as a typical acceptor. A more detailed study of the behaviour of two selected dihydrides with a wide range of acceptors follows in Part XVII. The donors studied were: diethyl 1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate (the " Hantzsch ester ");[1] 1,2-dihydro-quinoline and -isoquinoline; 1,2-dihydro-1-methyl- and 1,2-dimethyl-quinoline; and 9,10-dihydroacridine.

The Hantzsch Ester.—Homogeneous hydrogen transfer from the Hantzsch ester (I) to an equimolecular amount of chloranil is virtually complete in 15 minutes at room temperature, giving the dehydrogenated ester and tetrachloroquinol in 97% yield. Its kinetics were followed spectrometrically and found to be of the second order, with $k = 2{\cdot}60 \pm 0{\cdot}05$ l. mole^{-1} sec.$^{-1}$.



The donor activity of the Hantzsch ester is reflected by its ready disproportionation in concentrated mineral acid.[2] As in the hydrogen transfer to quinones, the mechanism may be formulated as a hydride-ion transfer (see formulæ).

* Part XV, *J.*, 1960, 3144.

[1] Singer and McElvain, *Org. Synth.*, 1934, **14**, 31.
[2] Knoevenagel and Fuchs, *Ber.*, 1902, **35**, 1788.

The process is then repeated with the intermediate (III) to give the hexahydro-compound. Compound (IV) is the salt of the oxidised Hantzsch ester. This postulated terminal addition of H^+ to the carbon end of the C=C–N< system, reminiscent of 1,4-addition to conjugated dienes, is suggested by analogy with Robinson's studies on the *C*-alkylation of certain derivatives of β-aminocrotonic acid:[3]

$$NEt_2{\cdot}CMe{:}CH{\cdot}CO_2Et + MeI \longrightarrow [NEt_2{:}CMe{\cdot}CHMe{\cdot}CO_2Et]^+I^-$$

1,2-*Dihydroquinoline.*—Monomeric 1,2-dihydroquinoline was first prepared by Johnson and Buell[4] by pyrolysis of 1,2,3,4-tetrahydro-4-phenethylaminoquinoline. Bohlmann showed that certain nitrogen-heterocyclic dihydro-compounds were readily prepared by reduction with lithium aluminium hydride;[5] from quinoline this reaction yielded an extremely unstable solid, considered by Bohlmann to be a mixture of 1,2- and 1,4-dihydroquinoline, from which 1,2-dihydroquinoline was indeed later isolated.[6,7]

In the present work 1,2-dihydroquinoline has been prepared many times by the reduction of quinoline with lithium aluminium hydride, and it is now considered very probable that some 1,4-dihydroquinoline is formed, at least transiently. 1,4-Dihydroquinoline would tend to rearrange to the 1,2-dihydro-isomer, and, since at least 3% of 1,2,3,4-tetrahydroquinoline is also found in the crude product, we postulate that the enamine structure of 1,4-dihydroquinoline is susceptible to further reduction. Supporting evidence is that pure 1,2-dihydroquinoline is recovered unchanged on attempted further reduction with lithium aluminium hydride, and does not disproportionate even under most vigorous thermal conditions. Furthermore, the reduction of isoquinoline under the same conditions yields much more (16%) of the tetrahydro-compound.

The crude solid product, containing about 70% of dihydroquinoline (by chloranil estimation), obtained by the lithium aluminium hydride reduction of quinoline could not be stored under any conditions. At 0·08 mm. it rapidly decomposed to a yellow syrup, which, when acetylated and fractionally distilled, yielded quinoline and a mixture which analysed as 1-acetyl-1,2-dihydroquinoline with some acetylated tetrahydro-compound. Direct fractional distillation of the crude product gave quinoline and a solid fraction, predominantly 1,2-dihydroquinoline contaminated with a little quinoline and 1,2,3,4-tetrahydroquinoline.

The above process is a convenient route to substantial quantities of 1,2-dihydroquinoline, and it is noteworthy that the purified product may be stored indefinitely at 10^{-5} mm., whereas the undistilled material rapidly decomposes under these conditions.

1,2-Dihydroquinoline and chloranil reacted almost instantaneously in solution at room temperature to form quinoline and tetrachloroquinol. This affords an excellent procedure for estimation of 1,2-dihydroquinoline. Attempts to measure the kinetics of the hydrogen transfer to the quinone spectrometrically were hindered by the labile nature of the dihydro-product and the extreme speed of the reaction; only one estimate could be made of the second-order rate constant (k = 14,000 l. mole^{-1} sec.$^{-1}$).

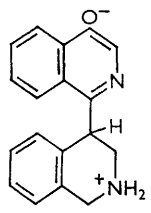
1,2-*Dihydroisoquinoline.*—1,2-Dihydroisoquinoline was first prepared by Jackman and Packham by the reduction of isoquinoline with lithium aluminium hydride.[8] Our first preparative attempt gave only a poor yield of crude product, and a higher-melting by-product was isolated; this we found to be due to competing oxidation and over-reduction of the dihydro-product. Moreover, Jackman and Packham have since shown that this material is polymeric in concentrated solution and in the solid state:[9] from the infrared

[3] Robinson, *J.*, 1916, 1038.
[4] Johnson and Buell, *J. Amer. Chem. Soc.*, 1952, **74**, 4517.
[5] Bohlmann, *Ber.*, 1952, **85**, 390; 1953, **86**, 1419.
[6] Rosenmund, *Ber.*, 1953, **86**, 37; Rosenmund, Zymalkowski, and Schwarte, *Ber.*, 1954, **87**, 1229.
[7] Craig and Gregg, *J. Amer. Chem. Soc.*, 1953, **75**, 2252.
[8] Jackman and Packham, *Chem. and Ind.*, 1955, 360.
[9] Jackman and Packham, personal communication.

absorption of solutions of the isolated "dihydroisoquinoline" it seems that the Ph·CH:CH·NH· system is present only in dilute solution.

In addition to the associated dihydro-compound (formed in about 60% yield) we isolated isoquinoline, 1,2,3,4-tetrahydroisoquinoline, 4-hydroxyisoquinoline, and a high-melting compound (A) $C_{18}H_{16}N_2O$.

The amount of tetrahydroisoquinoline (16% isolated) was much higher than that of tetrahydroquinoline in the analogous reduction, which supports the view that reduction to the tetrahydro-level is by addition of hydrogen to an enamine grouping. 1,2-Dihydroisoquinoline already has such a structure, whereas 1,2-dihydroquinoline must undergo rearrangement unless some 1,4-dihydroquinoline has previously been formed.


(V)

The ready oxidation of associated 1,2-dihydroisoquinoline by molecular oxygen to 4-hydroxyisoquinoline is comparable with Witkop's observation [10] that *trans*-decahydroquinoline with molecular oxygen at 100° forms 5,6,7,8-tetrahydro-3-hydroxyquinoline.

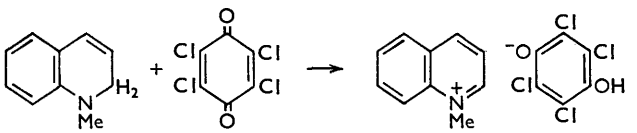
Compound (A) showed points of similarity to 4-hydroxyisoquinoline in ultraviolet and infrared absorption. Neither had hydroxyl absorption in the infrared region: 4-hydroxyisoquinoline must therefore exist as a zwitterion, and a similar salt structure is thought to be present in compound (A). Compound (A) formed a neutral *ON*-dibenzoate ($\nu_{max.}$ 1734 and 1629 cm.$^{-1}$) and is therefore formulated as (V or a double-bond isomer) (though the neutrality of the dibenzoate is not thereby accounted for).

It has already been shown [8] that with a high-potential quinone the associated 1,2-dihydroisoquinoline gives isoquinoline rapidly at room temperature.

1,2-*Dihydro*-1-*methylquinoline*.—Schmid and Karrer [11] who obtained 1,2-dihydro-1-methylquinoline in 37% yield by reduction of quinoline methiodide with ethereal lithium aluminium hydride described it as an extremely unstable oil. We have simplified their procedure and raised the yield of pure distilled product to 93%. Pure 1,2-dihydro-1-methylquinoline is a very pale yellow, mobile oil which can be stored indefinitely if immediately sealed in ampoules at 0·1 mm. On exposure to air it is even more unstable than the parent 1,2-dihydroquinoline, absorption of oxygen initiating rapid polymerisation to a resin of at least 24 monomer units.

1,2-Dihydro-1-methylquinoline and chloranil in homogeneous solution at room temperature give instantly a green amorphous precipitate (B) in amount corresponding to a 1 : 1 addition product. With *p*-benzoquinone it gave more slowly a dull mauve, amorphous powder (C) in 84% yield. These products are sparingly soluble in most solvents (except light petroleum and ether), in which however they are not stable, and they could not be purified. Their infrared spectra were complex and their ultraviolet spectra indicated no more than a quinoline nucleus.

When an aqueous solution or suspension of product (B) was treated with a slight excess of dilute hydriodic acid, the green colour was instantly discharged. There remained



a suspension of brown tetrachloroquinol, and evaporation of the aqueous filtrate yielded quinoline methiodide. Product (C) was similarly decolorised. The compounds are therefore considered to be salts, formed as indicated in the annexed formula for compound (B).

The green salt (B) has one of its absorption maxima at λ 452 mμ (ε ~3600) where

[10] Witkop, *Experientia*, 1954, **10**, 419.
[11] Schmid and Karrer, *Helv. Chim. Acta*, 1949, 960.

neither reactant absorbs. The intensity of absorption at 452 mμ of a mixture of the reactants rises rapidly to a maximum, then more slowly declines. The theoretical maximum value was therefore obtained by extrapolation. Measurements were made fairly satisfactorily at room temperature and give a second-order constant $k = 600 \pm 20$ l. mole^{-1} sec.$^{-1}$ for formation of the salt.

Formation of such phenol salts in this series can occur only by removal of a hydride ion from the position next to the nitrogen atom, followed by quaternisation. The primary hydride transfer accords with the mechanism thought to operate in the dehydrogenation of hydroaromatic homocyclic compounds by quinones. The above compound (B) is a relatively stable " half-way " stage which is rapidly reached in treating 1,2-dihydro-1-methylquinoline with chloranil; for the parent 1,2-dihydroquinoline this stage would involve a proton attached to quaternary nitrogen, and removal of this proton, which would be easy, would then complete the dehydrogenation. It is therefore relevant that quinoline and tetrachloroquinol form a loosely associated complex, which could involve donation of a proton to the base from the feebly acidic phenol. Similar colourless complexes of heterocyclic bases and dihydric phenols are recorded in the literature and have been described as " molecular complexes " [12] and " salts." [13] The extent of their " salt " character is thought to be less than that of the highly coloured compounds (B) and (C) described above.

The very ready quaternisation-dehydrogenation of 1,2-dihydro-1-methylquinoline by loss of a hydride ion probably represents the first stage of enzymic reduction by diphosphopyridine nucleotide ($DPNH_2$). In the biological process, the reaction is completed with the assistance of phosphoric acid residues in the molecule: *in vitro*, the second stage was effected by addition of dilute mineral acid to the phenol salt.

1,2-*Dihydro*-1,2-*dimethylquinoline.*—1,2-Dihydro-1,2-dimethylquinoline,[14,15] which still has one hydrogen atom next to the nitrogen, gives an intensely green colour at once with chloranil, but the reaction leads to a mixture of ill-defined products. In cold anhydrous ether 1,2-dihydro-1,2-dimethylquinoline and *p*-benzoquinone gave an insoluble, very dark blue, amorphous powder very different in properties from the monomethyl analogue. It showed no melting or decomposition range, was completely insoluble in water, and was not decolorised by mineral acid. Analysis showed that it was composed of 1 mol. of dihydrodimethylquinoline and 2 mol. of benzoquinone. Its formation could not have involved a hydrogen transfer process of the kind which led to a phenol salt with 1,2-dihydro-1-methylquinoline.

9,10-*Dihydroacridine.*—Acridine is reduced by lithium aluminium hydride to form 9,10-dihydroacridine in high yield and purity.[5] The product forms colourless needles which are stable under pure dry nitrogen or in a high vacuum. In air, slow oxidation produces the yellow colour of crude acridine.

On treatment with chloranil in homogeneous solution, 9,10-dihydroacridine showed rapid hydrogen transfer to form the quinol and acridine. Spectrometric kinetic work on this transfer system in benzene at room temperature, however, gave no satisfaction. Two runs at different concentrations gave closely similar series of falling second-order k values. The explanation probably follows from Dr. Packham's observation [16] that acridine and 9,10-dihydroacridine form indeterminate, bright yellow complexes with great ease (similar highly coloured complexes are formed from phenazine and 9,10-dihydrophenazine [17]) and these would interfere in the kinetic work. The original preparative reaction with chloranil, in solution at 66°, gave an almost quantitative yield of quinol, so that the hydrogen transfer still proceeds to completion under appropriate conditions.

[12] Cavalla, *J.*, 1954, 4701.
[13] Bothner-By, *J. Amer. Chem. Soc.*, 1955, 749.
[14] Freund, *Ber.*, 1904, 4660; 1909, 1101.
[15] Bradley and Jeffrey, *J.*, 1954, 2770.
[16] Packham, personal communication.
[17] Morley, *J.*, 1952, 4011.

Experimental

M. p.s were determined on a Kofler block and are corrected; unstable or volatile compounds were contained in sealed capillaries (about 0·2 mm. in diameter) which were laid flat on the glass slide of the Kofler block in the usual way. Microanalyses and spectral measurements were carried out in the microanalytical (Miss J. Cuckney) and spectrographic (Mrs. A. I. Boston and Dr. R. L. Erskine) laboratories of this Department.

Diethyl 1,4-*Dihydro*-2,6-*dimethylpyridine*-3,5-*dicarboxylate* (I).—The procedure in *Org. Synth.*[1] gave this compound in high yield as a yellow solid easily purified by crystallisation from ethanol. Further crystallisation from degassed ethanol in an evacuated vessel was necessary to obtain the ester pure for spectrometric kinetic work as bright yellow needles, m. p. 189—190°, $\lambda_{max.}$ 230 and 372 mμ (ε 16,000, 7250). Transfer reactions were carried out with the once recrystallised product, m. p. 184—185°, of >97% purity.

Reaction of Ester (I) *with Chloranil.*—An orange solution of chloranil (0·500 g., 1·0 mol.) in tetrahydrofuran (25 ml.) at 25° was added, all at once, to a pale yellow solution of the ester (0·515 g., 1·0 mol.) in tetrahydrofuran (17 ml.). There was a suggestion of a greenish colour, which almost instantly faded to pale yellow-brown. The mixture remained homogeneous, and during the next 15 min. no further change was observed. Solvent was then evaporated at reduced pressure, and the residue was separated by extraction with hydrochloric acid. The acid-insoluble pale-brown powder was tetrachloroquinol (0·489 g., 97%), m. p. and mixed m. p. 233—236° (sealed capillary) (pure, m. p. 234—236°). The basic component, precipitated from the acid extract by alkali as a colourless powder, was diethyl 2,6-dimethylpyridine-3,5-dicarboxylate (0·493 g., 96%), m. p. and mixed m. p. 70·5—72°. Recrystallisation from ethanol gave the pure oxidised ester, m. p. 73·5—74·5°, $\lambda_{max.}$ 236, 273, and 282 mμ (ε 13,200, 4120, and 3380).

1,2-*Dihydroquinoline.*—(*a*) A solution of quinoline (10·00 g., 1·0 mol.) in anhydrous ether (100 ml.) was added dropwise in about 20 min. to a boiling solution of lithium aluminium hydride (6·0 g., 2·0 mol.) in anhydrous ether (300 ml.). The mixture was then boiled under reflux for 5 hr. The mixture was chilled to 0°, and the complex was decomposed by addition of a slight excess of water. The sludge was filtered off and washed with ether (100 ml.). Evaporation of the filtrates under reduced pressure yielded the crude crystalline product (11·00 g., theor. 10·15 g.), m. p. ~47—52°, which at 0·08 mm. changed in 60 hr. to a yellow, syrup (9·77 g.).

The oil was boiled with acetic anhydride (3·7 ml., 0·6 mol.) for 15 min., then fractionally distilled, giving (*a*) a mixture of acetic acid and anhydride, (*b*) a colourless oil (4·56 g.), b. p. 108—110°/18 mm., n_D^{22} 1·5952 [largely quinoline (picrate, m. p. and mixed m. p. 205—207°)], and higher-boiling materials which on refractionation gave a pale yellow oil (3·23 g.), b. p. 101—109°/0·08 mm., n_D^{22} 1·5939—1·5911 (Found: C, 75·6; H, 6·7; N, 8·2%).

(*b*) The ethereal solution of the reduction product (15·00 g.), obtained as above, was concentrated and distilled through a 10 × 1 cm. Stedman column, affording a fraction (4·08 g.), b. p. up to 117°/18 mm., yellow oil (A) (2·01 g.), b. p. 117—120°/18 mm., n_D^{22} 1·6166, and a sticky solid (B) (5·14 g.), b. p. 128—130°/18 mm., melting over a wide range up to 70° and having $\lambda_{max.}$ 230, 279, and 349 mμ (ε 29,300, 1640, and 1940); pure 1,2-dihydroquinoline [4] has $\lambda_{max.}$ 228, 278, and 343 mμ (ε 30,200, 1510, and 2240).

Fraction (A) crystallised under pure dry nitrogen and was combined with fraction (B) for a second distillation which removed a small oily fore-run and gave the bulk of material as a pale yellow oily solid, b. p. 129—130°/18 mm., m. p. up to 65°. The solid was crystallised twice from hot degassed petroleum (b. p. 60—80°), yielding colourless needles (2·21 g.), m. p. 71—74° (sealed capillary) and similar needles (1·50 g.), m. p. 66—69° (sealed capillary). Both materials were stored at 10^{-5} mm. pressure.

All the mother-liquors were combined and evaporated at reduced pressure. The residual yellow oil was combined with the low-boiling fractions from the first distillation and the total oil component (6·58 g.) was twice fractionally distilled at reduced pressure. Fractions were collected, of b. p. 111—117°/16 mm., n_D^{25} 1·6156—1·6050, the last of which was a yellow oil (0·56 g.). Analytical values for this product indicated ~70% of tetrahydroquinoline (Found: C, 81·3; H, 7·5; N, 10·8. Calc. for C_9H_7N: C, 83·7; H, 5·5; N, 10·8. Calc. for $C_9H_{11}N$: C, 81·15; H, 8·3; N, 10·5%). Benzoylation in pyridine afforded 1-benzoyl-1,2,3,4-tetrahydroquinoline (84%), m. p. and mixed m. p. 76—77°.

The first fractions (4·61 g.) of the above distillation were shown by light absorption and isolation of the pure picrate [(m. p. and mixed m. p. 205—207° (sealed capillary)] to contain about 80% of quinoline.

(*c*) A solution of 1,2-dihydroquinoline (2·263 g., m. p. 71—74°) in pure degassed phenetole (10 ml., b. p. 172°) was boiled under reflux in a sealed vessel for 2 hr. The base was recovered and with acetyl chloride in pyridine (15 min. at 100°) gave 1-*acetyl*-1,2-*dihydroquinoline* (1·51 g.), b. p. 102°/0·08 mm., n_D^{23} 1·6028 (Found: C, 76·5; H, 6·6; N, 8·2. $C_{11}H_{11}NO$ requires C, 76·3; H, 6·4; N, 8·1%).

(*d*) Of 1,2-dihydroquinoline (3·000 g.), treated with lithium aluminium hydride (1·73 g.) in ether (70 ml.), most (2·921 g.) was recovered.

Reaction of 1,2-*Dihydroquinoline with Chloranil.*—An orange solution of chloranil (0·936 g., 1·0 mol.) in dioxan (30 ml.) was added all at once to a solution of crude, undistilled 1,2-dihydroquinoline (0·500 g.) in dioxan (5 ml.) at room temperature: a deep wine-red colour was immediately produced, and after 10 min. solvent was evaporated at reduced pressure. The residual oil was dissolved in benzene and extracted with hydrochloric acid. Basic material was recovered from the aqueous acid extract as a dark brown oil (0·481 g.), giving quinoline picrate, m. p. and mixed m. p. 205—207° (sealed capillary). Evaporation of the benzene solution afforded a yellow-brown solid (1·072 g.), m. p. 172—205°, all of which was dissolved in hot 4N-sodium hydroxide. The solution was filtered into an excess of hydrochloric acid and the precipitate was filtered off as a brown powder (0·693 g., 73%), m. p. 228—232° (sealed capillary), not depressed on admixture with tetrachloroquinol, m. p. 234—236° (sealed capillary). Continuous ether-extraction of the deep red filtrate from the quinol yielded an orange-red solid (0·220 g.), m. p. 282—284° (decomp.; sealed capillary) alone or mixed with 2,5-dichloro-3,6-dihydroxy-1,4-benzoquinone. This accounts for the balance (27%) of acceptor. This process serves as an excellent procedure for estimation of 1,2-dihydroquinoline.

1,2-*Dihydroisoquinoline.*—Redistilled isoquinoline (10·00 g., 1·0 mol.; m. p. 21—24°) was reduced with ethereal lithium aluminium hydride (6·0 g., 2·0 mol.) as with quinoline: crystallisation of the crude oily product from methanol afforded a powder (2·69 g.), m. p. 126—132°, which, recrystallised from aqueous and then from anhydrous dimethylformamide, gave pale fawn plates (0·22 g.), m. p. 194° (slight decomp.) (Found: C, 77·8; H, 6·1; N, 10·4. $C_{18}H_{16}N_2O$ requires C, 78·2; H, 5·8; N, 10·1%). Sublimation at 165°/5 × 10^{-3} mm. gave a very pale yellow powder (0·14 g.), m. p. 178—180° (decomp.) (Found: C, 78·1; H, 5·9; N, 10·6%).

The above reduction was repeated with pure isoquinoline (20·00 g., 1·0 mol.) and ethereal lithium aluminium hydride (6·0 g., 1·0 mol.) in an atmosphere of pure dry nitrogen. Chloroform (200 ml.) was also added to keep all organic material in solution after the complex was decomposed with a slight excess of water. The crude product was an oil whence crystallisation from methanol (50 ml.) gave a series of indefinite crystalline products (X) (13·45 g.). Evaporation of the mother-liquors yielded an oil (7·23 g.) which was twice distilled to give a series of strongly blue-fluorescent, colourless oils (2·77 g.), b. p. 111—113°/16 mm., n_D^{23} 1·5777—1·5842. Part (0·100 g.) of a middle fraction was heated in pyridine with a slight excess of benzenesulphonyl chloride, for 10 min. on the steam-bath; the neutral product (0·176 g., 86%) had m. p. 153—154° alone or mixed with 1-benzenesulphonyl-1,2,3,4-tetrahydroisoquinoline, m. p. 153—154°.

The product (X) was extracted with cold chloroform (5 × 20 ml.; 5 × 5 ml.): insoluble material was a fawn powder (1·052 g.) (A), m. p. 189—190°, which, crystallised twice from 1 : 1 aqueous dioxan, gave fawn needles (0·632 g.), m. p. 189·5—190° (Found: C, 77·8; H, 6·1; N, 10·5%), $\lambda_{max.}$ 239, 274, 305, and 330 mμ (ε 26,600, 3270, 4680, and 5630), $\nu_{max.}$ 2567, 2535, and 1625 $cm.^{-1}$.

Material (A) (0·200 g., 1·0 mol.) was heated in pyridine (12 ml.) with benzoyl chloride (0·25 ml., 3·0 mol.) for 10 min. on the steam-bath, then the neutral *product* was isolated (0·338 g., 97%). Crystallisation twice from ethanol afforded colourless prisms (0·259 g.), m. p. 201·5—202° [Found: C, 79·4; H, 5·0; N, 5·9; O, 10·2%; *M*, 485 (Rast). $C_{32}H_{24}N_2O_3$ requires C, 79·3; H, 5·0; N, 5·8; O, 9·9%; *M*, 490], $\nu_{max.}$ 1734s, 1629s, 1601m, and 1581m $cm.^{-1}$.

The chloroform-soluble solid from the isoquinoline reduction was twice fractionally extracted by chloroform and precipitated from solution with light petroleum. The main product was then a colourless crystalline powder (3·40 g.), m. p. 112—121°, showing no trace of a higher-melting component. This was fairly pure associated 1,2-dihydroisoquinoline. All the other fractions (total, 6·48 g.) showed traces of higher-melting impurity in the range 155—195°.

These fractions were combined and shaken with chloroform (25 ml.) at 23°. Oxygen was bubbled through the solution or suspension. In ~15 min. the temperature had risen to 35° and the amount of solid had increased. Thereafter the temperature slowly declined (to 19° in 1 hr.). Filtration afforded a fawn powder (1·800 g.), m. p. 196—198° (decomp.). This material was crystallised from aqueous dioxan, then from aqueous ethanol, sublimed at 150°/9 × 10^{-5} mm., and finally crystallised from anhydrous ethanol to give 4-hydroxyisoquinoline as pale fawn prisms (0·963 g.), m. p. 228—229·5° (sealed capillary) alone or mixed with material prepared as described by Gilman *et al.*[18] (Found: C, 74·8; H, 5·2; N, 9·7; O, 11·1. Calc. for C_9H_7NO: C, 74·5; H, 4·9; N, 9·7; O, 11·0%), $\lambda_{max.}$ 234, 295, 320, and 330 mμ (ε 17,910, 4700, 5320, and 5700), $\nu_{max.}$ (strong) 2427, 1803, 1770, and 1624 $cm.^{-1}$.

The hydroxyisoquinoline was heated in pyridine with a slight excess of benzoyl chloride on a steam-bath for 10 min. and the basic benzoate was isolated quantitatively. Two crystallisations from light petroleum (b. p. 60—80°) gave colourless prisms, m. p. and mixed m. p. 109—109·5°.

Concentration of the chloroform filtrate from the 4-hydroxyisoquinoline gave a second crop of similar material (0·250 g.), m. p. 180—198° (decomp.). This was benzoylated and the crude product (0·40 g.) was separated by fractional crystallisation from petroleum (b. p. 60—80°) and from ethanol into 4-hydroxyisoquinoline benzoate (0·128 g.), m. p. 107—109°, and the less soluble *ON*-dibenzoate (A) (0·106 g.), m. p. 200·5—202°.

Total evaporation of the chloroform mother-liquor and distillation of the residue (3·81 g.) gave mainly an oil (1·07 g.), b. p. 87—90°/0·002 mm., n_D^{22} 1·6160—1·6203, which with methyl iodide yielded isoquinoline methiodide as needles (1·81 g., 80%), m. p. and mixed m. p. 160—161° (from ethanol).

1,2-*Dihydro*-1-*methylquinoline*.—Anhydrous, finely ground quinoline methiodide (10·00 g., 1·0 mol.; m. p. 145—146°) was added in small portions in about 20 min. to a stirred solution of lithium aluminium hydride (1·54 g., 1·1 mol.) in anhydrous ether (50 ml.). A slight excess of saturated aqueous ammonium chloride was then added at 0°. The inorganic precipitate was filtered off and the filtrate was evaporated at 14 mm. on the steam-bath. The residue was fractionally distilled, to give a yellow oil (4·98 g., 93%), b. p. 52—53°/0·08 mm., $n_D^{22·5}$ 1·6195—1·6201, $\lambda_{max.}$ 231, 289, and 348 mμ (ε 32,600, 2490 and 2110 in EtOH).

A less successful distillation gave a resin which on repeated precipitation from benzene by ethanol afforded an unstable powder, m. p. 214—216° [Found: C, 81·9; H, 7·7; N, 10·1%; *M*, 5000 (Rast), 3500 (ebullioscopic in C_6H_6)].

Reaction of 1,2-*Dihydro*-1-*methylquinoline with Chloranil*.—Chloranil (3·12 g., 1·0 mol.) in dioxan (110 ml.) was quickly added at room temperature to 1,2-dihydro-1-methylquinoline (1·84 g., 1·0 mol.) in dioxan (15 ml.), giving a green precipitate which was filtered off, washed with dioxan, and dried in a vacuum to an amorphous green powder (4·96 g.) (B), m. p. ~123—130° (decomp.), $\lambda_{max.}$ 235, 316, 426, and 452 mμ (ε 41,290, 12,430, 3380, and 3480 in EtOH), $\nu_{max.}$ (weak) 1628, 1591, 773, and 763 $cm.^{-1}$.

When this compound (1·000 g.) was suspended in water (10 ml.) and treated with a slight excess of N-hydriodic acid (3 ml.) at room temperature, the green colour was discharged and brown material remained in suspension. Filtration afforded a powder (0·656 g.; theor. for tetrachloroquinol, 0·634 g.), m. p. 205—210°. Crystallisation from benzene yielded pale brown leaflets (0·351 g.), m. p. 221—223°. Sublimation at 130° (bath)/6 × 10^{-5} mm. gave pale fawn crystals (0·325 g.), m. p. and mixed m. p. 234—236° (sealed capillary). The aqueous filtrate from the quinol, evaporated at reduced pressure, yielded a sticky yellow solid (0·794 g.; theor. for quinoline methiodide monohydrate, 0·739 g.). Recrystallisation from 50% aqueous ethanol gave yellow plates (0·525 g.), m. p. and mixed m. p. 71—73° (sealed capillary). When slowly heated in air, the sample was dehydrated and had m. p. and mixed m. p. 145—146°.

Reaction of 1,2-*Dihydro*-1-*methylquinoline with* p-*Benzoquinone*.—*p*-Benzoquinone (0·80 g., 1·0 mol.) in ether (25 ml.) was added at room temperature to 1,2-dihydro-1-methylquinoline (1·07 g., 1·0 mol.) in ether (25 ml.). A dark brown colour appeared immediately and a flocculent solid began to separate. The mixture was sealed under nitrogen for 10 min. The solid was then filtered off, washed with ether, and obtained as a dull mauve, amorphous powder (1·57 g.) (C), m. p. 105—140° (decomp.) $\lambda_{max.}$ 235 and 303 mμ (ε 27,900 and 7000 in EtOH), $\nu_{max.}$ 1208s 839s, and 767s, 1644m, 1620m, 1592m, and 780m $cm.^{-1}$.

Quinoline–Tetrachloroquinol Complex.—A solution of quinoline (0·400 g., 2·0 mol.) and

[18] Gilman and Gainer, *J. Amer. Chem. Soc.*, 1947, **69**, 1946.

tetrachloroquinol (0·384 g., 1·0 mol.) in ethyl acetate (10 ml.) was boiled under reflux. Concentration and cooling afforded light brown prisms (0·583 g.) readily subliming as plates and needles from about 98° before melting at 125—173°. On attempted sublimation at 5×10^{-5} mm. decomposition occurred at about 90°.

Reaction of 1,2-*Dihydro*-1,2-*dimethylquinoline with* p-*Benzoquinone*.—1,2-Dihydro-1,2-dimethylquinoline[15] (1·000 g., 1·0 mol.) in anhydrous ether (15 ml.) was quickly added at room temperature to *p*-benzoquinone (0·679 g., 1·0 mol.) in ether (25 ml.). A dark turquoise-blue colour appeared immediately and a solid slowly separated. The mixture was sealed under nitrogen for 5 hr. Filtration then afforded a dark blue powder which was washed with ether and immediately heated at 50°/10^{-5} mm. for 2 hr. After being cooled at this pressure, a specimen of the *product* (0·648 g.) was analysed at once (Found: C, 73·8; H, 5·3; N, 3·8. $C_{23}H_{21}NO_4$ requires C, 73·6; H, 5·6; N, 3·7%), $\lambda_{max.}$ 235, 324, and 650 mμ (ε 33,320, 11,380, and 3870), $\nu_{max.}$ 1604m, 829m, and 759m, 1620w, and 1582w cm.$^{-1}$. Addition of more *p*-benzoquinone (1·0 g.) in ether (30 ml.) to the filtrate from the blue complex produced an identical reaction. Filtration after 14 hr. at room temperature afforded more of the complex (0·957 g.), to make the total yield 68%.

9,10-*Dihydroacridine*.[5]—A solution of acridine (5·00 g., 1·0 mol.) in anhydrous 1 : 1 benzene–ether (50 ml.) was added in about 10 min. to lithium aluminium hydride (2·12 g., 2·0 mol.) in anhydrous ether (100 ml.). The mixture was set aside in a sealed flask at room temperature for 18 hr., and worked up as for dihydroquinoline. The crude product crystallised from ethanol as needles (4·34 g., 87%), m. p. 170—172°. Recrystallisation from degassed ethanol in a vacuum yielded needles, m. p. 172—172·5°, $\lambda_{max.}$ 290 mμ (ε 15,200).

Reaction of 9,10-*Dihydroacridine with Chloranil*.—A colourless solution of 9,10-dihydroacridine (0·736 g., 1·0 mol.) in anhydrous tetrahydrofuran (6 ml.) was quickly added to a yellow solution of chloranil (1·000 g., 1·0 mol.) in hot tetrahydrofuran (15 ml.). There was immediately an intense, transient, blue coloration, changing at once to deep wine-red. The homogeneous solution was boiled under reflux for 1 hr. in a sealed vessel, and showed no further change in appearance. Solvent was distilled off at reduced pressure and the residual solid was separated by extraction with hot alkali. The alkali-soluble, acid-insoluble component was tetrachloroquinol (0·930 g., 92%), m. p. and mixed m. p. 232—236° (sealed capillary). The alkali-insoluble component was acridine (0·701 g., 97%), m. p. and mixed m. p. 106—109°.

Kinetic Experiments.—(1) *The Hantzsch ester and chloranil.* The freshly crystallised ester (7·21 mg., 1·0 mol.) was dissolved in redistilled " AnalaR " benzene (50·00 ml.). A portion was diluted to exactly half concentration, and the absorption was measured in a 1·0 cm. stoppered cell (*E* 0·818 at 392 mμ). A similar process with chloranil (7·00 mg., 1·0 mol.) led to the value *E* 0·273. The oxidised Hantzsch ester and the quinol have no significant absorption at this wavelength, and it was assumed that in solutions containing equimolecular quantities of the reagents, $E_{donor} = 0{\cdot}750\,E_{obs}$. Immediately after the above measurements, 5·00 ml. of each solution were mixed and the diminishing absorption of an aliquot part was followed spectrophotometrically at 24° (see Table).

Time (min.)	2	4	6	8	10	12	16	20	26
E_{obs}	0·942	0·895	0·831	0·779	0·735	0·687	0·618	0·556	0·494
E_{donor}	0·706	0·671	0·623	0·584	0·551	0·515	0·463	0·417	0·370
Time (min.)	30	40	60	80	100	190	360	1260	
E_{obs}	0·461	0·392	0·295	0·239	0·199	0·115	59	20	
E_{donor}	0·346	0·294	0·221	0·179	0·149	86	44	15	

$k = 2{\cdot}60 \pm 0{\cdot}05$ l. mole^{-1} sec.$^{-1}$.

(2) 1,2-*Dihydroquinoline–chloranil*. For 1,2-dihydroquinoline (0·0010%, 1·0 mol.) in benzene, $E_{\frac{1}{2}conc.} = 0{\cdot}221$ at 350 mμ, and for chloroanil (0·00187%, 1·0 mol.) in benzene $E_{\frac{1}{2}conc.} = 0{\cdot}184$. The products of hydrogen transfer showed no significant absorption at this wavelength. However that at these concentrations the reaction was >80% complete in 40 sec. at 23°.

When extremely dilute solutions were used at 350 mμ, an estimate was made of the second-order rate constant, from the simple equation from $t = 0$:

Donor, 0·00050%; acceptor, 0·000937%; in benzene at 23°.

Time (sec.)	55	65	80
E_{obs}	0·052	0·047	0·040
E_{donor}	0·0284	0·0257	0·0190
k (l. mole^{-1} sec.$^{-1}$)	13,800	13,400	13,400

(3) 1,2-*Dihydro*-1-*methylquinoline–chloranil.* Dihydromethylquinoline (4·00 mg., 1·0 mol.) was dissolved in benzene (100·0 ml.), also chloranil (6·76 mg., 1·0 mol.) was dissolved in benzene (100·0 ml.); 1·40 ml. of each solution were mixed in a 1·0 cm. absorption cell in position in the spectrometer. Quantitative reaction produced the green phenol salt in 0·00538% concentration which is sufficiently low for complete solubility in benzene. The increasing absorption of the system at 452 mμ was then measured. The expected zero-time value of E, less than 0·005, was neglected in calculating the extent of reaction.

Heterocycle, 0·0020%; quinone, 0·00338%; in benzene at 23°.

Time (sec.)	25	35	45	55	70	90	120
E_{obs}	0·345	0·375	0·395	0·411	0·429	0·441	0·455
Reaction (%)	69	75	79	82	86	88	91
Time (sec.)	180	240	600	720	1000	16 hr.	
E_{obs}	0·470	0·480	450	430	420	287	
Reaction (%)	94	96	—	—	—	—	

The extrapolated, final value for E was 0·500, corresponding to $\varepsilon_{max.}$ 3640. The second-order rate equation (up to 180 sec.) gave $k = 600 \pm 20$ l. mole^{-1} sec.$^{-1}$.

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