

several hours and the piperidine hydrobromide was filtered off. To the filtrate an absolute alcohol solution of hydrogen bromide (at least 0.3 g. per cc.) was added until no further precipitation occurred. The product precipitated as a finely divided, white solid, or as a golden oil which solidified to a finely divided, white solid on standing at 0°.

The dimethylamino- derivative was crystallized from absolute methanol, the diethylamino- compound from an absolute butanol solution saturated at 70°, and the di-*n*-propylamino- compound by dissolving it in three volumes of absolute butanol (1 g. per 10 cc.) at 65° and adding two volumes of petroleum ether. The dimethylamino-

diethylamino- and di-*n*-propylamino- derivatives, when they crystallized rapidly from solution, formed finely divided white powder. When crystallization was slow, colorless, thick, hexagonal plates were formed.

From the oil obtained as a final product in the attempt to prepare the di-*n*-butylamino- and the di-*n*-amylamino- derivatives, only the corresponding di-*n*-alkylamine hydrobromide and piperidine hydrobromide could be isolated. When subjected to vacuum distillation the oil darkened rapidly and formed a tar.

Summary

Five new β -bromo- α -di-*n*-alkylaminopropiophenone hydrobromides have been prepared.

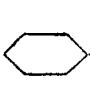
Three new β -N-piperidino- α -di-*n*-alkylaminopropiophenone dihydrobromides have been prepared.

The β -N-piperidino- α -di-*n*-alkylaminopropiophenone dihydrobromides do not show vaso-pressor or local anesthetic activity.

CHICAGO, ILLINOIS

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TABLE II

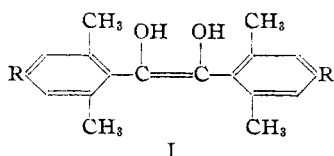
DIHYDROBROMIDES OF: 						
R =	M. p., °C.	Nitrogen, %		Bromine, %		Yield, %
		Calcd.	Found	Calcd.	Found	
CH ₃	190-191	6.63	6.68	37.86	37.76	58.54
C ₂ H ₅	164-165	6.22	6.19	35.51	35.38	73.28
<i>n</i> -C ₃ H ₇	154-155	5.85	5.71	33.41	33.34	54.97

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

Enediols. VII.¹ Bromostilbenediols

BY REYNOLD C. FUSON, S. L. SCOTT AND R. V. LINDSEY, JR.²

When it was discovered that 1,2-dimesityl-acetylene glycol (I, R = CH₃) was stable,³ a program of exploratory research was instituted to



study the relation of the various structural features of the molecule to its remarkable behavior. One problem was to determine the effect of substituents in the aromatic rings. However, the types of substituents, which can be so introduced and which at the same time can be tolerated under the experimental conditions necessary to produce an enediol, are greatly limited. One of the simplest of these is the bromine atom. The present report deals with its incorporation into various enediol molecules.

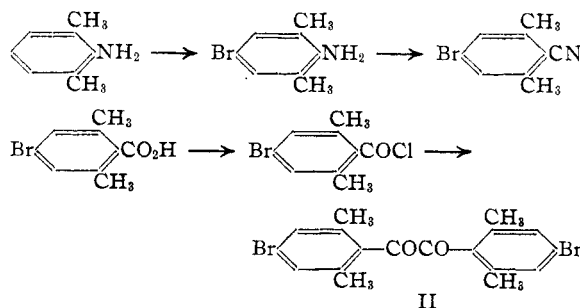
The first bromo enediols to be prepared were those derived from 4,4'-dibromo-2,6-xylyl (II).

(1) For the preceding communication in this series see Fuson and Kelton, *THIS JOURNAL*, **63**, 1500 (1941).

(2) Abbott Research Fellow, 1940-1941.

(3) Fuson and Corse, *THIS JOURNAL*, **61**, 975 (1939); Thompson, *ibid.*, **61**, 1281 (1939).

The latter was made from 2,6-xylydine according to the following scheme.



The hydrolysis of the nitrile was facilitated by the presence of the halogen atom. Yields of 70 to 80% of the acid were obtained by heating the nitrile for three hours at 170-180° with 70% sulfuric acid. Addition of sodium nitrite to the diluted sulfuric acid hydrolysis mixture, according to the method of Gattermann, Fritz and Beck,⁴ gave an almost quantitative yield of the bromo acid.

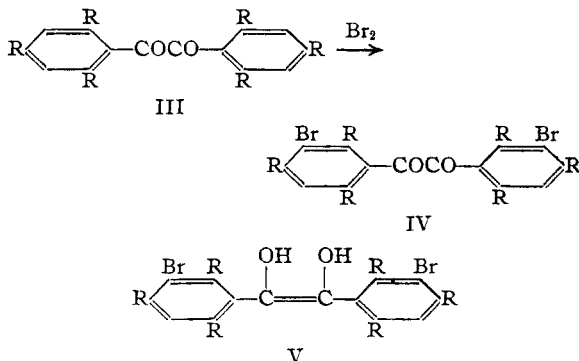
The bromine atoms had a similarly marked effect on the properties of the enediols. Whereas the enediols from 2,6-xylyl (I, R = H) could be

(4) Gattermann, Fritz and Beck, *Ber.*, **32**, 1122 (1899).

exposed to air for hours without appreciable change,⁵ their dibromo derivatives (I, R = Br) were extremely sensitive; a few minutes of exposure to the air suffice to produce a yellow coloration.

Since the bromine atom is ortho-para directing, it seemed likely that its pronounced activation of the enediol group might depend on its orientation with respect to that group. To test this, enediols have been made which hold bromine atoms in positions meta to the diol group. Results show that in this position the bromine atom brings about no very great change in the behavior of the enediol.

The enediols of this group (V, R = CH₃ or C₂H₅) were derived from mesitol (III, R = CH₃) and its ethyl analog (III, R = C₂H₅) by direct bromination followed by reduction.



Experimental

4-Bromo-2,6-xyloinitrile.—2,6-Xylidine was brominated according to the method described by Noelting, Braun and Thesmar,⁶ and the product, 4-bromo-2,6-xyloinitrile hydrobromide, was converted to the nitrile according to the procedure described in "Organic Syntheses"⁷ for *o*-tolunitrile. The solid nitrile was collected and recrystallized from methanol or ethanol; m. p. 71–72°; yield 84 g. (40%).

*Anal.*⁸ Calcd. for C₉H₈NBr: C, 51.43; H, 3.81. Found: C, 51.60; H, 3.94.

4-Bromo-2,6-xylic Acid.—A mixture of 15 g. of nitrile, 25 g. of concentrated sulfuric acid and 11 g. of water was heated for two hours at 150°. The flask was cooled to room temperature, 47 cc. of water was added, and heating was resumed until the solution boiled gently. To the hot solution was added slowly 100 cc. of a 10% solution of sodium nitrite.⁴ The flask was cooled to room temperature and the solid which separated was collected and recrystallized from benzene; m. p. 197–198°; yield 15.5 g.

Anal. Calcd. for C₉H₈O₂Br: C, 47.16; H, 3.93. Found: C, 46.95; H, 3.93.

The acid was also prepared from the nitrile by heating with 70% sulfuric acid for three hours at 170–180°. The yields varied from 70 to 80%.

4-Bromo-2,6-xyloyl Chloride.—A mixture of 24 g. of 4-bromo-2,6-xylic acid and 30 g. of thionyl chloride was heated over a small flame until complete solution was effected and then allowed to stand overnight. The excess thionyl chloride was removed and the product purified by distillation under reduced pressure; b. p. 105–106° (4 mm.). The acid chloride solidified in the receiver and was recrystallized from low-boiling petroleum ether in fine, white crystals; m. p. 56–57°; yield 25 g.

Action of the Binary Mixture on 4-Bromo-2,6-xyloyl Chloride.—The procedure was that described for the preparation of 1,2-di-(2,4,6-triethylphenyl)-acetylene glycol from 2,4,6-triethylbenzoyl chloride.⁹ The crude product, a dark red oil, was taken up in low-boiling petroleum ether and allowed to stand. A mixture of white and yellow crystals was obtained which was separated mechanically. Each component was recrystallized from high-boiling petroleum ether.

The yellow compound, 4,4'-dibromo-2,6-xylyl, melted at 211.5–212.5°; yield 4.2 g.

Anal. Calcd. for C₁₈H₁₆O₂Br₂: C, 50.94; H, 3.80. Found: C, 50.99; H, 3.98.

The white compound, 4,4'-dibromo-2,6-xyloin, melted at 143–144°; yield, 2.8 g.

Anal. Calcd. for C₁₈H₁₈O₂Br₂: C, 50.69; H, 4.26. Found: C, 50.77; H, 4.28.

The acetate of the xyloin was prepared in the usual manner by refluxing overnight a mixture of 0.5 g. of the xyloin and 10 cc. of acetic anhydride. The product was recrystallized from methanol; m. p. 163–164°; yield 0.5 g.

Anal. Calcd. for C₂₀H₂₀O₃Br₂: C, 51.28; H, 4.31. Found: C, 51.38; H, 4.40.

Oxidation of 4,4'-Dibromo-2,6-xyloin.—The oxidation was executed according to the procedure described in "Organic Syntheses"¹⁰ for the preparation of benzil. A mixture of 0.5 g. of the xyloin, 2 g. of copper sulfate, 10 cc. of pyridine and 10 cc. of water was heated under reflux for four hours. The product was recrystallized from high-boiling petroleum ether and identified as 4,4'-dibromo-2,6-xylyl by a mixed melting point determination.

cis-2,2',6,6'-Tetramethyl-4,4'-dibromostilbenediol.—The enediol was prepared by hydrogenating 1 g. of 4,4'-dibromo-2,6-xylyl in 50 cc. of methanol using a platinum catalyst. In one hour the solution was colorless and the reaction was complete. The reaction mixture was filtered and evaporated, leaving glistening white crystals which were washed with low-boiling petroleum ether and dried in a stream of dry nitrogen; m. p. 124–125°; yield 1 g.

Anal. Calcd. for C₁₈H₁₈O₂Br₂: C, 50.69; H, 4.26. Found: C, 50.79; H, 4.31.

The enediol was very unstable, turning yellow in a few minutes on exposure to air.

The diacetate was prepared in the usual manner by hydrogenating a mixture of 0.5 g. of the diketone, 0.1 g.

(5) Fuson, Scott, Horning and McKeever, *THIS JOURNAL*, **62**, 2091 (1940).

(6) Noelting, Braun and Thesmar, *Ber.*, **34**, 2242 (1901).

(7) "Organic Syntheses," Coll. Vol. I, p. 500.

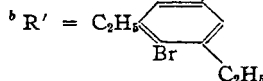
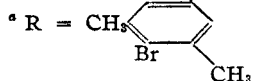
(8) Microanalyses by Mr. L. G. Fauble and Miss Mary S. Kreger.

(9) Fuson, Corse and McKeever, *THIS JOURNAL*, **61**, 2010 (1939).

(10) "Organic Syntheses," Coll. Vol. I, p. 80.

TABLE I

Compd.	M. p. (cor.)	Solvent	Analyses, %				Bromine	
			Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Calcd.	Found
	181.5-182.5 ^a	CCl ₄	53.09	53.04	4.42	4.53	35.39	35.53
	158-160 ^f	Bz.-pet. ether	52.86	53.04	4.84	4.99		
	204.5-205.5 ^f	Ether-pet. ether	52.86	53.03	4.84	5.11		
	197-198	Methanol	53.53	53.18	4.83	4.83	29.74	29.69
	237.5-239	Ethyl acetate	53.53	53.94	4.83	4.90	29.74	29.39
	133.5-135	Aq. methanol	52.86	53.01	4.84	5.06		
	113-114	Ethanol	58.23	58.08	5.97	5.99	29.84	29.95
	138-139 ^f	Pet. ether	57.99	58.24	6.32	6.60		
	179.5-180.5 ^f	Ether-pet. ether	57.99	58.14	6.32	6.44		
	152-152.7	Methanol	57.87		6.11		25.72	
	211.5-212.5	Ethyl acetate	57.87	58.06	6.11	6.18	25.72	25.84
	210-211	Bz. abs. alc.	64.34	64.54	5.63	5.79		
	207.5-208	CCl ₄	44.95	45.06	4.32	4.48	46.10	45.93



^c Prepared by direct bromination of the corresponding hexa-

alkylbenzil in gently refluxing carbon tetrachloride using powdered iron catalyst. ^d This benzil was cleaved with alkaline peroxide by the method of Weitz and Scheffer, *Ber.*, **54**, 2327 (1921), to give an acid which was identical with a sample of 3-bromomesitoic acid prepared by the method of Schildneck and Adams, *THIS JOURNAL*, **53**, 349 (1931). ^e Prepared by hydrogenation of the benzil in low-boiling petroleum ether-benzene solution according to the method of Thompson.³ ^f Determined in nitrogen-filled capillary. ^g Obtained by prolonged hydrogenation of the benzil as described by Thompson.⁸ ^h In the methyl series a 1:1 mixture of methanol and low-boiling petroleum ether was used as the solvent. Methyl alcohol was employed in the ethyl series. ⁱ Prepared by hydrogenating the corresponding benzil in acetic anhydride.³ ^j Prepared by refluxing the enediol with acetic anhydride.⁸ ^k Obtained together with some *trans* enediol by allowing a solution of the reduced benzil to stand in contact with hydrogen and platinum catalyst for twenty hours. Oxidation of the 3,3'-dibromomesitoins with copper sulfate in pyridine produced 3,3'-dibromomesitol.¹⁰ ^l Prepared by the action of the binary mixture, Mg + MgI₂, on the benzil. See Fuson, McKeever and Corse, *THIS JOURNAL*, **62**, 600 (1940). ^m Prepared by refluxing the enediol in benzoyl chloride.⁹ Only one form of the dibenzoate was isolated and hence its configuration is not known. ⁿ Prepared by brominating 2,2',4,4',6,6'-hexaethyl-3,3'-dibromobenzil in refluxing carbon tetrachloride using iron catalyst.

of platinum oxide, 0.1 g. of fused zinc chloride, four drops of concentrated hydrochloric acid and 50 cc. of acetic anhydride. The diacetate was recrystallized from methanol; m. p. 186.5-187.5°; yield 0.5 g.

Anal. Calcd. for C₂₂H₂₂O₄Br₂: C, 51.74; H, 4.35. Found: C, 51.87; H, 4.48.

Ketonization of 2,2',6,6'-Tetramethyl-4,4'-dibromostilbenediol.—The rearrangement was effected in methanol saturated with dry hydrogen chloride. From 0.12 g. of the enediol there was obtained 0.11 g. of 4,4'-dibromo-2,6-

xyloin, identified by a mixed melting point determination.

***trans*-2,2',6,6'-Tetramethyl-4,4'-dibromostilbenediol.**—One gram of the xylin, suspended in 50 cc. of methanol containing a drop of piperidine, was treated with hydrogen for forty-one and one-half hours in the presence of 0.1 g. of platinum oxide catalyst. The enediol, obtained in the usual fashion, was washed with high- and low-boiling petroleum ether and dried in a stream of dry nitrogen; m. p. 183-184°; yield 1 g. This enediol differed very little in stability from the *cis*-isomer.

Anal. Calcd. for $C_{18}H_{18}O_2Br_2$: C, 50.69; H, 4.26. Found: C, 50.87; H, 4.38.

The diacetate was prepared by refluxing 0.3 g. of the high-melting enediol in 20 cc. of acetic anhydride for three hours. The product was recrystallized from high-boiling petroleum ether; m. p. 241–242°; yield 0.3 g.

Anal. Calcd. for $C_{22}H_{22}O_4Br_2$: C, 51.74; H, 4.35. Found: C, 51.47; H, 4.42.

A dibenzoate of the enediol was prepared by refluxing a mixture of 0.3 g. of the enediol, 5 cc. of benzoyl chloride and 20 cc. of pyridine for three hours. The dibenzoate crystallized from a mixture of benzene and absolute alcohol in glistening white leaflets; m. p. 265–267°; yield 0.28 g.

Anal. Calcd. for $C_{32}H_{26}O_4Br_2$: C, 60.55; H, 4.13. Found: C, 60.76; H, 4.27.

Reaction of 4,4'-Dibromo-2,6-xylyl with Hydroxylamine.—A mixture of 0.5 g. of hydroxylamine hydrochloride, 0.5 g. of potassium hydroxide, 0.3 g. of the diketone and 20 cc. of ethanol was heated under reflux overnight. The light orange solution was cooled, poured into 200 cc. of water and the mixture made slightly acidic with dilute hydrochloric acid. The white, flocculent precipitate which formed was extracted with ether; the ether solution was

washed with water, 10% potassium bicarbonate solution, and again with water. It was then treated with Norit, filtered and the ether was evaporated. The residue separated from a benzene–high-boiling petroleum ether mixture in fine, white crystals; m. p. 222–223°; yield 0.28 g.

Anal. Calcd. for $C_{18}H_{17}O_2NBr_2$: C, 49.19; H, 3.90; N, 3.19. Found: C, 49.41; H, 3.97; N, 3.18.

The melting points and analytical data for the new compounds in the mesityl and triethylphenyl series have been collected in Table I.

Summary

Enediols have been prepared from 4,4'-dibromo-2,6-xylyl (II), from 3,3'-dibromomesityl (IV, $R = CH_3$) and from 3,3'-dibromohexaethylbenzil (IV, $R = C_2H_5$). Those in which the bromine atoms are meta to the diol group are not greatly different from the corresponding bromine-free compounds. Bromine atoms which are in positions para to the diol group, however, render the enediols much more sensitive to oxidation by the air.

URBANA, ILLINOIS

RECEIVED MARCH 31, 1941

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE UNIVERSITY OF MICHIGAN]

Some Modifications of the Synthesis of 3,4-Benzpyrene from Pyrene

BY W. E. BACHMANN, MARVIN CARMACK¹ AND S. R. SAFIR

In the Cook and Hewett² synthesis of the carcinogenic hydrocarbon 3,4-benzpyrene, pyrene is condensed with succinic anhydride, the resulting β -3-pyrenoylpropionic acid (I) is reduced to γ -3-pyrenylbutyric acid, the latter is cyclized to 4'-ketotetrahydrobenzpyrene and the ketone is converted to the hydrocarbon. In this paper we are reporting some modifications of this synthesis which we found useful for preparing the hydrocarbon.³

Usually β -aroylpropionic acids are reduced by the Clemmensen method, but Cook and Hewett² and also Martin⁴ have shown that the method fails with β -3-pyrenoylpropionic acid. Neither the acid nor its ester was reduced by zinc and hydrochloric acid with or without the use of toluene, and the employment of acetic acid in the reducing mixture resulted in the formation of resinous products. Although Cook and Hewett succeeded in reducing the keto acid by means of zinc and

alkali, a reaction which Vollmann, Becker, Corell and Streeck⁵ carried out most successfully in an autoclave at 80–100 atmospheres pressure, it seemed desirable to reinvestigate the Clemmensen method because of the simplicity of the procedure employed and because it was of interest to know whether conditions could be found for reducing the compound by this method. After considerable experimentation, it was found that the keto acid is reduced to γ -3-pyrenylbutyric acid when a mixture of chlorobenzene, xylene and acetic acid is used in the Clemmensen mixture. The yields of fairly pure reduced acid varied from 68 to 84% and depended chiefly on the amounts being reduced. It is noteworthy that under the conditions employed the reaction proceeds extremely rapidly for a Clemmensen reaction in spite of the slight solubility of the keto acid; thus, on a 2-g. run a 70% yield of the reduced acid was obtained when only two hours were allowed for the reaction.

A small amount of a rather insoluble colorless solid is formed as a by-product in the reaction;

(1) From the Ph.D. dissertation of Marvin Carmack.

(2) Cook and Hewett, *J. Chem. Soc.*, 398 (1933).

(3) Fieser [*Am. J. Cancer*, **34**, 76 (1938)] has discussed the relative merits of the procedures that have been employed to prepare the hydrocarbon and its intermediates.

(4) Martin, *THIS JOURNAL*, **58**, 1438 (1936).

(5) Vollmann, Becker, Corell and Streeck, *Ann.*, **531**, 1 (1937).