[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Organometallic Derivatives of Carbazole and Quinoline. Amides of 3-Quinolinecarboxylic Acid

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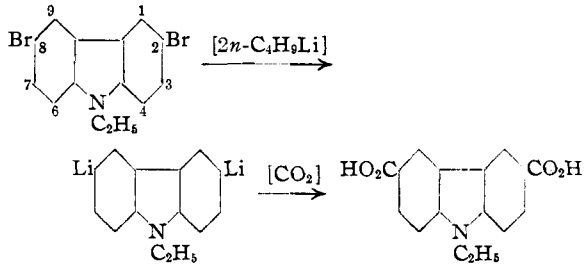
Two general procedures have been used hitherto for the preparation of organometallic derivatives of carbazole.[1] One of these involves a direct synthesis from RX compound and magnesium or lithium in poor yields. The other is a metalation reaction which also suffers from the disadvantage of low yields; however, this is compensated by the introduction of the metal in positions not generally accessible by other nuclear substitution reactions. The halogen–metal interconversion reaction now reported is one of choice for three reasons: (1) the highly satisfactory yields from monohalogen derivatives; (2) the splendid yields of dimetallic compounds from di-halogen derivatives; and (3) the possibility of effecting preferential X–M interconversion with di-halogen derivatives.

An illustration of di-metal formation is the reaction of 5-ethyl-2,8-dibromocarbazole with *n*-butyllithium to give, subsequent to carbonation, an 84% yield of dibasic acid.



In the quinoline series, the X–M interconversion reaction has a special interest from the viewpoint of synthesis. Sachs and Sachs[2] reported that Grignard reagents could not be prepared from bromoquinolines. Their findings were later confirmed by Howitz and Kopke[3] who, however, reported the preparation of an RMgBr compound from a lateral bromine derivative, 8-bromomethylquinoline.

In the X–M reactions with pyridine[4] and quinoline types it is essential to use moderately low temperatures and short time reaction periods. Otherwise, secondary reactions predominate, particularly addition of the RLi agent to the azomethylene linkage. The X–M reaction and addition to the N=C group are rapid, competitive reactions. Actually, under conditions effective for X–M reaction in a compound like 3-bromoquinoline, quinoline itself adds *n*-butyllithium promptly to give excellent yields of *n*-butylquinoline. There are several possible explanations for the preferential X–M reaction and two of these might be mentioned. First, the nuclear halogen may deactivate the azomethylene group toward RLi addition. Second, the C–Li linkage that forms after the X–M reaction may also reduce the activity of the N=C group. In support of the first suggestion is the observation that there is no evidence for either any appreciable X–M reaction or addition to N=C with 2-chloroquinoline. A chlorine–metal interconversion reaction has been observed only rarely.[5] Its essential absence in the case of 2-chloroquinoline is particularly noteworthy because of the relatively high reactivity of this chlorine in other reactions like hydrolysis, ammonolysis, and etherification by alkoxides.

The general order of decreasing reactivities of some interconversion reactions is: M–M > X–M > H–M. This finds support in the observation that 2-iodo-4-methylquinoline with *n*-butyllithium gives, subsequent to carbonation, 4-methyl-2-quinolinecarboxylic acid. There was no evidence of any lateral metalation of the otherwise active methyl group under the selected experimental conditions.

Amides of 3-Quinolinecarboxylic Acid.—A series of 3-quinolinecarboxylic acid amides prepared from secondary amines was needed for other studies. The reaction between the acid halide hydrochloride[6] and R_2NH compounds was found by us to give poor yields. A distinctly better procedure,[7a] which also obviates the inconvenience of preparing the acyl halide first, is to heat the acid itself with the amine in the presence of phosphorus oxychloride. Attempts to prepare the diallylamide in this manner gave only tarry

(1) Gilman and Kirby, *J. Org. Chem.*, **1**, 146 (1936).

(2) Sachs and Sachs, *Ber.*, **37**, 3088 (1904).

(3) Howitz and Kopke, *Ann.*, **396**, 38 (1913).

(4) Gilman and Spatz, THIS JOURNAL, **62**, 446 (1940). A later report will describe X–M reactions with mono- and poly-halogenated pyridines.

(5) Gilman, Langham and Moore, *ibid.*, **62**, 2327 (1940). See, also, Wittig, *Angew. Chem.*, **53**, 241 (1940).

(6) Kolber, Ruppersberg and Strang, *Monatsh.*, **52**, 59 (1929).

(7) (a) French Patent 793,633 [*C. A.*, **30**, 4626 (1936)]; (b) Fricker, French Patent 791,783 [*C. A.*, **30**, 4178 (1936)].

TABLE I

ORGANOMETALLIC DERIVATIVES OF CARBAZOLE AND QUINOLINE

Starting material	Interconverting agent	Time	Temp.	Product[a]	Yield,[b] %
2-Bromocarbazole (0.02m)	n-C_4H_9Li (0.05 m)	60 min.	Reflux	2-Lithiocarbazole	57.8
5 - Ethyl - 2 - bromocarbazole (0.012m)	n-C_4H_9Li (0.02m)	70 min.	Reflux	5-Ethyl-2-lithiocarbazole	71.1[c]
5 - Ethyl - 2 - iodocarbazole (0.016m)	n-C_4H_9Li (0.027m)	20 hr.	Reflux (only ether)	5-Ethyl-2-lithiocarbazole	67.0[d]
5 - Ethyl - 2,8 - dibromocarbazole (0.05m)	n-C_4H_9Li (0.11m)	90 min.	Reflux	5-Ethyl-2,8-dilithiocarbazole	84[e]
5 - Ethyl - 2,8 - diiodocarbazole (0.007m)	n-C_4H_9Li (0.015m)	75 min.	Reflux	5-Ethyl-2,8-dilithiocarbazole	79
5 - Ethyl - 2,8 - diiodocarbazole (0.015m)	n-C_4H_9MgBr (0.06m)	20 hr.	Reflux	5 - Ethyl - 2 - iodo - 8 - carbazolylmagnesium bromide	3.7
5 - Ethyl - 2,8 - dibromocarbazole (0.04m)	n-C_4H_9MgBr (0.08m)	24 hr.	Reflux	No reaction	
3-Bromoquinoline (0.07m)	n-C_4H_9Li (0.09m)	15 min.	−35°	3-Quinolyllithium	52
3-Bromoquinoline	n-C_4H_9Li	15 min.	Reflux	Few % of highly impure acid	
3-Bromoquinoline	n-C_4H_9Li	2 min.	Reflux	3-Quinolyllithium	12.7
3-Bromoquinoline	n-C_4H_9Li	5 min.	−45°	3-Quinolyllithium	35–47.5
Quinoline (0.1m)	n-C_4H_9Li[g] (0.12m)	15 min.	−35°	2-n-Butylquinoline	93.5[f]
2 - Iodo - 4 - methylquinoline (0.037m)	n-C_4H_9Li (0.042m)	8 min.	−40°	2-Lithio-4-methylquinoline	28.1[h,i]
2 - Iodo - 4 - methylquinoline (0.037m)	n-C_4H_9Li (0.076m)	8 min.	−40°	2-Lithio-4-methylquinoline	29.4[h,i]
2 - Iodo - 4 - methylquinoline (0.019m)	n-C_4H_9Li (0.05m)	15 min.	− 5°	2-Lithio-4-methylquinoline	53[j]

[a] The prefixes, lithio- and sodio-, are used in accordance with the suggestions of Drs. L. T. Capell and A. M. Patterson. [b] The yields are expressed in terms of the corresponding carboxylic acids, obtained subsequent to carbonation of the RLi or RMgX product. All of the carbazole acids are difficultly soluble in water, and easily isolated. [c] The 5-ethyl-2-carbazolecarboxylic acid was identified by mixed m. p.[1] [d] By I. Banner. [e] Identification of the 5-ethyl-2,8-carbazoledicarboxylic acid was completed by conversion to 5-ethyl-2,8-dicarbomethoxycarbazole[1] (m. p. 185–7°). [f] The 2-n-butylquinoline was characterized by its picrate, m. p. 162–3° [Ziegler and Zeiser, *Ann.*, **485**, 174 (1931)]. [g] In this experiment neither X–M interconversion nor metalation is involved. The intermediate product, 1-lithio-2-n-butyl-1,2-dihydroquinoline, is not a quinolyllithium compound. As a control reaction, this experiment shows that addition of RLi to the N=C linkage is not retarded at the low temperature and short reaction time, and that therefore in the reaction between a bromo- or iodoquinoline and RLi agent in a similar environment, other factors must be in operation which permit an X–M interconversion. (See introductory part of this paper.) [h] A positive color test [Gilman and Swiss, THIS JOURNAL, **62**, 1847 (1940)] showed the presence of unused n-butyllithium. [i] The extremely water-soluble 4-methyl-2-quinolinecarboxylic acid, isolated through its copper salt, melted at 153–4° [Koenigs and Mengel, *Ber.*, **37**, 1322 (1904)], and the yellow crystalline oxalate melted at 178.5° with gas evolution. The m. p. of the oxalate very probably varies with the rate of heating, for K. and M. found the oxalate to melt at 182°. Our m. p. of the free acid agrees exactly with theirs. [j] The yield of organometallic product was determined by hydrolysis to 4-methylquinoline, which was identified by a mixed m. p. of its picrate with an authentic specimen.

products. However, the diallylamide was prepared successfully from the acid and amine when phosphorus pentoxide[7] was used as the condensing agent. All of the amides listed in Table II form water-soluble crystalline hydrochlorides and yellow monopicrates.

Directions are provided for the improved preparation of 3-cyanoquinoline, which we find can be hydrolyzed quantitatively to the corresponding acid.

Experimental

General Procedure for Carbazoles.—A filtered ether solution of n-butyllithium and a thiophene-free benzene solution of the halogenated carbazole were mixed, stirred and refluxed for one to one and one-half hours in a nitrogen atmosphere, and then carbonated by pouring jet-wise into a slush of ether and solid carbon dioxide. Benzene was used not only to effect solution of the halogenated carbazoles which are sparingly soluble in ether alone, but also to obtain the desirable higher reflux temperature provided by an ether-benzene mixture.[8] The general procedure, relative quantities of each solvent and concentrations of the reactants are represented in the preparation of 2-lithiocarbazole. Table I summarizes the data on the several lithiocarbazoles.

2-Lithiocarbazole.—A solution of 0.02 mole of 2-bromocarbazole in 50 cc. of benzene and 0.05 mole of n-butyllithium in 100 cc. of ether was refluxed for one hour. The

(8) This higher reflux temperature was also used in X–M interconversions in the related dibenzofuran series: Gilman, Swiss and Brown, THIS JOURNAL, **62**, 348 (1940).

yield of 2-carbazolecarboxylic acid was 57.8%; m. p. 276–7°.[1,9] The acid was esterified quantitatively to the ethyl ester (m. p., 165°) by the procedure of Plant and Williams.[9]

Bromocarbazoles.—2-Bromocarbazole was prepared by acetylation of carbazole[10]; bromination to 5-acetyl-2-bromocarbazole[11]; followed by alcoholic potash hydrolysis.[11]

5-Ethyl-2-bromocarbazole was prepared, with modification of the procedure of Stevens and Tucker,[12] by refluxing and stirring 2-bromocarbazole in acetone with ethyl sulfate and concd. aqueous potassium hydroxide for one and one-half hours.

Preparation of 5-Ethyl-2,8-dibromocarbazole.—To a hot solution of 17.65 g. (0.05 mole) of 2,8-dibromocarbazole[13] in 100 cc. of acetone was added in one portion 30.8 g. (0.2 mole) of practical ethyl sulfate. Then, a 60% aqueous solution of 39 g. of potassium hydroxide was added over a forty-five minute period to the vigorously stirred and refluxing solution. Refluxing was continued for an additional one and one-half hours; the mixture was poured into ice-water; and crystallization of the precipitate from wet acetone gave a 97% yield of 5-ethyl-2,8-dibromocarbazole melting at 142–143°.

Anal. Calcd. for $C_{14}H_{11}NBr_2$: Br, 45.27. Found: Br, 45.03, 45.77.

Preparation of 5-Ethyl-2,8-diiodocarbazole [By I. Banner].—In contrast to previous methods,[1] 5-ethyl-2,8-diiodocarbazole was obtained easily and in excellent yields by direct iodination of 5-ethyl-2-iodocarbazole. To a solution of 5 g. (0.0156 mole) of 5-ethyl-2-iodocarbazole and 1.6 g. (0.01 mole) of potassium iodide in 100 cc. of glacial acetic acid was added 2.5 g. (0.012 mole) of potassium iodate, the free iodine color being allowed to disappear before the successive small additions of potassium iodate. The mixture was refluxed for ten to fifteen minutes; and addition of the hot straw-yellow solution to a large quantity of ice water gave 6.7 g. (96%) of pale-brown crystals melting at 144–147°. Recrystallization from ethanol containing a little acetone gave 5.9 g. (85%) of the diiodo compound; m. p. and mixed m. p., 154°.[14]

5-Ethyl-2-iodo-8-carbazolylmagnesium Bromide.—A solution of 6.7 g. (0.015 mole) of 5-ethyl-2,8-diiodocarbazole and 4 equivalents of *n*-butylmagnesium bromide in 60 cc. of ether and 50 cc. of benzene was refluxed for twenty hours. In addition to a recovery of 77.7% of the initial diiodo compound there was isolated 3.7% (or 16.3% on the basis of recovered diiodo compound) of pure 5-ethyl-2-iodo-8-carbazolecarboxylic acid which melted at 280–282° after crystallization from a pyridine–water solution.

Anal. Calcd. for $C_{15}H_{12}O_2NI$: N, 3.84. Found: N, 3.71. No acidic material was obtained from a corresponding experiment starting with 5-ethyl-2,8-dibromocarbazole.

Subsequent X–M interconversion studies indicate that methyllithium might be more effective in a selective mono-interconversion.

(9) Plant and Williams, *J. Chem. Soc.*, 1142 (1934).
(10) Böeseken, *Rec. trav. chim.*, **31**, 364 (1912).
(11) Ciamician and Silber, *Gazz. chim. ital.*, **12**, 276 (1882).
(12) Stevens and Tucker, *J. Chem. Soc.*, **123**, 2140 (1923).
(13) McClintock and Tucker, *ibid.*, 1216 (1927).
(14) Tucker, *ibid.*, 546 (1926), reported a m. p. of 152–153°.

Reduction of 5-Ethyl-2-iodo-8-carbazolecarboxylic Acid.—Catalytic reduction of 50 mg. of the iodo acid by the palladium–calcium carbonate procedure[15] gave a 94% yield of 5-ethyl-2-carbazolecarboxylic acid (mixed m. p., 224–226°).

3-Quinolyllithium.—In the preparation of the quinolyllithium compounds the solvent is exclusively sodium-dried ethyl ether, the temperature low, and the reaction period short. To a filtered solution of 1.25 equivalents of *n*-butyllithium, cooled[16] externally to −35°, was added over a two-minute period with stirring 14.6 g. (0.07 mole) of 3-bromoquinoline[17] in 50 cc. of ether also cooled to −35°. The mixture was stirred at this temperature for fifteen minutes, and the dark-red solution was then carbonated by jet-wise addition to finely powdered, solid carbon dioxide. The yield of 3-quinolinecarboxylic acid was 52%. The acid was shown (mixed m. p.) to be identical with the hydrolysis product of 3-cyanoquinoline; and the ethyl esters of the acid prepared by these two procedures were also shown to be identical.

The experiments starting with 3-bromoquinoline listed in Table I show the importance of low temperature and short reaction time in X–M interconversions in the quinoline series. When these conditions are not observed, the activity of the azomethylene linkage becomes manifest in a series of secondary reactions which account for the tarry residues obtained by Harris[18] and by Banner,[19] who treated 2-bromopyridine, 2-bromoquinoline and 3-bromoquinoline with *n*-butyllithium for twenty hours at the temperature of refluxing ether, whereas under similar conditions the *m*- and *p*-bromodimethylanilines,[20] which do not contain an anil group, yield interconversion products in favorable quantity.

Ethyl 3-Quinolinecarboxylate.—Although this ester has been reported,[21] no mention is made concerning the method of its preparation. A mixture of 93 g. (0.54 mole) of 3-quinolinecarboxylic acid, 16 moles of anhydrous ethanol and 33 cc. of concd. sulfuric acid was refluxed for ten hours. The thick viscous liquid remaining after removal of the ethanol by distillation had a pronounced odor of quinoline. Treatment of the viscous residue with cold dilute sodium carbonate precipitated the ester, and after standing overnight in an icebox, the solid was separated by filtration. The oily material that came through to the filtrate was shown to be quinoline.[22] The crude ester (m. p. 68°) crystallized from aqueous ethanol as fine white needles or from Skelly B as thick heavy crystals (m. p. 69–69.5°). Kindler[21] reported the m. p. as 66–67°. The yield was 33.7%; and in a run starting with 10 g. of acid the yield was 36%.

(15) Busch and Stöve, *Ber.*, **49**, 1063 (1916).
(16) Cooling is conveniently effected by adding chips of solid carbon dioxide from time to time to a cooling bath of acetone–solid carbon dioxide.
(17) Claus and Collischon, *Ber.*, **19**, 2763 (1886).
(18) Harris, *Iowa State Coll. J. Sci.*, **6**, 425 (1932) [*C. A.*, **27**, 279 (1933)].
(19) I. Banner, M. S. Thesis, Iowa State College, Ames, Iowa, 1939.
(20) Gilman and Banner, THIS JOURNAL, **62**, 344 (1940).
(21) Kindler, *Ber.*, **69B**, 2807 (1936).
(22) Van der Kolf and Van Leent, *Rec. trav. chim.*, **8**, 218 (1889), reported that ethyl 4-quinolinecarboxylate could not be purified by distillation under reduced pressure because of decomposition to quinoline.

Anal. Calcd. for $C_{12}H_{11}O_2N$: N, 6.96. Found: N, 6.95.

The picrate of the ester, m. p. 182–183°, crystallized as bright yellow, fine needles from hot ethanol.

Anal. Calcd. for $C_{18}H_{14}O_9N_4$: N, 13.02. Found: N, 13.17, 13.12.

2-Chloroquinoline and RLi Compounds.—In two separate reactions between 2-chloroquinoline and *n*-butyllithium at −35° for fifteen minutes, no interconversion product was obtained from the purple solution after carbonation. An unidentified crystalline acid was obtained from each of these experiments (1–2% yield) which on the basis of a chlorine test and a nitrogen analysis may be a 2-chloro-*x*-quinolinecarboxylic acid possibly formed by metalation.

Anal. Calcd. for $C_{10}H_6O_2NCl$: N, 6.75. Found: N, 6.74.

This compound has the peculiar melting point behavior characteristic of both 2-chloro-3-quinolinecarboxylic acid[23] and 2-chloro-4-quinolinecarboxylic acid.[24]

Possibly related to this reaction is the low yield of a chloro acid obtained from α-chloronaphthalene and *n*-butyllithium.[25]

From 0.09 mole of methyllithium and 0.07 mole of 2-chloroquinoline in 175 cc. of ether (fifteen minutes at −35°) no acid was obtained subsequent to carbonation and hydrolysis, and 81.6% of the 2-chloroquinoline was recovered.

3-Cyanoquinoline.—Employing the procedure of Craig[26] for the preparation of 2-cyanopyridine, Jansen and Wibaut[27] obtained 3-cyanoquinoline in a 60% yield from 3-bromoquinoline and anhydrous cuprous cyanide. Inasmuch as we have prepared this nitrile consistently in yields of 80%, and as high as 92%, we are reporting some details. One and one-half quivalents of cuprous cyanide[28] were used with one equivalent of the bromoquinoline. The reactants were placed in a 250-cc. Claisen flask, set up for immediate vacuum distillation, and heated with a faintly smoky flame, until almost all of both reactants were changed to the molten state, whereupon the system was immediately evacuated to a pressure of about 50 mm. The vacuum used was never much less than this; otherwise the nitrile would come over as a vapor and condense as fine flakes in the tube of the receiving vessel leading to the pump. The side-arm of the Claisen flask was 6 mm. in diameter to prevent plugging. Whenever this occurred, the time consumed in re-opening the plugged side-arm reduced the yield considerably, and a hard resinous product formed from which very little nitrile could be obtained. Craig[26] reported a similar observation in the preparation of 2-cyanopyridine. The neck of the receiving vessel was kept warm throughout the distillation; the side-arm of the receiving vessel was removed as far as possible from the cooled receiving bulb to prevent clogging. The entire reaction consumed about fifteen minutes and sometimes less. In this way, the following yields of 3-cyanoquinoline were obtained. The first run was made in an apparatus smaller than the one described, but on a proportionate scale.

In the following six preparations, the first figure is g. of 3-bromoquinoline; the second figure, g. of cuprous cyanide; and the third figure, g. and % of 3-cyanoquinoline. (1) 4.2, 2.73, 2.6 (84%); (2) 30.6, 19.8, 18 (79.5%); (3) 24.8, 16.4, 14.3 (78%); (4) 33.5, 21.8, 21.8 (88%); (5) 24.7, 16.1, 16.8 (92%); (6) 62.9, 40.8, 37.2 (80%).

The melting points of three different unrecrystallized samples were 107–108°, 107° and 106–108°, which check with the reported[27] value of 107°. Despite the close check in melting point, the product was contaminated with traces of 3-bromo-quinoline which may be removed by recrystallization from ethanol.

3-Quinolinecarboxylic Acid.—Hydrolysis of 3-cyanoquinoline to the acid was accomplished in a number of ways: (1) in 70% yield by boiling in a 20% aqueous solution of sodium hydroxide; (2) in 83% yield by boiling in 20% hydrochloric acid solution; (3) in 97% yield by boiling in 70% sulfuric acid solution; and (4) in 98.3% yield by heating in an aqueous-alcoholic sodium hydroxide solution. For example, 5.45 g. of the nitrile, added to 4 g. of sodium hydroxide in 15 cc. of water and 30 cc. of ethanol, was refluxed for about one hour until the evolution of ammonia ceased. The solvent was removed by distillation almost to dryness, and the residue redissolved in water, filtered and the filtrate carefully acidified to give a copious white precipitate of the acid, m. p., 270–272°. The yield was 6.02 g. (98.3%). The acid crystallizes in small white needles from glacial acetic acid diluted with a little water.

The hydrolysis of 3-cyanoquinoline, and the direct interconversion of 3-bromoquinoline with RLi followed by carbonation, constitute the most straightforward methods of preparing 3-quinolinecarboxylic acid. For other methods of making this compound see Mills and Watson.[23]

N,N-Diethyl-3-quinolinecarboxamide.—Eight grams (0.046 mole) of the finely powdered acid was treated with slightly more than one equivalent of diethylamine, and to the mixture 4.5 g. of phosphorus oxychloride was added carefully through the condenser. The reaction was vigorous, evolving considerable heat. The contents were heated in an oil-bath at 110° for twelve hours, and the melt which formed was decomposed with 30% sodium hydroxide; the dark oily product was extracted with ether, and dried. (Benzene is a better extracting solvent for the dimethyl homolog in this series.) A 6.1 g. (64%) yield of the diethylamide was obtained from the ether layer, and 0.65 g. of unused acid was recovered from the alkaline layer. Table II lists essential information on the several amides.

N,N-Diallyl-3-quinolinecarboxamide.—To 7 g. (0.04 mole) of the acid was added 4.85 g. (0.05 mole) of diallylamine and a mixture of 3.55 g. of phosphorus pentoxide and 3.5 g. of fine sand. The contents were mixed, and then heated in an oil-bath at 145–150° for one hour. Decomposition of the glassy melt with aqueous alkali gave an oil, which was extracted with ether. After drying the ether extract, there was obtained a little quinoline and 3.1 g. (30.4%) of the amide. The decarboxylation of some of the acid is probably due to the high heat of reaction, characteristic of these condensations.

In the preparation of the other amides, listed in Table II, phosphorus oxychloride was used as the condensing agent

(23) Mills and Watson, *J. Chem. Soc.*, **97**, 741 (1910).
(24) Aeschlimann, *ibid.*, 2902 (1926).
(25) Gilman and Moore, THIS JOURNAL, **62**, 1843 (1940).
(26) Craig, *ibid.*, **56**, 232 (1934).
(27) Jansen and Wibaut, *Rec. trav. chim.*, **56**, 709 (1937).
(28) "Organic Syntheses," Coll. Vol. I, p. 38.

TABLE II

DIALKYLAMIDES OF 3-QUINOLINECARBOXYLIC ACID

Compound	B. p. °C.	Mm.	M. p., °C.	Form	Yield	N, % Calcd.	Found	
N,N-Dimethyl-3-quinolinecarboxamide	157–160	2		Thick yellow oil	75.3			
Hydrochloride			191–192	Fine white needles		11.84	11.91	
Picrate			195	Yellow crystals		16.31	16.21	
N,N-Diethyl-3-quinolinecarboxamide	190–194	10		Viscous yellow oil	64	12.27	12.19	
Hydrochloride			159–160 dec.	Colorless rhombohedra		10.58	10.66	
Picrate			sinters 188–190 m. 190–192	Yellow platelets		15.33	15.46	
N,N-Di-*n*-propyl-3-quinolinecarboxamide	173	1.5		Viscous oil				
Hydrochloride			153–154	Acicular	58.5	9.57	9.39	9.51
Picrate			159–160	Yellow platelets		14.43	14.67	
N,N-Di-*iso*-propyl-3-quinoline-carboxamide	169–170	1.5	81–84	Crystalline	35.2–40.5			
Hydrochloride			173.5–174.5 dec.	Colorless crystals		9.57	9.41	
Picrate			225–227	Yellow blades		14.43	14.43	
N,N-Diallyl-3-quinolinecarboxamide	178–180	2		Viscous yellow oil	30.4			
Hydrochloride			152.5–153.5	Pale brown crystals		9.70	9.83	
Picrate			152–152.5	Yellow shining platelets		14.55	14.58	
3-Quinoline-carboxylic acid piperidide	198–202	2.5	88–89	Crystalline	67	11.66	11.66	
Hydrochloride			122–158 dec.	Fine white needles		10.12	9.94	
Picrate			195.5–196.5	Fine yellow needles		14.89	14.94	

and the reactants were heated at 145° for eight hours. Where possible, the oxychloride was preferred to the pentoxide, because the physical state of the former permits a more intimate contact between amine, acid and condensing agent, which prevents or at least reduces to a minimum the decarboxylation of the acid by the high heat of reaction.

The hydrochlorides of the amides were precipitated in crystalline form from alcoholic solution by dilution with ether.

Summary

The halogen–metal interconversion reaction with halogen derivatives of carbazole and quinoline provides a very satisfactory procedure for the preparation of RM compounds of these nitrogen heterocycles. The essential absence of reaction between 2-chloroquinoline and RLi compounds supports the suggestion that a halogen deactivates the azomethylene linkage for its otherwise prompt addition with RLi compounds. Directions are given for the preparation of a series of substituted amides of 3-quinolinecarboxylic acid.

AMES, IOWA RECEIVED FEBRUARY 14, 1941