[CONTRIBUTION FROM THE JOHN HARRISON LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF PENNSYLVANIA]

Condensations of Aromatic Amines with Formaldehyde in Media Containing Acid. II. Formation of Some Diarylmethane Bases

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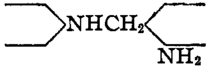
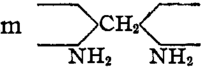
The common methods for preparation of diarylmethane bases from primary and secondary amines by use of formaldehyde involve heating with excess amine and amine-salt (a) the methyleneamines, (b) the methylenediimines, (c) the anhydroaminobenzylalcohols, or (d) the arylaminobenzylanilines.[1] These methods are cumbersome, as a large excess of amine must be removed by steam distillation in order to isolate the product. This necessity is largely avoided by the simpler procedure of heating the amine and about one-half equivalent of formaldehyde in acid solution, as used previously with some secondary aromatic amines, especially by v. Braun, and more recently with aniline by Rivier and Farine.[2] This procedure has now been extended to *n*-propyl-, *n*-butyl- and isoamylaniline, and to *o*- and *m*-toluidines. Most of the products are new or have not previously been made in this way; a number of new derivatives are reported. The reactions yielded the usual higher condensation products or resins, found in some cases to be stable bases distillable *in vacuo*, but obtained in quantities insufficient to permit purification and study.

Attempted preparation of 2,2′-diamino-5,5′-dimethyldiphenylmethane from *p*-toluidine by this method under various conditions was almost wholly fruitless. Yields by the original method of Eberhardt and Welter were trivial. Formation of the base from *o*-amino-*m*-xylyl-*p*-toluidine by heating with *p*-toluidine and its hydrochloride at 120–130° was more successful, yields being about 50%.

The difficulty encountered in the preparation of the diphenylmethane base from *p*-toluidine is apparently due to the necessity for two ortho couplings (with respect to NH_2) during the "rearrangement," instead of the usual para couplings, and is therefore to be expected with other *p*-substituted amines. The occurrence of single ortho couplings has been observed in the formation of aminobenzylanilines such as *o*-amino-*m*-xylyl-*p*-toluidine.[3] The only 2,2′-diaminodiarylmethanes (formed by double ortho coupling) reported as made in this way appear to be those from *p*-toluidine (Eberhardt and Welter), *p*-nitroaniline (Meyer and Stillich), and methyl-*p*-toluidine (v. Braun), yields being small and products incompletely characterized. The obstruction to the formation of diarylmethane bases from *p*-substituted amines is probably the reactivity of the system  $>NHCH_2<\underset{NH_2}{}$ present in the intermediate base of aminobenzylamine type,[4] or of the system  $\underset{NH_2}{>}CH_2\underset{NH_2}{<}$ present in the diphenylmethane base,[5] leading to complications which decrease formation of the latter or involve it in further reactions and so operate against its survival. This view will be discussed in a later paper dealing with the mechanism of the condensations of *p*-substituted amines with formaldehyde in media containing acid.

Experimental

General Procedure for Formation of Diaminodiarylmethanes from Amines and Formaldehyde in Dilute Hydrochloric Acid Solution

The method used was essentially that of v. Braun. The base, in 1.1 to 2.5 equivalents of 6 *N* hydrochloric acid, was treated with slightly less than one-half equivalent of formaldehyde (37%), and the mixture heated on the water-bath, or refluxed, for twelve to twenty-nine hours. Excess of sodium hydroxide was added and uncombined amine (usually only a few grams) recovered by steam distillation, the residue consisting of the diarylmethane base together with resins, etc. The isolation and purification procedures varied and are indicated later. Yields are calculated from the weight of amine not recoverable. New compounds are designated by asterisks.

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[1] (a) German Patent 53,937, *Friedl.*, **2**, 53; 58,072, *Friedl.*, **3**, 79; 70,402, *Friedl.*, **3**, 80; Pat. Anm. C4640, *Friedl.*, **2**, 54; (b) Eberhardt and Welter, *Ber.*, **27**, 1804 (1894); Gnehm and Blumer, *Ann.*, **304**, 87 (1899); Ullmann, *Ber.*, **36**, 1017 (1903); Auwers, *et al.*, *Ann.*, **356**, 124 (1907); v. Braun, *Ber.*, **41**, 2145 (1908); Craig, THIS JOURNAL, **55**, 3723 (1933); (c) German Patent 83,544, *Friedl.*, **4**, 50; 96,762, *Friedl.*, **5**, 77; Meyer and Rohmer, *Ber.*, **33**, 250 (1900); Meyer and Stillich, *ibid.*, **35**, 739 (1902); (d) German Patent 87,934, *Friedl.*, **4**, 66; 107,718, *Friedl.*, **5**, 78; Cohn and Fischer, *Ber.*, **33**, 2586 (1900).

[2] V. Braun, *loc. cit.*; Rivier and Farine, *Helv. Chim. Acta*, **12**, 865 (1929).

[3] German Patent 105,797, *Friedl.*, **5**, 84; v. Walther and Bamberg, *J. prakt. Chem.*, [2] **71**, 153 (1905); *cf.* King, *J. Chem. Soc.*, **117**, 988 (1920).

[4] Lepetit, Maffei and Maimeri, *Gazz. chim. ital.*, **57**, 867 (1927); Maffei, *ibid.*, **58**, 261 (1928); **59**, 3 (1929); Eisner and Wagner, THIS JOURNAL, **56**, 1938 (1934).

[5] Ullmann, *Ber.*, **36**, 1017 (1903).

Diarylmethane Bases from Alkylanilines.—The products were recovered by reduced pressure distillation of the oily residues not volatile with steam. In each case two main fractions were secured, one at 9–10 mm. and the higher-boiling products at about 1 mm. These were redistilled within narrower temperature limits, yielding essentially pure diarylmethane bases, and higher products which were still mixtures. The latter were viscous oils, which generally solidified without visible crystallization. Values for nitrogen indicated in each case a composition approximately that of the diarylmethane base. The bis-(alkylamino)-diphenylmethanes yield dinitrosamines which for the methyl, ethyl and *n*-propyl compounds are useful derivatives; those from the butyl and amyl compounds melt too low. Attempts to prepare picrates of these bases failed to yield solid or crystalline products. Data for the compounds obtained from alkylanilines are given in Table I.

TABLE I

DIARYLMETHANE BASES FROM ALKYLANILINES

Product	Method of preparation	Yield, %[a]	M. p. or b. p.,[b]	corr., °C.	Mm.	Nitrogen analyses, % Formula	Calcd.	Found
$(CH_3NHC_6H_4)_2CH_2$	General procedure	58	B	261–262	9	$C_{15}H_{18}N_2$	12.39	12.30
*Diacetyl deriv.	AcCl in pyridine; cryst. ligroin + C_6H_6	. .	M	121		$C_{19}H_{22}O_2N_2$	9.03	9.04
Higher cond. prod.	General procedure		B	310–313	1			12.2
$(C_2H_5NHC_6H_4)_2CH_2$	General procedure	62	B	265–267	9	$C_{17}H_{22}N_2$	11.02	11.06
Higher cond. prod.	General procedure		B	290–305	2			10.9
*$(n\text{-}C_3H_7NHC_6H_4)_2CH_2$	General procedure	57	B	275–276	9	$C_{19}H_{26}N_2$	9.93	10.0
						Mol. wt.	282	282
*Dinitrosamine	In water; cryst. ether + ligroin	81	M	49.5		$C_{19}H_{24}O_2N_4$	16.47	16.4
Higher cond. prod.	General procedure		B	310–317	1			9.7
*$(n\text{-}C_4H_9NHC_6H_4)_2CH_2$	General procedure	53.5	B	292	9	$C_{21}H_{30}N_2$	9.03	9.04
			M	41–42		Mol. wt.	310	305
*Dibenzoyl deriv.	Schotten-Baumann; cryst. alc.	86	M	95		$C_{35}H_{38}O_2N_2$	5.41	5.44
Higher cond. prod.	General procedure		B	315–320	1			8.95
*$(i\text{-}C_5H_{11}NHC_6H_4)_2CH_2$	General procedure	46	B	301–303	9	$C_{23}H_{34}N_2$	8.28	8.10
						Mol. wt.	338	331
Higher cond. prod.	General procedure		B	320–328	1			8.07

[a] Yields of bases calculated on ratio $(2RNHC_6H_5 + CH_2O - H_2O):2RNHC_6H_5$. [b] Some of the reduced-pressure boiling points are affected by a positive error due to superheating which the usual devices failed to prevent during the final distillations of the pure high-boiling bases.

Diarylmethane Bases from Aniline and the Toluidines.—The general procedure applied to aniline gave only 41% of diaminodiphenylmethane, but considerable higher-boiling material; the method of Rivier and Farine was found to be more satisfactory. The higher condensation product (b. p. 329–334° at 1–2 mm.) gave results for nitrogen (13.75%) and molecular weight (351) which indicate a mixture of tri- and tetra-nuclear bases, *e. g.*, $C_{20}H_{21}N_3$ and $C_{27}H_{28}N_4$ (mol. wt. 303 and 408; nitrogen 13.86 and 13.73%).

The diarylmethane bases from *o*-toluidine and *m*-toluidine were obtained readily and in good yields. That from *o*-toluidine was solid following removal of unreacted amine by steam distillation, and could be crystallized directly from alcohol. The diarylmethane base from *m*-toluidine (not previously reported) was isolated as the hydrochloride, which was precipitated from water solution by excess concd. hydrochloric acid. The base itself was found to be very soluble in the usual solvents, and was best crystallized from hot water containing some alcohol. Its structure was indicated by complete analysis, and by the fact that nitrous acid gave no precipitate (no secondary nitrogen), the diazotized solution coupling strongly with β-naphthol. Data for the bases mentioned, and for a number of derivatives, are given in Table *II*.

2,2′-Diamino-5,5′-dimethyldiphenylmethane.—Trials of the method of Eberhardt and Welter (mixture of di-*p*-toluidinomethane, *p*-toluidine and *p*-toluidine hydrochloride heated at 100°) gave crude yields of 4.5 and 16.4%, much decreased upon crystallization from ligroin; m. p. 93°; picrate, m. p. 195°.

Attempted preparation by the general procedure yielded in various trials some 3-*p*-tolyl-6-methyl-3,4-dihydroquinazoline (m. p. 158°), some Tröger's base (m. p. 135°), a number of unidentified products isolated as high-melting acetyl, benzoyl or nitroso derivatives, and only in one experiment a small amount of 2,2′-diamino-5,5′-dimethyldiphenylmethane, identified as the picrate. The isolation procedures used in numerous trials of this method under various conditions were tedious and complicated, and will not be outlined.

Preparation of 2,2′-diamino-5,5′-dimethyldiphenylmethane from *o*-amino-*m*-xylyl-*p*-toluidine by heating with twice its weight (each) of *p*-toluidine and *p*-toluidine hydrochloride for nine to fourteen hours at 120–130° in an oil-bath was the only method found to be even moderately satisfactory. After removal of excess *p*-toluidine by steam distillation, the black and tarry residue was extracted with warm dilute hydrochloric acid, and undissolved tar separated by use of considerable charcoal. The cooled and filtered solution was neutralized gradually by sodium hydroxide solution, the gluey resins being separated at intervals with the aid of charcoal to prevent clogging of the filter. The diarylmethane base was obtained from the somewhat fluorescent solution as the neutral point was approached. The charcoal residues were worked over similarly, giving a small additional yield. After crystallization from ligroin the best yield of 56% was decreased to 48%; m. p. 95°, mixed melting point with Eberhardt and Welter base 94°; the picrates also were identical.

2,2′-Diamino-5,5′-dimethyldiphenylmethane, made as outlined, and recrystallized from ligroin, melted at 96° corr. *Analysis*. Calcd. for $C_{15}H_{18}N_2$: C, 79.65; H,

TABLE II

DIARYLMETHANE BASES FROM ANILINE AND *o*- AND *m*-TOLUIDINE

Product	Method of preparation	Yield, %	M. p., or b. p., corr., °C.	Mm.	Analyses, %		
					Formula	Calcd.	Found
$(NH_2C_6H_4)_2CH_2$	General procedure	41[a]	B 249 M 93	9	$C_{13}H_{14}N_2$	N 14.14	13.98
*Picrate (B.2 picr.)	Made in dil. AcOH; cryst. hot aq. + alc.	88	No m. p.; blackened 225				
*Tetracetyl deriv.	Made by excess Ac_2O;[b] cryst. alc. + benzene	40	M 170–171		$C_{21}H_{22}O_4N_2$	N 7.65	7.67
Diacetyl deriv.	Made by glac. AcOH; cryst. dil. alc.[c]	..	M 233.8		$C_{17}H_{18}O_2N_2$	9.93	9.88
Higher cond. prod.	General procedure		B 329–334	1		 Mol. wt.	13.75 351
4,4'-Diamino-3,3'-dimethyldiphenylmethane	From *o*-toluidine by gen. proc.; 11 hrs. heating	70[d]	M 158		$C_{15}H_{18}N_2$	C 79.65 H 7.97 N 12.39	79.8 7.92 12.32
*Picrate, B.2 picr.	Made in dil. alc.	80	M 192–193				
*Diacetyl deriv.	By glac. AcOH; cryst. dil. alc.	68	M 224		$C_{19}H_{22}O_2N_2$	N 9.03	9.04
*Tetracetyl deriv.	By excess Ac_2O; cryst. dil. alc.	93	M 119		$C_{23}H_{26}O_4N_2$	N 7.11	7.05
*Dibenzoyl deriv.	PhCOCl in pyridine; cryst. alc.	76[d]	M 214.5		$C_{29}H_{26}O_2N_2$	N 6.45	6.35
*4,4'-Diamino-2,2'-dimethyl-d. p. m.	From *m*-toluidine by gen. proc., 13 hrs. heating	69.6[e]	M 123		$C_{15}H_{18}N_2$	C 79.65 H 7.97 N 12.39 Mol. wt. 226	79.74 7.87 12.33 225
*Hydrochloride	Aq. sol. pptd. by concd. HCl	..	M 258 dec.		$C_{15}H_{18}N_2HCl \cdot H_2O$	Cl 23.0 N 8.33	22.6 8.76
*Picrate (B.2 picr.)	Made in dil. AcOH; cryst. hot water	73	M 216.5 dec.				
*Diacetyl deriv.	By glac. AcOH; cryst. alc.		M 228		$C_{19}H_{22}O_2N_2$	N 9.03	8.80

[a] The method of Rivier and Farine (*loc. cit.*) gave higher yield and less resin. [b] Staedel and Haase [*Ann.*, **283**, 151 (1894)] reported acetic anhydride to yield the diacetyl derivative. [c] Method of Gram, *Ber.*, **25**, 302 (1892). [d] Crude yield nearly quantitative. [e] Weighed as hydrochloride first obtained from crude product.

7.97; N, 12.39; mol. wt. 226. Found: C, 79.48; H, 7.94; N, 12.30; mol. wt. 219. The **picrate*** was prepared in alcohol, and crystallized by diluting and chilling. After recrystallization from dilute alcohol, the small golden needles melted at 198.7° corr. (dec.). The **diacetyl derivative** 2,2'-bis-(acetamino)-5,5'-dimethyldiphenylmethane* was obtained in 88% yield by refluxing the base with glacial acetic acid, and purified by two recrystallizations from dilute alcohol, m. p. 226.5° corr.; nitrogen, 8.93; calcd. for $C_{19}H_{22}O_2N_2$, 9.03. The **tetracetyl derivative** 2,2'-bis-(diacetamino)-5,5'-dimethyl-diphenylmethane* was obtained similarly by use of acetic anhydride, the yield being nearly quantitative. Crystallized from dilute alcohol, the compound melted at 152° corr.; nitrogen, 7.08; calcd. for $C_{23}H_{26}O_4N_2$, 7.11.

The structure of this diaminoditolylmethane has never been determined, but was inferred by Eberhardt and Welter from its nitrogen content (found 12.75, calcd. 12.39), the fluorescence of its acid solutions, and the manner of its formation, the last being of reduced significance due to the very small yield. More satisfactory evidence is now available: (*a*) the complete analysis given above, (*b*) the preparation of the base from *o*-amino-*m*-xylyl-*p*-toluidine, (*c*) the base when diazotized gave a clear solution (which coupled strongly with β-naphthol) with no separation of nitrosamine, showing no secondary nitrogen, and (*d*) the base gave a tetracetyl derivative, showing both nitrogen atoms to be primary.

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Summary

1. The method of v. Braun for preparation of diaminodiarylmethanes from alkylanilines and alkyltoluidines by heating with formaldehyde in aqueous acid solution has been extended to other alkylanilines and also to aniline, *o*-toluidine and *m*-toluidine; it fails in the case of *p*-toluidine. Several of the diaminodiarylmethanes described are new, as are a number of derivatives.

2. The base 2,2'-diamino-5,5'-dimethyldiphenylmethane was prepared from *o*-amino-*m*-xylyl-*p*-toluidine. It is characterized more fully than hitherto, and a proximate structure proof is given.

3. Certain facts disclosed in this and earlier work are of significance with respect to the mechanism of the condensations of *p*-substituted amines with formaldehyde in media containing acid, and in conjunction with further results will be discussed in a later paper.

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