Experimental

General Preparation of Dialkylaminoalkyl Half Esters.—The preparation of mono-β-diethylaminoethyl *cis*-Δ^4-tetrahydrophthalate will illustrate the procedure followed.

A solution of 0.1 mole (11.7 g.) of diethylaminoethanol dissolved in 30 ml. of dry acetone was slowly added dropwise to 0.1 mole (15.2 g.) of *cis*-Δ^4-tetrahydrophthalic anhydride dissolved in 30 ml. of dry acetone. After the exothermic reaction was over the mixture was boiled for a few minutes and filtered from a small amount of insoluble material. On standing at room temperature overnight a heavy, colorless precipitate (23 g.) formed. The insoluble product was filtered off and washed with anhydrous ether. Recrystallization from dry acetone several times yielded the desired compound, m.p. 83–84°.

Preparation of Magnesium Salts.—A mixture of the amino acid and a slight molar excess of magnesium carbonate were refluxed for 4 hours in 5% alcohol. The solution was then filtered and concentrated to dryness *in vacuo* to obtain a colorless crystalline solid product, which in all cases was very soluble in water.

Preparation of Bis-(β-diethylaminoethyl)-*cis*-Δ^4-tetrahydrophthalate.—In a flask, equipped with a dropping funnel and a condenser carrying a calcium chloride drying tube, was placed 0.1 mole of β-diethylaminoethyl-*cis*-Δ^4-acid tetrahydrophthalate and 100 ml. of dry benzene. While the mixture was cooled in an ice-bath, 0.12 mole of oxalyl chloride dissolved in 100 ml. of benzene was added dropwise. The reaction was rapid as was evidenced by the rapid evolution of gas. When all the oxalyl chloride was added, the mixture was refluxed for one hour on a water-bath. The benzene and the unreacted oxalyl chloride were removed under vacuum, fresh benzene was added, and the stripping procedure repeated. The resulting gum was taken up in 200 ml. of dry benzene and 0.11 mole of diethylaminoethanol was slowly added to the solution. After refluxing for four hours the mixture was cooled and extracted with dilute hydrochloric acid. The water solution was separated, filtered, made alkaline with 10% sodium carbonate solution, and extracted with ether. Anhydrous sodium sulfate was added to dry the ethereal extract which was then filtered and concentrated from a water-bath. The resulting oil was fractionated in vacuum. The product was obtained as a clear, colorless oil with a boiling point of 166–171° at 0.5 mm.

Anal. Calcd. for $C_{20}H_{36}N_2O_4$: C, 65.2; H, 9.7; N, 7.6. Found: C, 65.3; H, 9.8; N, 7.7.

WASHINGTON 7, D. C.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Rearrangements in Amination by Alkali Amides in Liquid Ammonia and by Lithium Dialkylamides in Ether

BY HENRY GILMAN AND ROBERT H. KYLE

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Several extensions have been made on the scope of rearrangements in amination by alkali amides in liquid ammonia and by lithium dialkylamides in ether.

An earlier study[1a,b] reported a rearrangement of ortho-halogenated ethers by sodamide in liquid ammonia to give *m*-amino ethers. The rearrangement reaction was also shown to take place with an ortho-halogenated sulfide like 4-iododibenzothiophene.[1c] The rearrangement is apparently of a wider scope for it is shown not only with sodamide in liquid ammonia but also with lithium dialkylamides in ether, and with non-ether or -sulfide types like α-halogenated naphthalenes[1d,e] and *o*-bromodimethylaniline.[1f] It is also noteworthy that *p*-bromoanisole and lithium diethylamide give, in addition to *p*-methoxydiethylaniline, the rearrangement product, *m*-methoxydiethylaniline.[1g]

An extension of some of these reactions is now reported. First, results are reported on some optimal conditions for the reaction of *o*-chloroanisole with sodamide in liquid ammonia. Second, potassium amide gives a yield of rearrangement product comparable to that obtained with sodamide. Third, under corresponding conditions, lithium amide does not react appreciably with *o*-chloroanisole, but does show the rearrangement with *o*-bromoanisole. Fourth, lithium diethylamide in ether shows the rearrangement with *o*-iodo-, *o*-bromo-, *o*-chloro- and *o*-fluoroanisole to give *m*-diethylaminoanisole. The reaction with *o*-fluoroanisole is interesting, for α-fluoronaphthalene, unlike α-chloronaphthalene, does not rearrange with potassium amide in liquid ammonia,[1e] whereas the α-fluoro-, α-chloro- and α-bromonaphthalenes give β-diethylaminonaphthalenes with lithium diethylamide. Fifth, *m*-chloroanisole, as might have been expected, gives *m*-diethylaminoanisole. Sixth, lithium di-*n*-butylamide with *o*-chloroanisole gives a higher yield than lithium diethylamide. Seventh, the halogenated phenols may behave like the halogenated ethers, for *o*-bromophenol and lithium diethylamide give *m*-diethylaminophenol. Eighth, cyclic amides like lithium piperidide and morpholide show the same rearrangement observed with lithium dialkylamides.[1b]

In practically all reactions with the *o*-halogenated anisoles, some anisole is obtained. This does not, apparently, owe its formation to a halogen–metal interconversion reaction[1d] which would give an anisyllithium compound that would be hydrolyzed to anisole.

Experimental

***o*-Haloanisoles and Metal Amides.**—In a typical procedure, 0.5 mole of the *o*-haloanisole was added to one mole of sodamide[2] in liquid ammonia over a one-half-hour period. The color gradually changed, first to light green and finally to a deep reddish brown. The mixture was then stirred for an additional 20 minutes, and then one mole of am-

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[1] (a) H. Gilman and S. Avakian, THIS JOURNAL, **67**, 349 (1945); see, also, F. W. Bergstrom and W. C. Fernelius, *Chem. Revs.*, **20**, 437 (1937); and (b) C. H. Horning and F. W. Bergstrom, THIS JOURNAL, **67**, 2110 (1945); (c) H. Gilman and J. F. Nobis, *ibid.*, **67**, 1479 (1945); (d) H. Gilman, N. N. Crounse, S. P. Massie, R. A. Benkeser and S. M. Spatz, *ibid.*, **67**, 2106 (1945); (e) R. S. Urner and F. W. Bergstrom, *ibid.*, **67**, 2108 (1945); (f) H. Gilman, R. H. Kyle and R. A. Benkeser, *ibid.*, **68**, 143 (1946); (g) H. Gilman and R. H. Kyle, *ibid.*, **70**, 3945 (1948); see, particularly, R. A. Benkeser and R. G. Severson, *ibid.*, **71**, 3838 (1949).

[2] Prepared in accordance with directions by T. H. Vaughn, R. R. Vogt and J. A. Nieuwland, *ibid.*, **56**, 2120 (1934).

monium chloride was added over a period of 10–15 minutes which made the over-all time about one hour. Subsequent to the addition of 250 cc. of benzene and warming to expel the ammonia, the solids were filtered and extracted with benzene. Hydrogen chloride was bubbled into the combined benzene extracts to precipitate the *m*-anisidine hydrochloride, from which the free base was liberated, dried and distilled; b.p. 75–77° (0.15 mm.); n^{20}_D 1.5809.

Potassium amide was prepared in a manner similar to that used for sodamide. Lithium amide was prepared in essential accordance with the procedure of Campbell and Campbell.[3]

The general results are given in Table I. In each experiment there was used 0.5 mole of *o*-haloanisole; and, unless otherwise stated, the time from the start of the addition of the *o*-haloanisole until all of the ammonium chloride had been added was one hour.

TABLE I

REACTION OF *o*-HALOANISOLES WITH METAL AMIDES

Metal	Halogen	Mole ratio Amide: RX	Yield (gross) of *m* $CH_3OC_6H_4$-NH_2, %	Recovery of RX, %	Yield (net) of *m*-$CH_3OC_6H_4$-NH_2, %
Na	Cl	2:1	46.5		
Na	Cl	2:1	42.5		
Na	Cl	4:1	51.0		
Na	Cl	4:1	55.1	3.7	57.4
Na	Cl	4:1	51.5		
Na	Cl	4:1[a]	35.9	31.3	52.4
Na	Cl	4:1[b]	25.7		
Na	Cl	8:1	42.9		
Li	Cl	2:1	0.0	65.2	
Li	Cl	2:1	0.0	90.3	
Li	Br	2:1[c]	5.4	75.7	22.0
K	Cl	2:1	44.4	25.4	59.5
K	Cl	2:1[d]	33.3	26.6	45.4
K	Cl	4:1[e]	35.6	28.0	49.5

[a] The reaction time was 0.33 hour. [b] The reaction time was 2.5 hours. [c] The reaction time was 1.3 hours. [d] The reaction time was 0.75 hour. [e] The reaction time was 0.33 hour.

o-**Haloanisoles and Lithium Diethylamide**.—The following general procedure was used in the lithium diethylamide studies. To 0.28 mole of diethylamine in 150 cc. of ether contained in a flask provided with a dry nitrogen atmosphere was added 0.25 mole of methyllithium.[4] To this pale cream-colored mixture, which gave a negative color test I,[5] was added 0.25 mole of the *o*-haloanisole; the color generally turned red gradually. After refluxing and stirring for 24 hours, the mixture was hydrolyzed. The ether layer was extracted with hydrochloric acid, and the acid solution was treated with sodium hydroxide to give the free base, which was taken up in ether, dried over sodium sulfate, and distilled.

Some preliminary experiments of 0.5-mole size showed that the yield of rearrangement product was increased a few per cent. on extending the time of reflux from three or four hours to 24 hours.

Brown and Mason[6] have described *m*-methoxydiethylaniline as a colorless oil which darkens rapidly on standing and which boils at 146–148° (14 mm.). The following additional data were observed by us: b.p. 87–89° (0.5 mm.); n^{20}_D 1.5437. The picrate was obtained as yellow prisms melting at 145–146°.

Anal. Calcd. for $C_{17}H_{20}O_8N_4$: N, 13.7. Found: N, 13.7.

An authentic specimen was prepared from *m*-hydroxydiethylaniline, dimethyl sulfate, and sodium hydroxide. This compound had the same boiling point and refractive index as the rearrangement product; and its picrate was identical (mixed m.p.) with the picrate of the rearrangement product.

The general results of the reactions of the *o*-haloanisoles with lithium diethylamide are given in Table II.

TABLE II

REACTION OF *o*-HALOANISOLES WITH LITHIUM DIETHYLAMIDE[a]

o-Haloanisole	Yield (gross) of *m*-$(C_2H_5)_2$-$NC_6H_4OCH_3$, %	Recovery of *o*-haloanisole, %	Yield (net) of *m*-$(C_2H_5)_2$-$NC_6H_4OCH_3$, %	Yield of anisole, %
I[b]	5.4	22.9	6.9	22.2
Br	32.8	25.3	43.8	9.6
Cl	26.4	23.9	34.6	7.4
F[c]	26.2			

[a] In all runs there was used 0.25 mole of *o*-haloanisole, and the reaction time was 24 hours. [b] Because of the high yield of anisole (identified by conversion to 2,4,6-tribromophenol), the reaction mixture from one run was sprayed upon Dry Ice to determine whether any anisyllithium might have been formed by a halogen–metal interconversion reaction; however, no *o*-methoxybenzoic acid was isolated. [c] The *o*-fluoroanisole [J. English, J. F. Mead and C. Niemann, THIS JOURNAL, **62**, 350 (1940); W. F. Anzilotti and B. C. Curran, *ibid.*, **65**, 607 (1943)] was prepared from *o*-fluorophenol by methylation with dimethyl sulfate. The authors are grateful to Dr. Carl Niemann for the *o*-fluorophenol used in this study.

m-**Chloroanisole and Lithium Diethylamide.**—In a 0.2-mole run there was an immediate reaction on adding *m*-chloroanisole to lithium diethylamide. The solution turned brown at the outset, but after a few hours of stirring and refluxing the color changed to orange. The yield of *m*-methoxydiethylaniline (mixed m.p. of the picrates unchanged) was about 48%.

o-**Bromophenol and Lithium Diethylamide.**—To a suspension of 0.2 mole of lithium diethylamide in 150 cc. of ether was added 0.1 mole of *o*-bromophenol in 50 cc. of ether, and the mixture was refluxed for 98 hours. The yield of *m*-diethylaminophenol was 15%, or, allowing for a 43% recovery of *o*-bromophenol, the net yield was 26%. Identity of the product was established by first converting the *m*-diethylaminophenol to *m*-diethylaminoanisole by means of dimethyl sulfate, and then preparing the picrate. The m.p. and mixed m.p. of the picrate of *m*-diethylaminoanisole was 145.5–146°.

o-**Chloroanisole and Lithium Di-*n*-butylamide.**—From this reaction, effected in essential accordance with the lithium diethylamide procedure, there was obtained 42% of *m*-methoxydi-*n*-butylaniline, or a net yield of 48% after allowing for recovered *o*-chloroanisole: b.p. 136.5–138.5° (1.9 mm.); n^{20}_D 1.5205; d^{20}_4 0.951; mol. ref. calcd., 76.7; found, 75.4. The picrate of *m*-methoxydi-*n*-butylaniline was obtained as yellow prisms melting at 95–96°.

Anal. Calcd. for $C_{21}H_{28}O_8N_4$: N, 12.1. Found: N, 12.8, 12.3, 12.9 and 12.4.

An authentic specimen of *m*-methoxydi-*n*-butylaniline was prepared in accordance with a general procedure of Hickinbottom and Lambert[7] by heating 0.18 mole of *m*-anisidine, 0.54 mole of *n*-butyl iodide, 0.24 mole of sodium carbonate and 250 cc. of water on a boiling water-bath for five hours. After treatment with acetic anhydride and 20% sodium hydroxide, and then extraction with hydrochloric acid, the amine was isolated and found to have the same boiling point and refractive index as the rearrangement product from *o*-chloroanisole, and the picrate melted at 95–96° (mixed m.p.).

o-**Chlorophenetole and Lithium Diethylamide.**—A mixture of 0.25 mole of lithium diethylamide and 0.25 mole of *o*-chlorophenetole in 250 cc. of ether was refluxed with stirring for 24 hours. The products isolated and identified were: 21% of *o*-chlorophenetole; 27% of phenetole (characterized by cleavage to phenol and preparation of 2,4,6-tribromophenol, mixed m.p.); and a yield of 38% of *m*-diethylaminophenetole, after making allowance for the recovered *o*-chlorophenetole. An authentic specimen of *m*-diethylaminophenetole, prepared from *m*-diethylaminophenol and diethyl sulfate, distilled at 97–98° (0.6 mm.); n^{20}_D 1.5342.

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[3] K. N. Campbell and B. K. Campbell, *Proc. Indiana Acad. Sci.*, **50**, 123 (1940).

[4] H. Gilman, E. A. Zoellner, W. M. Selby and C. H. Boatner, *Rec. trav. chim.*, **54**, 584 (1935).

[5] H. Gilman and F. Schulze, THIS JOURNAL, **47**, 2002 (1925).

[6] W. R. Brown and F. A. Mason, *J. Chem. Soc.*, 1269 (1933).

[7] W. J. Hickinbottom and E. W. Lambert, *ibid.*, 1383 (1939).

The picrate of *m*-diethylaminophenetole melted at 132–133° (mixed m.p.).

o-**Bromoanisole and Lithium Piperidide.**—The lithium piperidide was prepared from 0.22 mole of piperidine and 0.2 mole of methyllithium (negative color test I). On the addition of 0.2 mole of *o*-bromoanisole the mixture assumed a reddish tinge. At the end of a 24-hour period of refluxing with stirring almost no precipitate had appeared and the mixture was translucent. The yield of *m*-piperidylanisole was 41%, after allowing for a 34% recovery of *o*-bromoanisole: b.p. 110° (0.2 mm.); $n^{20}{}_D$ 1.5628; $d^{20}{}_4$ 1.059; mol. ref. calcd., 58.9; found, 58.8. The picrate of *m*-piperidylanisole was obtained as yellow needles melting at 159.5–160°.

Anal. Calcd. for $C_{18}H_{20}O_8N_4$: N, 13.3. Found: N, 13.55.

The structure of the reaction product was established by comparison with the picrate of a sample prepared by the reaction of *m*-chloroanisole with lithium piperidide: m.p. and mixed m.p. 159–160°.

o-**Bromoanisole and Lithium Morpholide.**—To lithium morpholide, obtained as a thick white suspension from 0.2 mole of methyllithium and 0.23 mole of freshly distilled morpholine in ether, was added 0.2 mole of *o*-bromoanisole in 50 cc. of ether. The color gradually changed from white to yellowish during a 24-hour period of refluxing with stirring. The initial yield of *m*-morpholylanisole was 8.6%, but after allowing for a recovery of 75% of *o*-bromoanisole the net yield was 35%; b.p. 113° (0.15 mm.); $n^{20}{}_D$ 1.5650. The picrate was obtained as yellow plates melting at 196–197°.

Anal. Calcd. for $C_{17}H_{18}O_9N_4$: N, 13.3. Found: N, 13.5.

The *m*-morpholylanisole was also obtained by reaction of *m*-chloroanisole with lithium morpholide (mixed m.p. of picrates).

p-**Dibromobenzene and Lithium Diethylamide.**—To a suspension of 0.22 mole of lithium diethylamide in 150 cc. of ether was added 0.09 mole of *p*-dibromobenzene in 100 cc. of ether, and the mixture was refluxed for 25 hours. Among the products so far isolated are: 15% of diethylaniline (m.p. and mixed m.p. of picrates 137–138°); and 14% of *p*-bromodiethylaniline (m.p. and mixed m.p. of picrates 165–166°). From another experiment in which 0.1 mole of *p*-dibromobenzene and 0.1 mole of lithium diethylamide were used, there was obtained 23% of *p*-bromodiethylaniline, or a 28% yield when allowance is made for recovered *p*-dibromobenzene.

AMES, IOWA

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Quinone Imides. XIV. Addition of Hydrogen Chloride to *p*-Quinonedibenzimides and Related Compounds

BY ROGER ADAMS AND D. S. ACKER

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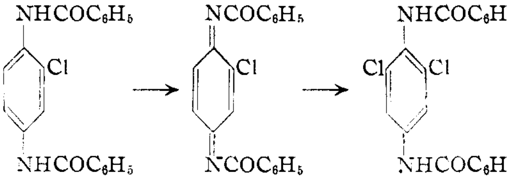
p-Phenylenedibenzamides may be oxidized to *p*-quinonedibenzimides by means of lead tetraacetate. Hydrogen chloride adds to the imides to give chloro amides. 2-Chloro-*p*-quinonedibenzimide is converted almost exclusively to 2,6-dichloro-*p*-phenylenedibenzamide, the structure of which was proved by an unequivocal synthesis, in contrast to the formation of a mixture of isomeric dichloro derivatives when 2-chloro-*p*-quinonedibenzenesulfonimide reacts under similar conditions. 2,6-Dichloro-*p*-quinonedibenzimide and hydrogen chloride react to give a complicated mixture from which only a small amount of trichloro diamide could be isolated. 2-Chloro-*p*-quinonedicarbethoxyimide adds hydrogen chloride to give a mixture of dichloro diamides from which two were isolated in pure state. 2-Chloro-*p*-quinonedicarbobenzoxyimide is likewise converted to a mixture of dichloro diamides which by oxidation and subsequent addition of hydrogen chloride give a good yield of 2,3,5-trichloro diamide. The substituted *p*-phenylenedibenzylcarbamates are quite readily hydrolyzed to the corresponding diamines by ethanolic hydrochloric acid.

The orientation of the chlorine atom when hydrogen chloride is added to various *p*-quinonedibenzenesulfonimides has been discussed in a previous paper.[1a] A similar study using various acyl and aroyl diimides has now been completed.

2-Chloro-*p*-phenylenedibenzamide (I) is formed when hydrogen chloride is added to *p*-quinonedibenzimide.[1b] This product was oxidized with lead tetraacetate in refluxing benzene or chloroform to 2-chloro-*p*-quinonedibenzimide (II). Subsequent addition of hydrogen chloride gave a good yield of a single product, 2,6-dichloro-*p*-phenylenedibenzamide, with little or no tendency to form isomers. The structure of this product was proved unequivocally by reducing the commercially available 2,6-dichloro-4-nitroaniline to the corresponding diamine and benzoylating. The entrance of the chlorine atom in the 6-position is in contrast to the addition of hydrogen chloride to 2-methyl-*p*-quinonedibenzenesulfonimide which yields exclusively the 2-methyl-5-chloro diamide; addition of hydrogen chloride to 2-chloro-*p*-quinonedibenzenesulfonimide yields primarily the 2,5-dichloro- and 2,3-dichloro diamides.



I II III

When the 2,6-dichloro-*p*-phenylenedibenzamide (III) was oxidized to the corresponding dichloro-*p*-quinonedibenzimide and treated with hydrogen chloride, the reaction was a complicated one, yielding a mixture from which only a small quantity of the expected 2,3,5-trichloro-*p*-phenylenedibenzamide was obtained. The other products were not identified.

2,3,5,6-Tetrachloro-*p*-phenylenedibenzamide was obtained by nitration of 1,2,4,5-tetrachlorobenzene to the dinitro compound, reduction to the corresponding diamine and benzoylation. This diamide was oxidized to the diimide by lead tetraacetate in refluxing benzene somewhat more slowly than the other dibenzamides reported in this paper.

2-Chloro-*p*-phenylenediethylcarbamate[1b] was oxidized by lead tetraacetate in anhydrous ether to

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(1) (a) R. Adams, E. F. Elslager and K. F. Heumann, THIS JOURNAL, **74**, 2608 (1952); (b) R. Adams and J. L. Anderson, *ibid.*, **72**, 5154 (1950).