minutes, and was between 80 and 125° in all cases. [b] L. Beregi (*Magyar Kém. Folyóirat*, **56**, 257 (1950); *C.A.*, **46**, 8000 (1952)) reports a 56% yield of *n*-butylamine, a 33% yield of benzylamine, a 51% yield of furfurylamine, and a 75% yield of 2-aminobutane from the oximes over Raney nickel with dioxane as a solvent at 15–18°. [c] R. Paul (*Bull. soc. chim. France*, [5] **4**, 1121 (1937)) reports a 20% yield of benzylamine and a 44% yield of furfurylamine over Raney nickel with alcohol as a solvent at 15–18° and 1 atm. pressure. At 60 atm. hydrogen pressure and 70–85°, a 79% yield of 2-aminobutane and a 97% yield of α-phenethylamine were reported. [d] M. Smith and H. Adkins (THIS JOURNAL, **60**, 660 (1938)) report a 40% yield with methanol as the solvent. [e] C. Winans and H. Adkins (*ibid.*, **55**, 2051(1933)) report a 77% yield of benzylamine using a nickel-on-kieselguhr catalyst. In ref. 6, page 92, the same authors report a 78% yield of α-phenethylamine from acetophenone oxime.

From the data, it is apparent that Raney cobalt is likewise an excellent catalyst for this reaction. In the case of the six oximes studied, the two catalysts were about equally effective in three cases as far as yield and purity of product were concerned. In the other three cases, the Raney nickel may have been slightly superior in two cases and the Raney cobalt in one. The advantage of using a Raney cobalt catalyst is that sometimes it is as good or better than Raney nickel even when it is used with a dioxane or ethanol solvent containing no ammonia, whereas Raney nickel may require an ammoniacal solvent for best results in hydrogenating nitriles,[7] and probably also oximes. The hydrogenation of butyraldoxime illustrates this advantage of Raney cobalt.

Experimental

Hydrogenations.—A standard 300-ml. Aminco steel hydrogenation vessel and standard accessory equipment were used. Conditions are in the footnote to Table I. High boiling amines were isolated by distillation. The *n*-butylamine, 2-aminobutane and pinacolylamine were converted to their hydrochlorides, the solvent removed by distillation under water-pump pressure, a saturated solution of sodium hydroxide in diethylene glycol added, and the amine distilled off. Pinacolylamine formed an azeotrope with water, b.p. 84–85°, consisting of about 80% amine. The water was removed by treatment with solid potassium hydroxide, and the amine layer separated and distilled.

Catalysts. Solvents and Compounds.—The Raney catalysts were prepared by the W-7 procedure of Adkins and Billica.[8] The age of the catalysts at the time of use varied from a few days to three months. Catalyst age within these limits did not appear to affect the yields obtained.

The absolute ethanol used as a solvent was shaken with Raney nickel under the usual hydrogenation conditions at 125° for 2 hours, the nickel filtered off, the ethanol distilled from calcium oxide, and the middle half collected and stored for future use. The dioxane was purified by refluxing over sodium, distilling, and the middle third of the distillate used. The ammoniacal solvents were prepared by bubbling ammonia gas through the cooled solvent for several hours.

All of the oximes were prepared by standard methods and had the physical constants reported in the literature. The benzaldoxime was a mixture of the *syn* and *anti* forms, b.p. 132° at 20 mm.

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(7) E. J. Schwoegler and H. Adkins, THIS JOURNAL, **61**, 3499 (1939).

(8) H. Adkins and H. R. Billica, *ibid.*, **70**, 698 (1948).

COLLEGE PARK, MARYLAND

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENTS OF BROOKHAVEN NATIONAL LABORATORY AND THE UNIVERSITY OF KANSAS]

The Rearrangement and Condensation of Reissert Compounds with Grignard Reagents[1]

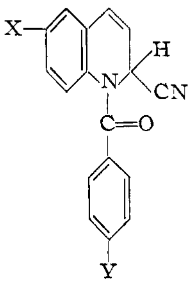
BY ALFRED P. WOLF,[2] WILLIAM E. MCEWEN[3] AND R. H. GLAZIER[3]

RECEIVED APRIL 18, 1955

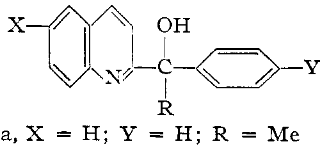
A series of 1-acyl-1,2-dihydroquinaldonitriles and 2-acyl-1,2-dihydroisoquinaldonitriles (Reissert compounds) have been rearranged and condensed with a variety of Grignard reagents. The mechanism of the rearrangement has been investigated, and it has been demonstrated that the rearrangement proceeds by an intramolecular process.

In a previous communication it was reported that 1-benzoyl-1,2-dihydroquinaldonitrile (Ia) reacts with methylmagnesium bromide in benzene or dioxane solution to give methylphenyl-2-quinolylcarbinol (IIa).[4] A similar rearrangement to form 2-benzoylquinoline (III) occurs when Ia is treated with sodium hydride in boiling xylene.[5] The Grignard reaction has now been extended to a variety of Reissert compounds and a variety of Grignard reagents, and the mechanism of the rearrangement has been investigated.

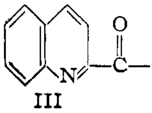
In the first series of reactions an ether solution of methylmagnesium bromide was added to a dioxane solution of the Reissert compound. The temperature was kept below 60° at all stages of the reac-



Ia, X = H; Y = H
b, X = OMe; Y = H
c, X = H; Y = Cl
d, X = H; Y = OMe
f, X = H; Y = Me



IIa, X = H; Y = H; R = Me
b, X = OMe; Y = H; R = Me
c, X = H; Y = Cl; R = Me
d, X = H; Y = OMe; R = Me
e, X = H; Y = H; R = C_6H_5



III

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(1) (a) A portion of this paper was abstracted from a thesis submitted by Robert H. Glazier in partial fulfillment of the requirements for the degree of Doctor of Philosophy, Kansas University, 1952; (b) work performed in part under the auspices of the U. S. Atomic Energy Commission.

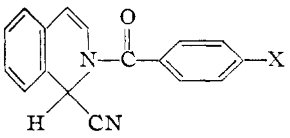
(2) Brookhaven National Laboratory, Upton, Long Island, N. Y.

(3) University of Kansas, Lawrence, Kansas.

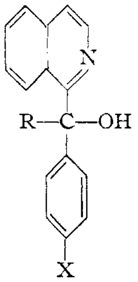
(4) W. E. McEwen, J. V. Kindall, R. N. Hazlett and R. H. Glazier, THIS JOURNAL, **73**, 4591 (1951).

(5) V. Boekelheide and J. Weinstock, *ibid.*, **74**, 660 (1952).

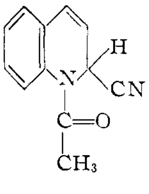
tion. Following is a summary of the results: from 1-benzoyl-1,2-dihydroquinaldonitrile (Ia) there was obtained a 59% yield of crude methylphenyl-2-quinolylcarbinol (IIa) plus a trace of 2-benzoylquinoline (III); from 1-benzoyl-6-methoxy-1,2-dihydroquinaldonitrile (Ib), 56% of methylphenyl-2-(6-methoxyquinolyl)-carbinol (IIb); from 2-benzoyl-1,2-dihydroisoquinaldonitrile (IVa), 32% of methylphenyl-1-isoquinolylcarbinol (Va); from 1-*p*-chlorobenzoyl-1,2-dihydroquinaldonitrile (Ic), 10% of methyl-*p*-chlorophenyl-2-quinolylcarbinol (IIc); from 1-anisoyl-1,2-dihydroquinaldonitrile (Id), 4% of methyl-*p*-anisyl-2-quinolylcarbinol (IId); 1-*p*-toluyl-1,2-dihydroquinaldonitrile (Ie) and 1-acetyl-1,2-dihydroquinaldonitrile (VI) failed to give products of rearrangement. The reaction of 1-anisoyl-1,2-dihydroquinaldonitrile (Id) with methylmagnesium bromide was also carried out at a temperature of about 130°, in xylene solution. There resulted only a very small increase in the yield of methyl-*p*-anisyl-2-quinolylcarbinol (IId).



IVa, X = H
b, X = Cl

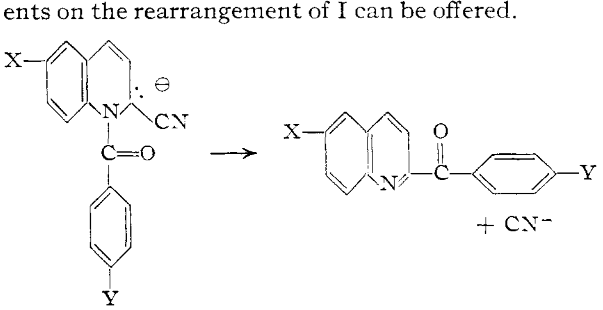


Va, X = H, R = Me
b, X = H, R = C_6H_5



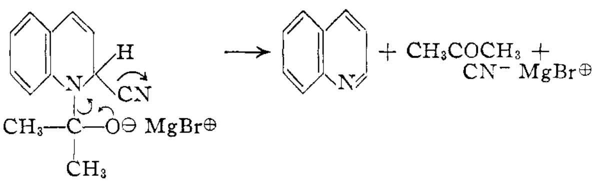
VI

It is evident from the above results that the presence of *para* substituents, both of the electron-donating type (OMe and Me) and of the electron-withdrawing type (Cl), in I inhibit the rearrangement. A Grignard anion could conceivably attack any of three positions in I: (*1*) *the carbon atom of the cyano group;* (*2*) *the acidic hydrogen atom in the 2-position of the quinoline ring; and* (*3*) *the carbonyl carbon atom of the 1-acyl group.* Clearly, each of these three reaction paths would give rise to different products. It has been suggested previously that the mechanism of the rearrangement involves formation of the anion VII of I, which then rearranges to VIII with expulsion of a cyanide ion.[4,5] On the basis of these considerations, a tentative explanation for the inhibiting effect of the *p*-substituents on the rearrangement of I can be offered.



VII VIII

The presence of an electron-withdrawing substituent in the *p*-position of I would tend to bring about an increase in the rate of reaction 3 relative to 1 and relative to the over-all rate of formation of the anion VII (reaction 2) and its rearrangement to VIII.[6] Obviously a reaction of this type would decrease the yield of rearrangement products II and VIII.



IX

The presence of an electron-donating substituent in I would be expected to lead to a decrease in the relative rate of reaction 3, but it would also lead to a decrease in the rate of rearrangement of the anion VII to VIII since this process also is dependent on the electrophilic reactivity of the carbonyl carbon atom. Hence other reactions, of type 1, for example, would be able to compete and thus decrease the yields of rearrangement-products II and VIII.

The reaction of aryl Grignard reagents with Reissert compounds was also studied. Only a trace of 2-benzoylquinoline (III) was obtained on reaction of phenylmagnesium bromide with 1-benzoyl-1,2-dihydroquinaldonitrile (Ia) in dioxane solution when the temperature of the reaction mixture was kept below 60°. When the reaction was carried out in boiling dioxane, however, there was obtained an 8.5% yield of pure diphenyl-2-quinolylcarbinol (IIe) plus a 4% yield of pure 2-benzoylquinoline (III). The lesser reactivity of phenylmagnesium bromide as compared to methylmagnesium bromide might be due to a steric factor or to the lesser tendency of aryl Grignard reagents to attack the α-hydrogen atom in reaction with a nitrile.[7] The beneficial effect of a higher reaction temperature in promoting the rearrangement has a parallel in the observation of Boekelheide and Weinstock on the rearrangement of Reissert compounds brought about by sodium hydride.[5] 2-Benzoyl-1,2-dihydroisoquinaldonitrile (IVa) reacted very smoothly with phenylmagnesium bromide in boiling dioxane to give a 50% yield of crude diphenyl-1-isoquinolylcarbinol (Vb).[8] The reaction of mesitylmagnesium bromide with 1-benzoyl-1,2-dihydroquinaldonitrile (Ia) in dioxane solution, at a temperature of about 60° led to the isolation of a trace of 2-benzoylquinoline (III). A reaction carried out in *p*-xylene solution, at a temperature of about 134°, led to the formation of a fairly large amount of quinoline and a trace of III.

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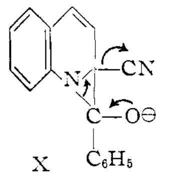
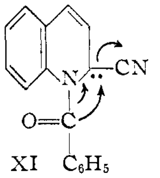
(6) The same would hold true for a Reissert compound having an aliphatic acyl group in the 1-position as compared to one having an aromatic acyl group. Thus in the reaction of 1-acetyl-1,2-dihydroquinaldonitrile (VI) with methylmagnesium bromide, quinoline was isolated as a reaction product. This probably was formed by addition of the Grignard reagent to the carbonyl group of VI to give IX, which then reacted further to form acetone, quinoline and the cyanide ion, the reaction scheme being analogous to that which occurs when a Reissert compound is cleaved by attack of a hydroxide ion. See V. Boekelheide and C. Ainsworth, THIS JOURNAL, **72**, 2134 (1950).

(7) C. R. Hauser and W. J. Humphlet, *J. Org. Chem.*, **15**, 359 (1950).

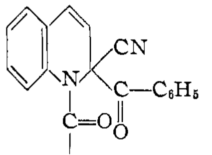
(8) The actual yield of Vb was greater than 50% since 21% of the starting material IVb was recovered.

Both intramolecular and intermolecular mechanisms have been considered for the rearrangement of the conjugate base of a Reissert compound to the α-acyl derivative with expulsion of a cyanide ion. For example, it has been proposed[9] that 2-benzoylquinoline (III) arises from the anion VII (X = Y = H) by an intramolecular process, possibly by way of the ethyleneimine intermediate X. An alternative intramolecular process presumably involving synchronous changes symbolized by the species XI has also been suggested.[5]

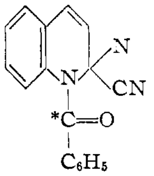

X

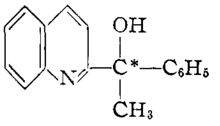

XI

The intermolecular process which has been considered is actually an ionic chain reaction involving formation of 1,2-dibenzoyl-1,2-dihydroquinaldonitrile (XII) as an intermediate.[5]


XII

A convincing proof that the rearrangement occurs by an intramolecular process now has been provided. Reaction of methylmagnesium bromide with a mixture of 1-benzoyl-6-methoxy-1,2-dihydroquinaldonitrile (Ib) and 1-benzoyl-(carbonyl-C_1^{14})-1,2-dihydroquinaldonitrile (XIII) gave active methylphenyl-2-quinolylcarbinol (XIV) and unlabeled methylphenyl-2-(6-methoxyquinolyl)-carbinol (IIb).


XIII


XIV

Before the results of the competition experiment could be accepted as proof of the intramolecular nature of the rearrangement, it was necessary to demonstrate that the rates of the two individual reactions were about equal under the indicated reaction conditions.[10] The data given in Table I demonstrate that the two rearrangement–condensation reactions proceed at very nearly identical rates. Furthermore, the visually apparent changes which occur during each of the individual reactions indicate that both proceed by the same sequence of steps.[11]

TABLE I

RELATIVE RATES OF REACTION OF METHYLMAGNESIUM BROMIDE WITH 1-BENZOYL-1,2-DIHYDROQUINALDONITRILE (Ia) AND 1-BENZOYL-6-METHOXY-1,2-DIHYDROQUINALDONITRILE (Ib) AT 56°

Reissert cmpd.	Yield of rearranged product after x minutes, %				
	x 8	10	15	30	*ca.* 120[a]
Ia	5.13(84.8)[b]	15.1(81.4)	16.9(77.6)	23.8(69.4)	59
Ib	4.89(82.8)	13.1(84.6)	14.4(77.9)	21.1(60.0)	56

[a] Yield obtained in preparative experiment. Total time of reaction at *ca.* 60°, including distillation period, was about 2 hours. [b] Percentage recovery of crude Reissert compound given in parentheses.

Difficulties were experienced in the initial attempts to effect a separation of the carbinols resulting from the competition reaction. Therefore a type of isotope dilution sometimes called the Carrier Addition Method[12] was used. A small amount of the mixture of active carbinols was diluted with one of the pure carbinols. The weight of either carbinol in the active mixture comprised 10–20% of the total sample weight after dilution. Each carbinol mixture was then recrystallized to constant specific activity and chemical purity.

Dilution of samples of the active mixture with inactive methylphenyl-2-(6-methoxyquinolyl)-carbinol (IIb) followed by several recrystallizations, gave samples whose activity was indistinguishable from background. Dilutions of samples of the active mixture with methylphenyl-2-quinolylcarbinol (IIa) resulted in the isolation of active samples which were demonstrably at constant specific activity.

The results are summarized in Table II. The results show that 100% of the expected activity is found in the diluted samples of methylphenyl-2-quinolyl-carbinol-C_1^{14} (XIV). The found activity in the diluted samples represents 95.6% of the

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(9) W. E. McEwen, J. V. Kindall, R. N. Hazlett and R. H. Glazier, paper presented at the 119th National Meeting of the American Chemical Society, Boston, Mass., 1951.

(10) Schmid and Schmid have discussed the importance of this requirement with reference to the determination of the intramolecular nature of the *ortho* Claisen Rearrangement: H. Schmid and K. Schmid, *Helv. Chim. Acta*, **35**, 1879 (1952).

(11) In each of the rate determinations, 10 ml. of a 4 *M* solution of methylmagnesium bromide (0.04 mole) was added in one portion to a solution of about 0.004 mole of Reissert compound in 15 ml. of dioxane, the reaction mixture being maintained at a temperature of 56°. In each case there was immediate formation of a colorless precipitate of halogen-containing salts. The precipitate is probably a mixture of methylmagnesium bromide and magnesium bromide with most of the base in solution being dimethylmagnesium. See, *e.g.*, C. R. Noller and W. R. White, THIS JOURNAL, **59**, 1354 (1937), and R. G. Jones and H. Gilman, *Chem. Revs.*, **54**, 835 (1954). However, without further investigation it is difficult to say whether there is extremely rapid reaction with the small amounts of methylmagnesium bromide left in solution or whether the proton abstraction is brought about by the more slowly reacting dimethylmagnesium. After about 4.5 minutes, red particles began to appear in the mixture and methane began to be evolved. By the end of 6 minutes the evolution of methane became quite rapid, and the reaction mixture consisted of a deep red precipitate suspended in a relatively pale solution. Methane evolution ceased after about 9.5 minutes. At the end of the desired reaction time, an excess of water was added to quench the reaction, whereupon a large volume of methane was evolved. On the basis of these observations and the data given in Table I, it is clear that both 1-benzoyl-1,2-dihydroquinaldonitrile (Ia) and 1-benzoyl-6-methoxy-1,2-dihydroquinaldonitrile (Ib) are converted to their conjugate bases during the first 10 minutes of reaction, then the anions rearrange to the 2-benzoyl derivatives with expulsion of a cyanide ion relatively slowly and possibly in the solid phase. Finally, the 2-benzoyl derivatives add methylmagnesium bromide, or perhaps dimethylmagnesium as is possible under these reaction conditions, to form the magnesium salts of the carbinols. Thus it is evident that the rearrangement–condensation reactions of both 1-benzoyl-1,2-dihydroquinaldonitrile (Ia) and 1-benzoyl-6-methoxy-1,2-dihydroquinaldonitrile (Ib) proceed not only at very similar over-all rates, but also by nearly identical time sequences of steps.

(12) G. A. Ropp and O. K. Neville, *Nucleonics*, [2] **9**, 22 (1951). An excellent theoretical treatment of the isotope dilution method can be found in H. Gest, M. D. Kamen and J. M. Reiner, *Archiv. of Biochem.*, **12**, 273 (1947).

total activity found in the initial active mixture. The method of analysis was that of Anderson, Delabarre and Bothner-By.[13]

TABLE II

ACTIVITIES OF REACTANTS AND PRODUCTS INVOLVED IN THE COMPETITION REACTION

Material	Activity,[a] mμc./mg. C Theor.	Activity,[a] mμc./mg. C Found
Benzoic acid-carboxyl-C_1^{14}	. . .	12.2[b]
Benzoyl chloride–carbonyl-C_1^{14}	0.698	0.703
1-Benzoyl-(carbonyl-C_1^{14})-1,2-dihydroquinaldonitrile	.287	0.298[c]
Methylphenyl-2-(6-methoxyquinolyl)-carbinol	.000[d]	Inact.[e]
Methylphenyl-2-quinolyl-carbinol-C_1^{14}	.287[f]	0.287[g]
Active mixture	.131[h]	0.137

[a] All theoretical activities are based on the value for benzoic acid. [b] This value is representative of assays carried out over a period of years on this material. [c] This material was not brought to constant specific activity and probably contains traces of benzoic acid. The deviation is only 3.8% which is well within the error of the assay. [d] Assuming no intermolecular reaction. [e] The activity of the diluted sample was indistinguishable from background. Under conditions of this determination, 1 c.p.m. could have been detected with a standard deviation of 20%. One count a minute would equal about 0.5–1% intermolecular reaction. [f] Assuming 100% intramolecular rearrangement and using the theoretical value for 1-benzoyl-(carbonyl-C_1^{14})-1,2-dihydroquinaldonitrile. [g] This value was obtained by using an average value of 44.2% by weight of methylphenyl-2-quinolylcarbinol-C_1^{14} in the active mixture. A value was calculated for each dilution. These were averaged to give the Table value. This value represents 100% of the expected theoretical activity. [h] This value is based on 100% intramolecular rearrangement. The theoretical value for the carbinol and the calculated weight of carbinol in the two samples used for dilution were used to calculate the theoretical activity in the active mixture. An average of these values is given in the Table. This represents 95.6% of the total activity found.

Two new Reissert compounds were prepared in the course of these studies, 1-*p*-toluyl-1,2-dihydroquinaldonitrile (Ie) and 2-*p*-chlorobenzoyl-1,2-dihydroisoquinaldonitrile (IVb). On treatment with a concentrated hydrochloric acid solution of 2,4-dinitrophenylhydrazine, Ie gave a 96% yield of *p* - tolualdehyde - 2,4 - dinitrophenylhydrazone. A 53% yield of quinaldic acid was also isolated. In a similar acid-catalyzed cleavage reaction, IVb gave a 50% yield of *p*-chlorobenzaldehyde-2,4-dinitrophenylhydrazone. The acid-catalyzed formation of aldehydes from Reissert compounds is probably the best known and most extensively investigated property of these compounds.[4,14]

Experimental[15]

Reaction of 1-Benzoyl-1,2-dihydroquinaldonitrile (Ia) with Methylmagnesium Bromide.—To 20.0 g. (0.077 mole) of 1-benzoyl-1,2-dihydroquinaldonitrile[16] (Ia), was added 150 cc. of pure, dry dioxane.[17] As dry nitrogen was passed over the reaction mixture, 50 cc. (0.20 mole) of 4 *M* methylmagnesium bromide in dry ether was added in the course of ten minutes, with stirring, the mixture turning a deep red color and becoming warm. Stirring was continued for 50 minutes, the last 30 minutes with sufficient heating on the steam-bath to keep the reaction mixture at about 60°. After standing at room temperature for an hour, the dioxane and ether were distilled *in vacuo*. The residual dark brown cake was treated with 100 cc. of ether and the suspension hydrolyzed with 32 cc. of saturated ammonium chloride solution. After the yellow precipitate had settled, the red-brown ether solution was decanted and the residue washed with three additional portions of ether. The combined ether solution was filtered and extracted with four 100-cc. portions of 5% hydrochloric acid. The combined acid extract was washed with ether, then made alkaline with sodium hydroxide solution. The resulting precipitate of crude methylphenyl-2-quinolylcarbinol (IIa), dried in a vacuum desiccator, amounted to 11.3 g. (59%), m.p. 80–100°. Several recrystallizations from absolute ethanol, then petroleum ether finally gave 5.8 g. (29%) of pure IIa, m.p. 102.2–102.8°. (The infrared absorption spectrum is available.[21]) The m.p. of an authentic sample of methylphenyl-2-quinolylcarbinol[18] was not depressed upon admixture with the above material.

The ether solution was washed with sodium bicarbonate solution, then dried over Drierite. Evaporation of the ether left a dark red-brown oil. The oil was mixed with petroleum ether, refluxed, and the red supernatant solution decanted. Relatively little of the dark oil had gone into solution. After several weeks crystals appeared in the petroleum ether solution. After several recrystallizations from petroleum ether (Norit), then ethanol, there was obtained 0.19 g. of 2-benzoylquinoline (III), m.p. 108.5–109°. The m.p. of an authentic sample of 2-benzoylquinoline[19] showed no depression upon admixture with the above material. (2-Benzoylquinoline is insoluble in 5% hydrochloric acid and was therefore obtained from the neutral rather than the amine fraction.)

Reaction of 1-Benzoyl-6-methoxy-1,2-dihydroquinaldonitrile (Ib) with Methylmagnesium Bromide.—Reaction of 20 g. (0.069 mole) of 1-benzoyl-6-methoxy-1,2-dihydroquinaldonitrile[20] with 50 cc. (0.20 mole) of 4 *M* methylmagnesium bromide solution in the manner described above afforded a yield of 10.4 g. (56%) of crude methylphenyl-2-(6-methoxyquinolyl)-carbinol (IIb), m.p. 74–84°. After several recrystallizations from petroleum ether–benzene (Norit), then petroleum ether, then absolute ethanol, there was obtained 4.7 g. (24%) of pure IIb, m.p. 98.5–99.0°. (The infrared spectrum is available.[21])

Anal. Calcd. for $C_{18}H_{17}NO_2$: C, 77.39; H, 6.14; N, 5.01. Found: C, 77.55, 77.53; H, 6.80, 6.36; N, 5.45, 5.48.

Picrate, needles from absolute ethanol, m.p. 174.5–175.5°.

Anal. Calcd. for $C_{24}H_{20}N_4O_9$: C, 56.67; H, 3.97; N, 11.02. Found: C, 56.72, 56.80; H, 3.97, 3.93; N, 10.8, 10.7.

Reaction of 2-Benzoyl-1,2-dihydroisoquinaldonitrile (IVa) with Methylmagnesium Bromide.—When 15 g. (0.058 mole) of 2-benzoyl-1,2-dihydroisoquinaldonitrile[22] (IVa) in 115 cc. of dry dioxane was treated with 37.5 cc. (0.15 mole) of 4 *M* methylmagnesium bromide solution and the amine fraction isolated as above, an orange-brown oil resulted. The oil was extracted with ether and dried over Drierite. Distillation of the ether left an oil, which partially crystallized after several days. There was obtained 4.6 g. (32%) of crude methylphenyl-1-isoquinolylcarbinol (Va). Recrystalliza-

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[13] R. C. Anderson, Y. Delabarre and A. A. Bothner-By, *Anal. Chem.*, **24**, 1298 (1952).

[14] W. E. McEwen and R. Lynn Cobb, *Chem. Revs.* **55**, 511 (1955).

[15] All m.p.'s are corrected. Microanalyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y., and Weiler and Strauss, Oxford, England. Radioassays were performed by P. Hansell and D. Christman of Brookhaven National Laboratory. A minimum of two assays were performed on each compound. The standard deviation for any given assay is 1–2% $\sigma = \sqrt{\text{total counts} \times 100}$/total counts. The root mean square error encompassing all errors inherent in the analysis is not greater than 5%.

[16] H. Rupe, R. Paltzer and K. Engel, *Helv. Chim. Acta*, **20**, 209 (1937).

[17] L. F. Fieser, "Experiments in Organic Chemistry," 2nd Ed., D. C. Heath and Co., New York, N. Y., 1941, p. 368.

[18] P. Dyson and D. L. Hammick, *J. Chem. Soc.*, 1724 (1937).

[19] E. Besthorn, *Ber.*, **41**, 2001 (1908).

[20] A. Gassmann and H. Rupe, *Helv. Chim. Acta*, **22**, 1241 (1939).

[21] The spectra in this paper have been deposited as Document No. 4683 with the ADI Auxiliary Publication Project, Photoduplication Service, Library of Congress, Washington 25, D. C. A copy may be secured by citing the document number and remitting in advance $2.50 for photoprints or $1.75 for 35 mm. microfilm payable to Chief, Photoduplication Service, Library of Congress.

[22] H. Rupe and W. Frey, *Helv. Chim. Acta*, **22**, 673 (1939).

tion from absolute ethanol gave 2.9 g. (20%) of pure Va, m.p. 92.2–93.3° (lit.[23] 93–95°).

The original ether solution of the neutral fraction was washed with 6 *N* hydrochloric acid. Some starting material, 2-benzoyl-1,2-dihydroisoquinaldonitrile (IVa), precipitated during this treatment. More of the same was obtained on evaporation of the ether. Recrystallization from absolute ethanol afforded 1.8 g. (12%) of IVa, m.p. 125.0–125.8° (lit.[22] 125–126°).

Reaction of 1-*p*-Chlorobenzoyl-1,2-dihydroquinaldonitrile (Ic) with Methylmagnesium Bromide.—A solution of 15.0 g. (0.051 mole) of 1-*p*-chlorobenzoyl-1,2-dihydroquinaldonitrile[24,25] (Ic) in 110 cc. of dry dioxane was treated with 30 cc. of 4 *M* methylmagnesium bromide (0.12 mole) as described above. When an emulsion formed in the hydrolysis step with 36 cc. of saturated ammonium chloride solution, the mixture was filtered. The residue was washed with several portions of ether.

The red ether solution was extracted five times with 80-cc. portions of 5% hydrochloric acid solution. An oil appeared when the solution was made basic with sodium hydroxide solution. The mixture was extracted with three portions of ether. Evaporation of the ether solution, dried over Drierite, left 3.73 g. of an oil. The oil was treated with ethanolic picric acid, and the resulting picrate was twice recrystallized from ethanol. There was obtained 2.45 g. (9.6%) of the picrate of methyl-*p*-chlorophenyl-2-quinolylcarbinol (IIc), m.p. 150–151.4°. Completely purified material showed a m.p. of 155.3–156.2°, also upon admixture with an authentic sample of IIc picrate (see below).

Anal. Calcd. for $C_{23}H_{17}N_4O_8Cl$: C, 53.86; H, 3.34; N, 10.93; Cl, 6.91. Found: C, 54.13; H, 3.23; N, 10.8; Cl, 6.95.

Slow evaporation of the main ether solution yielded a semisolid mass which was collected and washed with ethanol to give 1.4 g. (9.4%) of 1-*p*-chlorobenzoyl-1,2-dihydroquinaldonitrile (Ic), m.p. 140–142.8° (lit.[24] m.p. 142–144°) after recrystallization from ethanol.

Methyl-*p*-chlorophenyl-2-quinolylcarbinol (IIc) Picrate.—To 2.50 g. (0.0144 mole) of quinaldic acid was added 31.0 g. of freshly distilled *p*-chloroacetophenone, and the solution was heated at 200–230° for four hours, the solution turning black after the first half-hour. The cooled solution was poured into 5% hydrochloric acid solution and the excess ketone separated by ether extraction. The acid solution was made alkaline with sodium hydroxide solution and extracted with ether. Evaporation of the ether left an oil, which was converted to a mixture of picrates by addition of ethanolic picric acid solution. A fractional crystallization from absolute ethanol gave 2.40 g. (44%) of quinoline picrate, m.p. 203.0–203.5°) as the most insoluble component. On concentration of the mother liquor to about 5 cc., there was obtained 0.17 g. (2.3%) of methyl-*p*-chlorophenyl-2-quinolylcarbinol (IIc) picrate, m.p. 143–155°. Recrystallization from ethanol gave 0.08 g. of material of m.p. 154–155°.

Reaction of 1-Anisoyl-1,2-dihydroquinaldonitrile (Id) with Methylmagnesium Bromide.—A. After 23.0 g. (0.079 mole) of 1-anisoyl-1,2-dihydroquinaldonitrile[26] (Id) dissolved in 160 cc. of dry dioxane had been treated with 50 cc. (0.20 mole) of 4 *M* methylmagnesium bromide and the mixture handled as before, a small amount of viscous dark oil was obtained as the amine fraction. This was crystallized from ethanol, and 0.90 g. (4.1% crude yield) of methyl-*p*-anisyl-2-quinolylcarbinol (IId) was obtained. A recrystallization from petroleum ether (Norit) gave 0.40 g. (1.8%) of essentially pure product. The m.p., after four more recrystallizations from ethanol, was 122.2–123.0°.

Anal. Calcd. for $C_{18}H_{17}NO_2$: C, 77.39; H, 6.14; N, 5.01. Found: C, 77.16, 77.55; H, 5.74, 5.98; N, 5.34.

From the main ether solution there was recovered 1.9 g. (8%) of 1-anisoyl-1,2-dihydroquinaldonitrile (Id), m.p. 118.8–120.2° (lit.[26] m.p. 120–120.5°).

B. To 100 cc. of dry xylene (mixture of isomers) was added 28 cc. (0.11 mole) of 4 *M* methylmagnesium bromide in dry ether. The ether was distilled, and 9.5 g. (0.033 mole) of 1-anisoyl-1,2-dihydroquinaldonitrile (Id), dissolved in 150 cc. of dry xylene, was added in the course of 25 minutes to the Grignard solution, which was maintained at about 130°. The solution became red and a red-brown precipitate formed. The mixture was then refluxed for another 45 minutes. The reaction mixture was kept under a nitrogen atmosphere during the above operations.

After being cooled, the mixture was hydrolyzed with 27 cc. of saturated ammonium chloride solution. A red solution and yellow precipitate formed. The red solution was decanted, and the yellow slurry was washed with 50 cc. of fresh xylene. The combined xylene solution was extracted with five 100-cc. portions of 5% hydrochloric acid. The acid solution was made basic with sodium hydroxide solution. A precipitate consisting of 1.2 g. of granular material (A) and a small amount of gum was collected. The gummy material, after being washed with and crystallized from absolute ethanol, afforded 0.35 g. (3.8%) of methyl-*p*-anisyl-2-quinolylcarbinol (IId), m.p. 120–121°.

The xylene solution was extracted with two 100-cc. portions of 6 *N* hydrochloric acid. On making this extract basic with sodium hydroxide, an additional 0.3 g. of the granular material (A) was obtained. The combined 1.5 g. of granular material (A) was purified by crystallization, first from ethyl acetate, then benzene. Colorless crystals were obtained, m.p. 222.2–223.2°.

Anal. Calcd. for $C_{24}H_{19}N_2O_2$[27]: C, 78.45; H, 5.21; N, 7.62. Found: C, 78.38, 78.19; H, 5.40, 5.19; N, 7.71, 7.65.

Reaction of 1-*p*-Toluyl-1,2-dihydroquinaldonitrile (Ie) with Methylmagnesium Bromide.—After 13.6 g. (0.05 mole) of 1-*p*-toluyl-1,2-dihydroquinaldonitrile (Ie), prepared as shown below, dissolved in 130 cc. of dry dioxane, had been treated with 30 cc. (0.12 mole) of 4 *M* methylmagnesium bromide in the same manner as previously described for 1-benzoyl-1,2-dihydroquinaldonitrile (Ia), only a trace of dark oil was obtained as the amine fraction. This could not be purified or converted to a suitable derivative. A total of 1.4 g. (10.3%) of starting material, Ie, was recovered on evaporation of the neutral ether solution.

Reaction of 1-Acetyl-1,2-dihydroquinaldonitrile (VI) with Methylmagnesium Bromide.—After 10.0 g. (0.0505 mole) of 1-acetyl-1,2-dihydroquinaldonitrile[25] (VI), dissolved in 74 cc. of dry dioxane, had been treated with 32 cc. (0.13 mole) of 4 *M* methylmagnesium bromide, as above, a small amount of dark oil was obtained as the amine fraction. This was converted to a mixture of picrates, from which only 0.20 g. (1.1%) of quinoline picrate, m.p. 201.4–202.4° (lit.[28] m.p. 203°), could be separated in pure form by fractional crystallization from absolute ethanol. The m.p. of an authentic sample of quinoline picrate was not depressed upon admixture with the above material.

Reaction of 1-Benzoyl-1,2-dihydroquinaldonitrile (Ia) with Phenylmagnesium Bromide.—A. A solution of 18.0 g. (0.069 mole) of 1-benzoyl-1,2-dihydroquinaldonitrile (Ia) in 150 cc. of dry dioxane was added to 55 cc. (0.18 mole) of a 3.35 *M* ether solution of phenylmagnesium bromide in the course of five minutes, with vigorous mechanical stirring. The solution became colored almost black, and heat was evolved. The ether was distilled, and the dioxane solution was refluxed for one hour. After being cooled, the reaction mixture was worked up in the same manner as described for the reaction of 1-benzoyl-1,2-dihydroquinaldonitrile (Ia) with methylmagnesium bromide. There was one modification, however, in that the ether solution was extracted not only with four 100-cc. portions of 5% hydrochloric acid, but also with three 100-cc. portions of 6 *N* hydrochloric acid. On making the 5% hydrochloric acid solution alkaline with sodium hydroxide solution, an oil separated and then solidified. It was fractionally crystallized from absolute ethanol and consisted mainly of diphenyl-2-quinolylcarbinol (IIe) plus a small amount of 2-benzoylquinoline (III). On making the 6 *N* hydrochloric acid solution alkaline, a solid precipitated, which was also fractionally crystallized from absolute ethanol. The main product consisted of 2-benzoylquinoline (III) plus a small amount of the carbinol IIe. Altogether there was obtained an 8.5% yield of pure diphenyl-2-quinolylcarbinol (IIe), m.p. 188.9–190.4° (lit.[29] m.p. 189°)

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[23] J. J. Padbury and H. G. Lindwall, THIS JOURNAL, **67**, 1268 (1945).

[24] W. E. McEwen and R. N. Hazlett, *ibid.*, **71**, 1949 (1949).

[25] J. M. Grosheintz and H. O. L. Fischer, *ibid.*, **63**, 2021 (1941).

[26] S. Sugasawa and T. Tsuda, *J. Pharm. Soc. Japan*, **56**, 557 (1936); *C. A.*, **32**, 5836 (1938).

[27] Structure unknown.

[28] H. Decker, *Ber.*, **36**, 2568 (1903).

[29] M. R. F. Ashworth, R. P. Daffern and D. L. Hammick, *J. Chem. Soc.*, 809 (1939).

and a 4.0% yield of pure 2-benzoylquinoline (III), m.p. 107.8–108.4° (lit.[30] m.p. 110–111°). The m.p. of an authentic sample of 2-benzoylquinoline prepared by the method of Besthorn[19] was not depressed upon admixture with the above material.

B. When the reaction was carried out at a temperature not exceeding 60° at any time, only a trace of 2-benzoylquinoline (III) was isolated.

Reaction of 2-Benzoyl-1,2-dihydroisoquinaldonitrile (IVa) with Phenylmagnesium Bromide.—After 20.0 g. (0.077 mole) of 2-benzoyl-1,2-dihydroisoquinaldonitrile (IVa), dissolved in 150 cc. of dry dioxane, had been treated with 57.5 cc. (0.193 mole) of a 3.35 *M* ether solution of phenylmagnesium bromide and the reaction mixture worked up as described for the first reaction (A) of 1-benzoyl-1,2-dihydroquinaldonitrile (Ia) with phenylmagnesium bromide, a yield of 11.9 g. (49.8%) of crude diphenyl-1-isoquinolylcarbinol (Vb), m.p. 120–136°, was obtained on making the 5% hydrochloric acid extract alkaline. Recrystallization from absolute ethanol gave 9.25 g. (38.8%) of colorless crystals, m.p. 141–143.2°. After three additional recrystallizations from 95% ethanol and one from absolute ethanol, the m.p. was raised to 143.2–143.6°

Anal. Calcd. for $C_{22}H_{17}NO$: C, 84.86; H, 5.50; N, 4.50. Found: C, 85.00, 84.94; H, 5.59, 5.56; N, 4.18, 4.29.

On making the 6 *N* hydrochloric acid extract alkaline with sodium hydroxide solution, about 2 g. of oil precipitated. No pure substance was isolated from this oil.

The ether solution was washed with dilute sodium hydroxide solution. From the ether solution of the neutral fraction there was obtained 4.14 g. (20.7%) of recovered 2-benzoyl-1,2-dihydroisoquinaldonitrile (IVa), m.p. 124.2–125.8° (lit.[31] m.p. 125–126°) after recrystallization from ethanol.

Reaction of 1-Benzoyl-1,2-dihydroquinaldonitrile (Ia) with Mesitylmagnesium Bromide.—To 20.0 g. (0.077 mole) of 1-benzoyl-1,2-dihydroquinaldonitrile (Ia), dissolved in 250 cc. of dry *p*-xylene, was added in 15 minutes with mechanical stirring 110 cc. of a 1.25 *M* ether solution of mesitylmagnesium bromide (0.138 mole), prepared by the method of Barnes[32] and analyzed by the method of Fieser.[33] The apparatus was the same as that described for the second reaction (B) of 1-anisoyl-1,2-dihydroquinaldonitrile (Id) with methylmagnesium bromide. As the ether distilled, the temperature rose from an initial value of 80° to 134° in 45 minutes. The apparatus was modified for refluxing, which was continued for one hour and 15 minutes. The mixture was cooled, 500 cc. of ether was added, and the mixture was hydrolyzed with 26 cc. of saturated ammonium chloride solution. The deep red ether–xylene solution was filtered, and several ether washings of the solid residue were added to this solution. The solution was extracted with two 100-cc. portions of 5% hydrochloric acid. A dark oil which separated on the initial addition of the acid could not be purified and was discarded. The acid solution was made alkaline, causing an oil to separate, and this was taken up in ether. Evaporation of the ether, dried over anhydrous calcium sulfate, left 2.87 g. (29% crude yield) of quinoline. This was converted to the picrate and purified by digestion with hot absolute ethanol, followed by crystallization from chloroform, 2.57 g. (9.3%) of quinoline picrate, m.p. 199.3–200.6° (lit.[28] m.p. 203°) being obtained. The m.p. of an authentic sample of quinoline picrate was not depressed upon admixture with the above material.

The main ether–xylene solution was extracted five times with 100-cc. portions of 6 *N* hydrochloric acid. On making this acid solution alkaline with sodium hydroxide solution, a gum separated. This was crystallized from absolute ethanol, giving a small amount of gray powder. The powder was digested with ether and filtered. Evaporation of the ether and recrystallization of the residue from absolute ethanol gave a trace of 2-benzoylquinoline (III), m.p. 108–108.8°. The m.p. of an authentic sample of 2-benzoylquinoline (III) was not depressed upon admixture with the above material.

B. A reaction carried out in ether–dioxane, with the temperature not exceeding 60° at any time, led to the isolation of a trace of 2-benzoylquinoline (III) and the recovery of some starting material I. No quinoline was formed.

Benzoyl Chloride-carbonyl-C_1^{14}.—Benzoic acid-carboxyl-C_1^{14} (0.5887 g.[34]; *Anal.* Found: 12.2 mμc./mg. C) diluted with 9.6974 g. of inactive benzoic acid was converted to benzoyl chloride-carbonyl-C_1^{14} (8.7545 g., b.p. 195–196.5°) by the method described in Vogel.[35]

Anal. Calcd. activ. for C_7H_5OCl: 0.698 mμc./mg. C. Found: 0.703 mμc./mg. C.

The 1-Benzoyl-(carbonyl-C_1^{14})-1,2-dihydroquinaldonitrile (XIII).—Benzoyl chloride-carbonyl-C_1^{14} (6.8 g.) was used in the method described by Rupe, Paltzer and Engel[16] to prepare 1-benzoyl-(carbonyl-C_1^{14})-1,2-dihydroquinaldonitrile (XIII) (2.234 g., m.p. 148–151°).

Anal. Calcd. activ. for $C_{17}H_{12}ON$: 0.287 mμc./mg. C. Found: 0.298 mμc./mg. C.

Quinolylcarbinol-C_1^{14} from a 1-Benzoyl-(carbonyl-C_1^{14})-1,2-dihydroquinaldonitrile (XIII)–1-Benzoyl-6-methoxy-1,2-dihydroquinaldonitrile (Ib) Mixture.—A mixture of 1-benzoyl-(carbonyl-C_1^{14})-1,2-dihydroquinaldonitrile (XIII) (0.9884 g.) and 1-benzoyl-6-methoxy-1,2-dihydroquinaldonitrile (Ib) (1.1057 g.) was dissolved in 15 cc. of freshly purified dioxane. Methylmagnesium bromide (10 cc., 4 *M* in ethyl ether) was added with stirring over a ten-minute period. It was stirred another 50 minutes, the reaction mixture being kept at 60° during the last 30 minutes. The ether and dioxane were removed *in vacuo* after allowing the reaction mixture to stand 1 hour. The brown cake was broken up, 10 cc. of ether added, and then hydrolyzed with 3.2 cc. of saturated ammonium chloride solution. The ether was decanted and the residue was washed with three 10-cc. portions of ether. The combined ether solutions were filtered and then extracted with four 10-cc. portions of 5% hydrochloric acid. The combined acid extracts were washed with ether. A dark brownish-red oil precipitated when the washed acid extract was made alkaline with sodium hydroxide solution. The oil was washed several times with water. An alcohol solution of the oil was treated with charcoal and the alcohol removed on a water-bath. The oil was dried over calcium chloride in a vacuum desiccator. The dried oil (1.0943 g.) was kept at −10° under an atmosphere of nitrogen.

Purification of the Quinolylcarbinol-C_1^{14} Mixture.—Efforts to separate the carbinols by fractional crystallization were unrewarding. The oil was purified by chromatography on Harshaw Al_2O_3 (chromatography grade, activated at 400° for five hours). The column was prepared with purified carbon tetrachloride. The column was developed with 1,2-dichloroethane (b.p. 84°).[36] The column was dried with nitrogen and cut into several fractions. In this case most of the material was found in the top band. Continuous extraction of the aluminum oxide with anhydrous ethanol for 14 hours gave a yellow solution with a faint violet fluorescence. The alcohol was evaporated at 10 mm. and 30°. The oil obtained was seeded with methylphenyl-2-quinolylcarbinol. After standing in a vacuum desiccator overnight 0.5715 g. of a hard crystalline mass was obtained. Alumina was removed by hot filtration of a hexane solution. Two recrystallizations from hexane gave white crystals which were roughly a 50–50 mixture of methylphenyl-2-quinolylcarbinol (XIV) and methylphenyl-2-(6-methoxyquinolyl)-carbinol (IIb).

A second chromatogram using basic alumina (Woelm, Activity grade I) was carried out on the purified material (0.383 g.). Most of the material was recovered from the top layer. After purification, 0.1835 g. of mixed alcohols was obtained from 0.2634 g. of oil. (The infrared spectrum of the material is available.[21]) *Anal.* Found: 0.137 mμc./mg. C.

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[30] A. Kaufmann, P. Dändliker and H. Burkhardt, *Ber.*, **46**, 2935 (1913).

[31] A. Reissert, *ibid.*, **38**, 3415 (1905).

[32] R. P. Barnes, "Organic Syntheses," Vol. 21, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 77.

[33] L. F. Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Co., New York, N. Y., 1941, p. 407.

[34] Kindly provided by Dr. D. Christman of Brookhaven National Laboratory.

[35] A. I. Vogel, "Practical Organic Chemistry," Longmans, Green and Co., London, England, 1948, pp. 751–752.

[36] Chromatography with alumina seemed to afford a separation of the carbinols when tried with inactive materials. In one case. extraction of the top layer with alcohol followed by seeding the alcohol with methylphenyl-2-(6-methoxyquinolyl)-carbinol (IIb) gave a crop of pure methoxy compound. In all other cases, the solids isolated from the alcohol extracts proved to be mixtures of the two alcohols, usually in the ratio of the starting mixture.

The mixture contained 44.2 ± 2.2% methylphenyl-2-quinolylcarbinol-C_1^{14} (XIV) by weight when analyzed by ultraviolet absorption spectrophotometry. (The ultraviolet absorption spectra of the mixture and the pure materials are available.[21])

Methylphenyl-2-quinolylcarbinol-C_1^{14} (XIV) from the Mixed Carbinols by Isotope Dilution.—A 45.7-mg. sample of the mixed carbinols was added to 101.3 mg. of recrystallized inactive methylphenyl-2-quinolylcarbinol (IIa). Two recrystallizations from ether–hexane gave a material with m.p. 130–131°. Infrared spectra of this material and of authentic methylphenyl-2-quinolylcarbinol (IIa), m.p. 102.2–102.8°, were identical in every detail. (The infrared spectra of these two materials are available.[21]) This seems to be another example of polymorphism in this series of compounds. *Anal.* Found: 0.047 mμc./mg. C.

The material was recrystallized a third time from absolute ether and gave massive white needles. *Anal.* Found: 0.047 mμc./mg. C.

Using the value for the activity to be expected in the carbinol (based on the theoretical value for 1-benzoyl-(carbonyl-C_1^{14})-1,2-dihydroquinaldonitrile) and the above value found on dilution, calculation indicates that the mixed carbinols should contain 43.3% by weight of methylphenyl-2-quinolylcarbinol-C_1^{14} (XIV).

A second sample, 22.1 mg. of the mixed carbinols was added to 47.3 mg. of recrystallized methylphenyl-2-quinolylcarbinol (IIa). Two recrystallizations from ether–hexane gave material with the following activity. *Anal.* Found: 0.050 mμc./mg. C.

The material was recrystallized a third time from absolute ether and a drop of hexane to give massive white needles. *Anal.* Found: 0.050 mμc./mg. C.

This value indicates that the mixed carbinols should contain 45.1% by weight of methylphenyl-2-quinolylcarbinol-C_1^{14} (XIV).

The average of the values found by dilution and the value found by the ultraviolet absorption technique is 44.2% by weight.

Methylphenyl-2-(6-methoxyquinolyl)-carbinol (IIb) from the Mixed Carbinols by Dilution.—A 30.4-mg. sample of the mixed carbinols was added to 83.5 mg. of recrystallized inactive methylphenyl-2-(6-methoxyquinolyl)-carbinol (IIb). One recrystallization from ether–hexane gave fine needles, m.p. 96–98°. *Anal.* Found: 0.008 mμc./mg. C.

A second sample, 39.8 mg., of the mixed carbinols was added to 97.1 mg. of recrystallized methylphenyl-2-(6-methoxyquinolyl)-carbinol (IIb). Three recrystallizations from ether–hexane gave fine white needles, m.p. 98–99°. *Anal.* Found: inactive.[37]

A third sample, 24.5 mg., of the mixed carbinols was added to 65.8 mg. of recrystallized methylphenyl-2-(6-methoxyquinolyl)-carbinol (IIb). Four recrystallizations from ether–hexane gave fine white needles, m.p. 98–99°. *Anal.* Found: inactive.[37]

Relative Rates of Reaction of Methylmagnesium Bromide with 1-Benzoyl-1,2-dihydroquinaldonitrile (Ia) and 1-Benzoyl-6-methoxy-1,2-dihydroquinaldonitrile (Ib).—Each of the runs was carried out in the same manner with the exception of the time of reaction. A typical run is described below:

To 1.0214 g. of 1-benzoyl-1,2-dihydroquinaldonitrile (Ia) dissolved in 15 cc. of purified dioxane and maintained at a temperature of 56° was added in one portion 10 cc. of 4 *M* methylmagnesium bromide in ether. The visual observations typical of this and every one of the reactions with both Reissert compounds have been given in footnote 11. At the end of 10 minutes, the reaction was quenched by addition of 35 cc. of water. The mixture was extracted with four 50-cc. portions of ether, then the aqueous layer containing the precipitate of magnesium hydroxide was mixed with a filter aid and filtered. The precipitate was dried and digested with two 50-cc. portions of ether, and the filtrate was extracted with one additional 50-cc. portion of ether. The combined ether solution was extracted with five 12-cc. portions of 5% hydrochloric acid. The acid solution was extracted with 15 cc. of ether, then made basic by addition of sodium hydroxide solution. The precipitated amine was taken up in ether, the ether dried over Drierite and the solvent distilled. The residue was dried to constant weight in an oven maintained at 70° and amounted to 0.1552 g. (15.1% of crude methylphenyl-2-quinolylcarbinol). The infrared spectrum of a chloroform solution of the crude amine was practically identical with that of a chloroform solution of pure methylphenyl-2-quinolylcarbinol.

The ether solution of the neutral fraction was dried and concentrated. After drying to constant weight the residue amounted to 0.8319 g. The infrared spectrum of a chloroform solution of this material indicated that it consisted mainly of recovered 1-benzoyl-1,2-dihydroquinaldonitrile (Ia). Confirmation of this fact was obtained when treatment of the neutral fraction with a solution of 2,4-dinitrophenylhydrazine in concentrated hydrochloric acid as previously described[38] gave a 65% yield of benzaldehyde 2,4-dinitrophenylhydrazone.

The results of the other runs are summarized in Table I.

1-*p*-Toluyl-1,2-dihydroquinaldonitrile (Ie).—To a mixture of 31.3 g. (0.48 mole) of potassium cyanide, 20.8 g. of synthetic quinoline (0.16 mole) and 200 cc. of water was added 49 cc. (0.32 mole) of freshly distilled *p*-toluyl chloride in about five minutes, with vigorous mechanical stirring. After 30 minutes of additional stirring the aqueous solution was decanted from a tan, taffy-like solid, which was washed with dilute hydrochloric acid and then water. The precipitate, now completely solid, was broken up, dried and washed with ether. The remaining solid was twice recrystallized from carbon tetrachloride, affording 18.5 g. (42.3%) of 1-*p*-toluyl-1,2-dihydroquinaldonitrile (Ie), m.p. 148–149.5°. The m.p. after a total of seven recrystallizations from carbon tetrachloride was 149.5–150.2°.

Anal. Calcd. for $C_{18}H_{14}N_2O$: C, 78.81; H, 5.14; N, 10.21. Found: C, 78.40; H, 5.09; N, 10.3.

Acid-catalyzed Cleavages of 1-*p*-Toluyl-1,2-dihydroquinaldonitrile (Ie).—To a mixture of 4.45 g. (0.0162 mole) of 1-*p*-toluyl-1,2-dihydroquinaldonitrile (Ie) and 3.25 g. of 2,4-dinitrophenylhydrazine (0.0162 mole) was added 97.5 cc. of concentrated hydrochloric acid. The mixture was heated on the steam-bath for 30 minutes, then allowed to stand at room temperature for 52 hours. The mixture was diluted with an equal volume of water, heated to boiling and filtered. The precipitate, dried in an oven at 100°, amounted to 4.72 g. (96.3%) of *p*-tolualdehyde 2,4-dinitrophenylhydrazone, m.p. 233–234.2° (lit.[39] m.p. 235°).

Quinaldic acid was isolated from the acid filtrate by the same method employed by Padbury and Lindwall[23] for the isolation of isoquinaldic acid from the acid-catalyzed cleavage of 2-benzoyl-1,2-dihydroisoquinaldonitrile (IVa). The yield of quinaldic acid was 52.7%, m.p. 154° (lit.,[40] m.p. 157°). The m.p. of an authentic sample of quinaldic acid was not depressed upon admixture with the above material.

2-*p*-Chlorobenzoyl-1,2-dihydroisoquinaldonitrile (IVb).—To a mixture of 74.0 g. (1.14 mole) of potassium cyanide, 41.6 g. (0.32 mole) of isoquinoline and 500 cc. of water was added 122 g. (0.64 mole) of *p*-chlorobenzoyl chloride in 28 minutes, with vigorous mechanical stirring. After 45 minutes the stirring was stopped, a granular precipitate filtered, washed with water, sodium bicarbonate solution, water and dried. The solid was digested with several portions of ether, and the ether solution was extracted with dilute sodium hydroxide solution. Evaporation of the ether solution, dried over anhydrous magnesium sulfate, left a dark oil, which slowly solidified in an ice-bath. A total of 10.4 g. (11%) of very crude 2-*p*-chloro-benzoyl-1,2-dihydroisoquinaldonitrile (IVb), m.p. 129–134°, was obtained. The compound is extensively decomposed by recrystallization from alcohol; *p*-chlorobenzoic acid, which persists as an impurity, can be removed fairly well by recrystallization

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(37) Activity of sample indistinguishable from background. Two counting tubes were used for each sample.[18] The backgrounds on each of these were determined. The tubes were then filled with CO_2 from one combustion. The tubes were counted and then evacuated. They were refilled with counting gas and the background again determined. The standard deviation of the background due to the statistics of counting was not greater than 0.8%. The results obtained with samples used in the isotope dilution experiments were identical with those obtained by combustion of known inactive materials.

(38) W. E. McEwen, R. H. Terss and I. W. Elliott, THIS JOURNAL, **74**, 3605 (1952).

(39) W. Th. Nauta, M. J. E. Ernsting and A. C. Faber, *Rec. trav. chim.*, **60**, 915 (1941).

(40) A. Reissert, *Ber.*, **38**, 1603 (1905).

from benzene; the Reissert compound stays in solution and can be precipitated by addition of petroleum ether solvent. Recrystallization from diisopropyl ether is effective, provided only a small amount of the acid is present. By combining these methods a sample of pure 2-*p*-chlorobenzoyl-1,2-dihydroisoquinaldonitrile (IVb) was obtained, m.p. 155.2–155.8°.

Anal. Calcd. for $C_{17}H_{11}N_2OCl$: C, 69.27; H, 3.76; N, 9.51; Cl, 12.03. Found: C, 69.30; H, 3.60; N, 9.50; Cl, 12.04.

Acid-catalyzed Cleavage of 2-*p*-Chlorobenzoyl-1,2-dihydroisoquinaldonitrile (IVb).—To a mixture of 1.00 g. (0.0034 mole) of 2-*p*-chlorobenzoyl-1,2-dihydroisoquinaldonitrile (IVb) and 0.67 g. (0.0032 mole) of 2,4-dinitrophenylhydrazine was added 20 cc. of concentrated hydrochloric acid. The mixture was heated on the steam-bath for half an hour, allowed to stand at room temperature for 48 hours, then diluted with water, heated to boiling, filtered and the precipitate washed with hot water and dried. After crystallization from nitrobenzene 0.80 g. (50%) of *p*-chlorobenzaldehyde 2,4-dinitrophenylhydrazone, m.p. 267–268° (lit. m.p. 270°,[41] 265°,[42] 264°[43]) was obtained. No attempt was made to isolate isoquinaldic acid.

Dimorphism of Reissert Compounds.—Some evidence for the occurrence of dimorphism in various Reissert compounds has accumulated in the course of our work. On several occasions a sample of 1-benzoyl-1,2-dihydroquinaldonitrile (Ia) of m.p. 142.5–143.5° was obtained. On standing it gradually changed over to the usual form of m.p. 154–155°. Also, on one occasion for each case, we have observed a m.p. of 96–99° for 1-benzoyl-6-methoxy-1,2-dihydroquinaldonitrile (Ib), the usual value being 127°, and a m.p. of 56–57° for 2-benzoyl-1,2-dihydroisoquinaldonitrile (IVa), the usual value being 125–126°. In both of these cases, too, the lower melting variety was readily transformed into the higher melting form. Dimorphic forms of methylphenyl-2-quinolylcarbinol (IIa) were also isolated in these studies.

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[41] J. J. Blanksma and M. L. Wackers, *Rec. trav. chim.*, **55**, 659 (1936).

[42] J. Graymore and D. R. Davis, *J. Chem. Soc.*, 293 (1945).

[43] A. Eitel and G. Lock, *Monatsh.*, **72**, 385 (1939).

UPTON, LONG ISLAND, N. Y.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

Studies in the Bicyclo[2.2.1]heptane Series.[1] III. Some Aliphatic Bicyclo[2.2.1]-7-heptanones[2]

BY PELHAM WILDER, JR., AND ANTHONY WINSTON[3]

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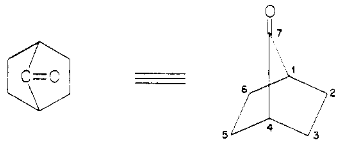
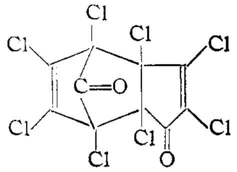
Three derivatives of bicyclo[2.2.1]-7-heptanone are reported. *endo-cis*-Bicyclo[2.2.1]-7-heptanone-2,3-dicarboxylic acid (IV), *exo-cis*-2,3-dimethylbicyclo[2.2.1]-7-heptanone (V) and *endo-cis*-2,3-dimethylbicyclo[2.2.1]-7-heptanone (VI) were prepared from adducts of 6,6-dimethylfulvene and maleic anhydride. These carbonyl bridge compounds are stable toward heat, form carbonyl derivatives, and exhibit strong absorption bands near 5.63 μ in the infrared.

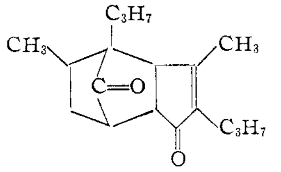
While many derivatives of bicyclo[2.2.1]-7-heptanone have been reported in the chemical literature, almost without exception they have been polyaryl or highly halogenated compounds and have contained an ethylenic double bond in the six-membered ring. In 1901, Zelinsky reported the preparation of the parent compound, bicyclo[2.2.1]-7-heptanone (I), by pyrolysis of the barium salt of *trans*-hexahydroterephthalic acid,[4] but on repeating Zelinsky's work Allen and his co-workers unequivocally demonstrated that Zelinsky had none of the ketone he reported.[5] In 1893, in an attempt to prepare tetrachlorocyclopentadienone from hexachlorocyclopenten-3-one, Zincke and Günther obtained hexachloroindone and phosgene.[6] In two later papers[7,8] Zincke explained the results of the previous investigation by suggesting that as soon as tetrachlorocyclopentadienone was formed, it dimerized to form II, perhaps the first synthetic bicyclo[2.2.1]-7-heptanone, which then readily lost carbon monoxide and chlorine to yield hexachloroindone. Polyaryl derivatives of bicyclo[2.2.1]-7-heptanone have been extensively investigated since 1933[9] and very recently the preparation of some halogenated bicyclic ketones of this type has been reported by McBee and his collaborators.[10] The only credible report of a bicyclo[2.2.1]-7-heptanone derivative with no phenyl groups or halogen atoms attached and with no double bond in the six-membered ring has been made by Allen and Van Allan[11] who prepared the tricyclic ketone III by catalytic hydrogenation of the dimer of allethrolone.[12] The purpose of the present paper



I



II



III

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[1] For paper II in this series, see P. Wilder, Jr., and A. Winston, THIS JOURNAL, **77**, 5598 (1955).

[2] Taken from a thesis submitted by Anthony Winston to the Graduate School of Duke University in partial fulfillment of the requirements for the Ph.D. degree, October, 1954.

[3] Du Pont Pre-doctoral Fellow, 1953–1954.

[4] N. Zelinsky, *Ber.*, **34**, 3798 (1901).

[5] C. F. H. Allen, T. Davis, D. W. Stewart and J. A. Van Allan, *J. Org. Chem.*, **20**, 306 (1955).

[6] T. Zincke and H. Günther, *Ann.*, **272**, 243 (1893).

[7] T. Zincke and K. H. Meyer, *ibid.*, **367**, 1 (1909).

[8] T. Zincke and W. Pfaffendorf, *ibid.*, **394**, 3 (1912).

[9] C. F. H. Allen and E. W. Spanagel, THIS JOURNAL, **55**, 3773 (1933). For a review of the literature of carbonyl bridge compounds, see C. F. H. Allen, *Chem. Revs.*, **37**, 209 (1945).

[10] E. T. McBee, W. R. Diveley and J. E. Burch, THIS JOURNAL, **77**, 385 (1955).

[11] C. F. H. Allen and J. A. Van Allan, *J. Org. Chem.*, **20**, 323 (1955).

[12] F. B. La Forge, N. Greene and M. S. Schechter, THIS JOURNAL, **74**, 5392 (1952).