

(98%).<sup>11-14</sup> A modification of this method is the procedure of Normant and Voreux,<sup>15</sup> in which the intermediate is the acetate of tetramethylene chlorohydrin. Furthermore, the chlorination of *n*-butyl bromide with atomic chlorine or sulfonyl chloride has been suggested as a method for the preparation of tetramethylene chlorobromide; in this reaction a yield of 35% is obtained.<sup>16</sup>

Attempts have been made to improve the conversion of tetramethylene chlorohydrin into the chlorobromide. However, the use of sodium bromide and concentrated sulfuric acid, or the application of phosphorus and bromine to this step, did not give better overall yields (58%; 40%) for the conversion of tetrahydrofuran into tetramethylene chlorobromide. Eventually, it was found that the treatment of tetrahydrofuran with a mixture of sodium chloride, sodium bromide, and concentrated sulfuric acid gives in a single step a 44% yield of the desired substance, which is accompanied by a 10% yield of tetramethylene dibromide. In our experience, this represents the easiest method for the preparation of tetramethylene chlorobromide.

#### EXPERIMENTAL

**Tetramethylene dibromide.** To a solution of sodium bromide (500 g; 4.85 mole) in water (600 ml.), there were added tetrahydrofuran (144 g.; 2.0 mole) and, with efficient agitation, concentrated sulfuric acid (750 ml.). The temperature was kept at 70–72°. The mixture was heated on the steam bath for 8 hr., then the two liquid layers were decanted from the solid phase and separated. The aqueous layer and the solid phase were washed with benzene (500 ml.), and the benzene extract was combined with the organic layer. The combined product was washed with sodium carbonate solution, sodium bisulfite solution, and water, dried, and distilled. Thus, 71 g. (86%) of the dibromide, b.p. 194–196°, was obtained.

**Tetramethylene chlorobromide.** (1) To a solution of sodium bromide (65 g.; 0.64 mole) in water (150 ml.), tetramethylene chlorohydrin (54.3 g.; 0.5 mole) and concentrated sulfuric acid (190 ml.) were added successively with efficient agitation. The temperature rose to 60–70°. The mixture was heated for 3 hr. on the water bath with continued agitation and kept at room temperature for 12 hr. Benzene was added and the organic layer separated, washed with 5% sodium hydroxide solution, sodium sulfite solution, and water, and then dried. Distillation gave 63.6 g., boiling at 87–95° (35 mm.). Fractionation of the product gave 49.9 g. (58%) of tetramethylene chlorobromide, b.p. 173–177°,  $n_D^{20}$  1.4870, and 9.5 g. (9%) of tetramethylene dibromide, b.p. 193–195°  $n_D^{20}$  1.5162.

(2) To a mixture of crude tetramethylene chlorohydrin,

prepared from 228 g. (3.2 mole) of tetrahydrofuran<sup>17</sup> and 33 g. (1.07 mole) of red phosphorus, bromine (240 g., 1.5 mole) was added within 3 hr., with cooling and agitation. The reaction product was poured into ice water and the organic layer separated, washed with sodium bicarbonate solution and water, and dried. Distillation under 30 mm pressure (b.p. 80–85°) and at atmospheric pressure (b.p. 172–176°) gave 221 g. (43%) of tetramethylene chlorobromide,  $n_D^{20}$  1.4872.

(3) Sodium bromide (124 g., 1.2 mole) and sodium chloride (76 g.; 1.3 mole) were dissolved in water (400 ml.), and tetrahydrofuran (72 g.; 1.0 mole) and, with agitation, concentrated sulfuric acid (400 ml.) were added, the latter at such a rate that the temperature did not exceed 70°. The mixture was then heated for 3 hr. at 100°, kept for 12 hr. at room temperature, and extracted with benzene or ether (250 ml.), and the extract was washed with 5% sodium hydroxide solution, sodium bisulfite solution, and water, dried and distilled. The product which collected between 65 and 100° at 6 mm. pressure was washed again with 20% sodium hydroxide solution and fractionated: 173–177°, tetramethylene chlorobromide,  $n_D^{20}$  1.4870, yield, 75.5 g. (44%); 193–195°, tetramethylene dibromide,  $n_D^{20}$  1.5162, yield, 22.7 g. (10%).

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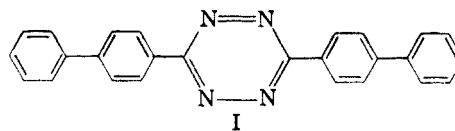
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### Heterocyclic Analogs of Terphenyl: 3,6-Diaryl-1,2,4,5-Tetrazines

RICHARD H. WILEY,<sup>1</sup> C. H. JARBOE, JR.,<sup>2</sup> AND F. N. HAYES

Received January 8, 1957

As part of a study of the heterocyclic analogs of terphenyl and quaterphenyl, which are of interest as solutes in liquid scintillation counting systems, we have devised improved syntheses for two previously known 3,6-diaryl-1,2,4,5-tetrazines (3,6-diphenyl<sup>3</sup> and 3,6-di-*m*-tolyl<sup>4</sup>) and synthesized for the first time 3,6-di-*p*-biphenyl-1,2,4,5-tetrazine (I) as well as the corresponding dihydrotetrazines.



The preparation of these compounds has been accomplished by a variation of the original Pinner synthesis in which the imido ester of an aromatic nitrile was reacted with hydrazine in an aqueous solution of either ammonium hydroxide or potassium hydroxide. Under these reaction conditions

(1) To whom inquiries should be sent.

(2) Atomic Energy Commission Postdoctoral Research Assistant.

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a complex mixture of products is formed and the desired dihydro-1,2,4,5-tetrazine is difficult to separate from the mixtures. In our variation of this procedure the reaction is carried out under anhydrous conditions in a mixture of methanol and triethylamine. The dihydrotetrazine precipitates from this reaction mixture, the reaction time is shortened, and the overall yields are improved to around 50%. Attempts to prepare those diaryltetrazines containing electron attracting substituents and 3,6-dipyridyl-1,2,4,5-tetrazine were unsuccessful by either procedure.

The infrared spectra of these 3,6-diaryl-1,2,4,5-tetrazines show a very strong ring stretching vibration at 1375–1390  $\text{cm}^{-1}$  which appears to be a characteristic of the tetrazine ring since it is absent from the spectra of the corresponding dihydrotetrazines. Another rather unique feature of these spectra is a strong band at 913–925  $\text{cm}^{-1}$ . A similar band was found in the spectrum of azobenzene at 920  $\text{cm}^{-1}$  but was absent from the spectrum of both freshly recrystallized hydrazobenzene and the dihydro derivative of 3,6-di-*p*-biphenyl-1,2,4,5-tetrazine. Although this would seem to indicate a connection between this frequency and the azo linkage, data for additional compounds is needed to establish this definitely. When examined by previously described techniques<sup>5,6</sup> none of these compounds showed relative pulse heights in excess of 0.12.

#### EXPERIMENTAL

Details are given for the preparation of a typical dihydro-tetrazine and tetrazine. Similar procedures were used in the preparation of 3,6-diphenyl-1,2,4,5-tetrazine, m.p. 195° (reported,<sup>1</sup> 192°), yield 55%, and 3,6-di-*m*-tolyl-1,2,4,5-tetrazine, m.p. 151° (reported,<sup>2</sup> 150–52°), yield 53%.

**1,2-Dihydro-3,6-di-*p*-biphenyl-1,2,4,5-tetrazine.** Dry hydrogen chloride gas was bubbled for 12 hr. into a solution of 10 g. (0.058 mole) *p*-biphenylcarbonitrile in 200 ml. of anhydrous methanol. At the end of this time the methanol solution was kept at 0° for 4 hr. to cause precipitation of the crystalline methyl *p*-biphenylimidate hydrochloride. This slurry of the imido ester hydrochloride in methanol was added very slowly and cautiously to a solution of 5 g. 95% hydrazine in 200 ml. anhydrous methanol and 100 g. triethylamine. After the addition was complete the mixture was heated on a steam bath until precipitation of the yellow-orange dihydro-tetrazine was complete. The precipitate was immediately filtered and washed with distilled water. Recrystallization from toluene yielded 6 g. (53.5%) of yellow-orange plates melting at 160° with resolidification. No attempt was made to obtain analytical data on this compound since it is so readily oxidized by air.

**3,6-Di-*p*-biphenyl-1,2,4,5-tetrazine.** To a solution of 5 g. of isoamyl nitrite in 100 ml. 95% ethanol was added 6 g. of 1,2-dihydro-3,6-di-*p*-biphenyl-1,2,4,5-tetrazine. This mixture was refluxed for 4 hr., cooled to room temperature, and filtered. The product was recrystallized from toluene to yield 5 g. (83.5%) of fuchsia needles, m.p. 297° (corr.).

*Anal.* Calcd. for  $\text{C}_{26}\text{H}_{18}\text{N}_4$ : C, 80.80; H, 4.70; N, 14.50. Found: C, 80.56; H, 4.56; N, 14.55.

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*Acknowledgment.* This research was completed in part under contract AT-(40-1)-2162 between the University of Louisville and the Atomic Energy Commission. The authors acknowledge this support with gratitude.

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LOUISVILLE 8, KY.

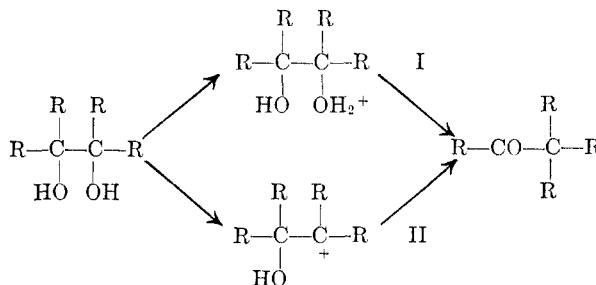
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UNIVERSITY OF CALIFORNIA  
LOS ALAMOS, N. M.

### The Pinacol Rearrangement<sup>1</sup>

NORMAN C. DENO AND CARL PERIZZOLO<sup>2</sup>

Received January 11, 1957

The pinacol rearrangement is acid-catalyzed and could conceivably proceed through an intermediate protonated glycol (I) or the free alkyl cation (II). Duncan and Lynn<sup>3</sup> concluded that for pinacol



itself (2,3-dimethyl-2,3-butanediol) the reaction proceeded *via* I. This conclusion was based on the observation that  $d \log k = -d H_0$ . However, the comparison was made using values of  $H_0$  measured at 25° with values of  $\log k$  measured at 70–150°.

We have now measured the rate of conversion of pinacol to pinacolone from 39–75% sulfuric acid at  $25 \pm 0.01^\circ$ . The data, which are summarized in Table I, show that the relation  $d \log k = -d H_0$  is precisely followed.

The conclusions of Duncan and Lynn can be extended as follows. The hypothesis has been developed<sup>4</sup> that if the transition state were of type I with the positive charge residing principally on the  $\text{OH}_2$  group,  $d \log k$  would equal  $-d H_0$ . For transition states of type II,  $d \log k$  would equal  $-d C_0$ . For transition states intermediate between I and II,  $d \log k$  would have values intermediate between

(1) Grateful acknowledgment is made of the support of this research by a grant from the Petroleum Research Fund of the AMERICAN CHEMICAL SOCIETY.

(2) Recipient of the Carbide and Carbon Fellowship for 1956–57.

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