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SYNTHESIS OF DISECONDARY AMINES: N,N′-DIPHENYL-α,ω-DIAMINOALKANES[1]

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The homologous series of N,N′-diphenyl-α,ω-diaminoalkanes, $C_6H_5NH(CH_2)_nNHC_6H_5$, is a group of compounds which has been the subject of little investigation. In order that the knowledge of the properties of this interesting group of compounds and their derivatives may be further extended, a study of their synthesis has been undertaken.

A survey of the literature reveals that compounds of this type have found use as stabilizers for polyvinyl acetal resins (1), as antioxidants for rubber (2, 3, 4), and as respiratory and vasomotor stimulants (5). There also exists the possibility that these diamines may be useful in the preparation of superpolyamides having special properties.

Of the procedures previously applied to the synthesis of N,N′-diphenyl-α,ω-diaminoalkanes, the most widely used method has been the reaction of aniline with an α,ω-dihaloalkane in the presence of either an alkali metal carbonate (6) or a large excess of aniline (7–11). However, this procedure frequently yields heterocyclic compounds as the principal products (12, 13, 14), especially in the cases of 1,4-dihalobutanes (12) and 1,5-dihalopentanes (13). Another procedure which has been applied to the synthesis of N,N′-diphenyl-α,ω-diaminoalkanes makes use of the thermal decarboxylation of the corresponding α,ω-dianilinodicarboxylic acids under reduced pressure (15). The pentane homolog, N,N′-diphenyl-1,5-diaminopentane has been prepared by cleavage of 1-phenylpiperidine with cyanogen bromide, followed by treatment with aniline and hydrolysis of the resulting N-cyano-N,N′-diphenyl-1,5-diaminopentane (16). It has also been prepared by cleavage of N,N′-dimethyl-N,N′-diphenyl-1,5-diaminopentane with cyanogen bromide and hydrolysis of the N,N′-dicyano-derivative (16).

The use of the sodium derivative of acetanilide as an intermediate in the synthesis of N-alkylanilines has been known since 1877 (17). However, the literature contains only one reference to a reaction of sodium acetanilide with a dihalide, dichloromethane, and this dihalide did not give the desired reaction (18). In the course of the present work it was found that dibromomethane could be made to give a low yield of the expected product.

A new general method of synthesis has been developed for the preparation of N,N′-diphenyl-α,ω-diaminoalkanes in relatively good yields, except in the case of the ethane homolog. This method involves the reaction of α,ω-dibromoalkanes with the sodium derivative of acetanilide to form the N,N′-diacetyl-

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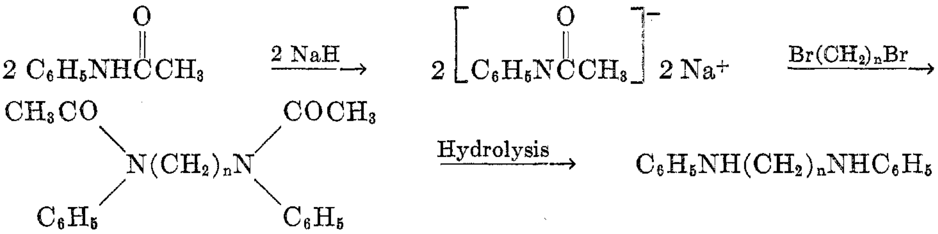
N,N′-diphenyl-α,ω-diaminoalkanes, which, with the exception of the methane homolog, are easily hydrolyzed to the corresponding diamines:



Sodium hydride was used in the preparation of the sodium derivative of acetanilide because it was found to give the sodium derivative more rapidly than does metallic sodium, and also because it does not react with organic halides (19). While this work was in progress, the use of sodium hydride for the preparation of sodium acetanilide was reported in the literature for the first time by Fones (20).

It is interesting and worth mentioning that the solubility of the diacetyl derivatives of the diamines in concentrated hydrochloric acid was quite appreciable, even at room temperature. However, the solubility decreased with an increase in the number of carbon atoms in the chain.

The ethane, propane, butane, and pentane homologs of the free diamines gave dihydrochlorides, as might be expected. However, the hexane, heptane, and decane homologs form sesquihydrochlorides. It may be noted in this connection that the compound reported in the literature (15) as the dihydrochloride of N,N′-diphenyl-1,8-diaminooctane gave a nitrogen analysis which corresponds more closely to that calculated for the sesquihydrochloride. The nonane homolog formed both a sesquihydrochloride, which precipitated from the hot hydrolysis mixture, and a monohydrochloride, which crystallized when the mixture was cooled. The N,N′-diphenyl-1,10-diaminodecane sesquihydrochloride decomposed at its melting point to give a monohydrochloride.

Attempts to convert these sesquihydrochlorides to dihydrochlorides by recrystallization from 7 *N* hydrochloric acid were unsuccessful. More strongly acid solutions could not be used for recrystallization because of the low solubility of the hydrochlorides.

The free diamines prepared were found to be colorless, odorless, crystalline solids, which were insoluble in water and soluble in organic solvents.

It is interesting that the melting points of the benzenesulfonyl and the *p*-toluenesulfonyl derivatives, as well as the melting points of the acetyl derivatives, follow the "sawtooth rule".

Studies of the preparation, and especially of the properties, of these and other N,N′-disubstituted-α,ω-diaminoalkanes are to be continued.

EXPERIMENTAL

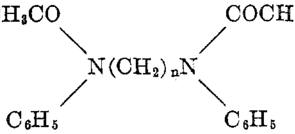
The general experimental procedure for each type of compound will be given, since identical procedures were used for each type of compound throughout the series. Exceptions will be noted where they occurred.

The sodium hydride used in this work was made by the E. I. du Pont de Nemours and Company Electrochemicals Divisions in 1946–1948.

Sodium acetanilide. A dry, two-liter, three-neck flask was set up with a dropping-funnel, stirrer, and reflux condenser (with calcium chloride drying tube), and the entire system was flushed with dry nitrogen for 20–30 minutes. Without interrupting the nitrogen flow, the dropping-funnel was removed, and 148.5 g. (1.10 moles) of acetanilide was placed in the flask through a powder funnel. One liter of anhydrous toluene was then rapidly added, followed by 25.0 g. (1.05 moles) of sodium hydride. A vigorous evolution of hydrogen began at once. The dropping-funnel was replaced immediately, the stirrer was started, and the nitrogen flow discontinued. The mixture was heated to 80–100° for two hours. At the end of this time the reaction mixture was white and pasty as the result of the formation of sodium acetanilide.

TABLE I

N,N'-DIACETYL-N,N'-DIPHENYL-α,ω-DIAMINOALKANES



$(CH_3CO)(C_6H_5)N(CH_2)_nN(COCH_3)(C_6H_5)$

n	M.P., °C. (CORR.)	YIELD,[a] %	ANALYSIS, NITROGEN	
			Calc'd	Found
1	83–83.5	30.9	9.93	9.96
2	156.5–157[b]	3.9	9.45	9.70
3	120.5–121[c]	67.3	9.03	9.10
4	132–133	78.7	8.64	8.51
5	124–125	74.1	8.28	8.29
6	179–180	99.3	7.95	7.84
7	78.5–79[d]	31.5[h]	7.64	7.67
9	(oil)[e]	80[f,h]	—	—
10	42.5–43	85[g]	6.86	6.93

[a] Based on $Br(CH_2)_nBr$. [b] M.p. 158°, Bischoff and Nastvogel, *Ber.*, **22,** 1783 (1889). [c] M.p. 119°, Veer, *Rec. trav. chim.*, **57,** 989 (1938). [d] M.p. 79–80°, Le Seuer, *J. Chem. Soc.*, **103,** 1119 (1913). [e] B.p. (8 mm.) 308–310° with decomposition. [f] Based on the yields of the hydrochlorides. [g] Estimated. [h] One-tenth the usual quantities of reactants were used in these cases.

N,N'-Diacetyl-N,N'-diphenyl-α,ω-diaminoalkanes (Table I). The heating of the sodium acetanilide suspension was stopped and 0.50 mole of the dibromoalkane, dissolved in 50 ml. of anhydrous toluene, was added through the dropping-funnel at the rate of 80–100 drops per minute. A more rapid addition resulted in a sudden, violent reaction. After 10–75 minutes the mass of sodium acetanilide began to break up and a vigorous ebullition commenced, accompanied by the precipitation of sodium bromide. After the ebullition had subsided, the mixture was heated so that it boiled gently for 1.5–2 hours.

The hot reaction mixture was then poured into 300 ml. of water containing 2 ml. of concentrated hydrochloric acid. The resulting mixture was chilled for 24 hours, and the product, which crystallized at the interface of the water and the toluene, was removed. The water layer was separated and discarded. The toluene layer was dried over magnesium sulfate and concentrated in order to effect complete recovery of the product.

The products were purified by recrystallization from ethyl ether or from ethanol.

The time required for the vigorous boiling of the reaction mixture to begin increased with the chain length of these compounds, with the exception of 1,2-dibromoethane and dibromomethane, each of which required longer than any of the other dibromides.

The nonane and decane homologs formed toluene-insoluble oils. These products were isolated by distilling the toluene. The decane homolog was crystallized from petroleum ether (30–60° fraction). The nonane homolog, however, melted below room temperature, and attempts at vacuum-distillation resulted in decomposition. The crude product from a second run was converted to the amine hydrochloride.

TABLE II

HYDROCHLORIDES OF N,N′-DIPHENYL-α,ω-DIAMINOALKANES

n	TYPE	YIELD,[a] %	M.P., °C.[b] (CORR.)	ANALYSIS, NITROGEN	
				Calc'd	Found
2	2 HCl	99.4	214–215[c]	9.82	9.99
3	2 HCl	94.3	193.5–194	9.36	9.54
4	2 HCl	98.1	217.5–218.5[d]	8.94	9.15
5	2 HCl	90.0	190–191[e]	8.56	8.45
6	1.5 HCl	96.9	217–218	8.67	8.65
7	1.5 HCl	74.2	194.5–195	8.31	8.44
9	1.5 HCl	65.3[f]	213–214	7.67	7.65
9	1 HCl	13.5[f]	185–186	8.07	7.99
10	1.5 HCl	88.9	211.5–212[g]	7.39	7.45
10	1 HCl	—	187–188	7.76	7.84

[a] Based on N,N′-diacetyl-N,N′-diphenyl-α,ω-diaminoalkanes. [b] Slow heating (one degree C. per minute). [c] M.p. on fast heating, 223–224°(uncorr.). [d] M.p. on fast heating, 228–229° (uncorr.). [e] M.p. 193–194°, von Braun, *Ber.*, **41**, 2165 (1908). [f] Based on $Br(CH_2)_9Br$. Total yield, 14.6 g. [g] Decomposes to the monohydrochloride.

TABLE III

N,N′-DIPHENYL-α,ω-DIAMINOALKANES $C_6H_5NH(CH_2)_nNHC_6H_5$

n	M.P., °C. (CORR.)	ANALYSIS, NITROGEN	
		Calc'd	Found
4	35–36	11.66	11.69
6	74.5–75.5[a]	10.44	10.46
9	47–48	9.02	9.14
10	76.5–77.5	8.63	8.85

[a] M.p. 74°, von Braun, *Ber.*, **43**, 2859 (1910).

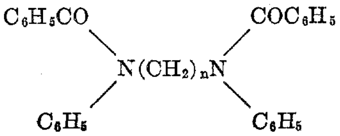
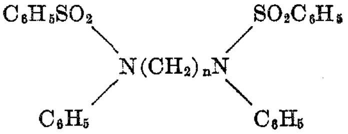
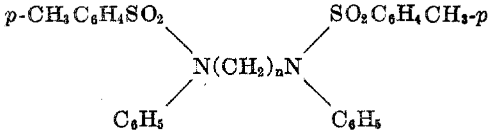
N,N′-Diphenyl-α,ω-diaminoalkane hydrochlorides (Table II), One-tenth mole of the N,N′-diacetyl derivative of the diamine was dissolved in 100–200 ml. of concentrated hydrochloric acid, and just enough water (150–250 ml.) was added to cause reprecipitation to begin. The resulting mixture was boiled under reflux for eight hours, cooled, and the crystallized product removed. Additional product was obtained by evaporation of the solvent under reduced pressure. The hydrochlorides were recrystallized from absolute ethanol.

Hydrochlorides of N,N′-diphenyldiaminomethane were not prepared because this amine is unstable towards acids (21). Attempts to hydrolyze its N,N′-diacetyl derivative with aqueous potassium hydroxide were unsuccessful, and the starting material was quantitatively recovered.

N,N′-Diphenyl-α,ω-diaminoalkanes (Table III). The hydrochloride (2 g.) was dissolved in 10 ml. of warm, distilled water, and 10 ml. of 20% sodium hydroxide was added.

TABLE IV

DERIVATIVES OF N,N′-DIPHENYL-α,ω-DIAMINOALKANES

n	M.P., °C. (CORR.)	ANALYSIS, NITROGEN	
		Calc'd	Found
A. N,N′-DIBENZOYL DERIVATIVES	 $(C_6H_5CO)(C_6H_5)N(CH_2)_nN(COC_6H_5)(C_6H_5)$		
2	193–194	6.66	6.84
4	131–131.5[a]	6.25	6.28
7	141–141.5	5.71	5.85
10	84–85	5.26	5.33
B. N,N′-DIBENZENESULFONYL DERIVATIVES	 $(C_6H_5SO_2)(C_6H_5)N(CH_2)_nN(SO_2C_6H_5)(C_6H_5)$		
2	231.5–232	5.69	5.96
3	95–96	5.53	5.83
4	189–190	5.38	5.55
5	144.5–145	5.24	5.54
6	154–155	5.11	5.27
9	77.5–78.5	4.74	4.98
10	130–131	4.60	4.90
C. N,N′-BIS-*p*-TOLUENESULFONYL DERIVATIVES	 $(p\text{-}CH_3C_6H_4SO_2)(C_6H_5)N(CH_2)_nN(SO_2C_6H_4CH_3\text{-}p)(C_6H_5)$		
2	223–223.5	5.38	5.60
3	131–132	5.24	5.53
4	206.5–207.5	5.11	5.38
5	127.5–128.5	4.98	5.25
6	158.5–159	4.86	5.14
7	102.5–103	4.74	4.89
10	144–145	4.43	4.79

[a] M.p. on fast heating, 120–121° (uncorr.).

The diamines separated as oils, which readily crystallized when the mixture was chilled, and were recrystallized from 10–15 ml. of a mixture containing equal parts of ethyl ether and petroleum ether (30–60° fraction).

N,N′-Dibenzoyl, N,N′-dibenzenesulfonyl, and N,N′-bis-p-toluenesulfonyl derivatives (Table IV). The diamine hydrochloride (0.5–1.0 g.) was completely dissolved in 10 ml. of water and 20–25 ml. of 20% sodium hydroxide was added to the solution, followed by 10 ml. of benzoyl chloride or benzenesulfonyl chloride, or 5 g. of *p*-toluenesulfonyl chloride, and the mixture was warmed. The flask was stoppered and shaken vigorously until a drop in temperature indicated that the reaction was complete. If the product separated as a solid, it was recrystallized from 25–50 ml. of absolute ethanol. If the product did not solidify, it was dissolved in 30–40 ml. of hot acetone, the solution filtered through 0.05–0.1 g. of charcoal, evaporated to 2–5 ml., and the product precipitated by the addition of 10–15 ml. of ethyl ether and 10 ml. of petroleum ether (30–60° fraction). The products obtained were recrystallized from a mixture of ethyl ether and petroleum ether, or from a mixture of ethyl ether and absolute ethanol.

SUMMARY

1. A new general method has been developed for the preparation of the N,N′ - diacetyl - N,N′ - diphenyl - α,ω - diaminoalkanes and the corresponding diamines.

2. A series of N,N′-dibenzoyl, N,N′-dibenzenesulfonyl, and N,N′-bis-*p*-toluenesulfonyl derivatives of the N,N′-diphenyl-α,ω-diaminoalkanes has been prepared. The hydrochlorides of these diamines have also been made.

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