

(yield 91%) as long golden yellow blades, m.p. 151–152°. Lit.<sup>3</sup> m.p. 149°.

*Anal.* Calcd. for  $C_{12}H_{10}N_4$ : C, 68.55; H, 4.80; N, 26.65. Found: C, 68.63; H, 4.63; N, 26.40.

The following five azines were similarly prepared.

*3-Pyridinaldazine*, golden yellow prismatic needles (4.1 g., yield 91%) from aqueous methanol, m.p. 148–149°. A specimen on admixture with 2-pyridinaldazine melted at 126–128°.

*Anal.* Calcd. for  $C_{12}H_{10}N_4$ : C, 68.55; H, 4.80; N, 26.65. Found: C, 68.45; H, 4.69; N, 26.45.

*4-Pyridinaldazine*, golden yellow needles (4.15 g., yield 92%) from aqueous methanol, m.p. 192–193°.

*Anal.* Calcd. for  $C_{12}H_{10}N_4$ : C, 68.55; H, 4.80; N, 26.65. Found: C, 68.60; H, 4.91; N, 26.35.

*1-Naphthaldazine*, yellow needles (3 g., yield 90%) from acetone-methanol, m.p. 155–156°. Lit.<sup>15</sup> m.p. 152°.

*2,2'-Dichlorobenzalazine*, long yellow needles (2.6 g., yield 87%) from methanol, m.p. 150–151°. Lit.<sup>16</sup> m.p. 143–145°.

*3,3'-Dinitrobenzalazine*, yellow blades (2.9 g., yield 89%) from acetic acid, m.p. 196–197°. Lit.<sup>17</sup> m.p. 194°.

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## Preparation of 2-Cyanotetrahydropyran<sup>1</sup>

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Although substituted 2-cyanotetrahydropyrans have been reported in the literature, they have been prepared either by addition of hydrogen cyanide to substituted dihydropyrans<sup>3</sup> or by reaction of appropriate acroleins and vinyl cyanides<sup>4</sup> in reactors at moderate pressure. There appeared to be no simple laboratory procedure for 2-cyanotetrahydropyran which was needed for other research. Accordingly the metathesis of 2-bromotetrahydropyran with metal cyanides has been partly evaluated as a method of synthesis.

2-Bromotetrahydropyran<sup>5</sup> solutions were treated in toluene with cuprous, mercuric, potassium, and silver cyanides in the manner reported for open chain,  $\alpha$ -chloro ethers.<sup>6</sup> Maximum conversions were obtained in experiments at 20–30°. None of the desired product was formed when potassium cyanide was used and the yield was only 12% from cuprous

cyanide. However, silver and mercuric cyanides gave 27–30% yields of 2-cyanotetrahydropyran.

The compound was characterized by hydrolysis in 63% yield to tetrahydropyran-2-carboxylic acid<sup>7</sup> and by reaction with benzylmagnesium chloride to form 2-(phenylacetyl)tetrahydropyran.

## EXPERIMENTAL

*2-Cyanotetrahydropyran.* A solution of 85 g. (1.0 mole) of 2,3-dihydro-4H-pyran in 300 ml. of dry toluene was maintained at –10 to 0° while a stream of hydrogen bromide was added with stirring until 73 g. (0.90 mole) had been absorbed. The 2-bromotetrahydropyran so obtained was used for the preparation of the 2-cyano compound since attempts to isolate the halopyran by vacuum distillation resulted in decomposition.<sup>8</sup>

The toluene solution was added dropwise with stirring to a suspension of 252 g. (1.0 mole) of mercuric cyanide in 200 ml. of dry toluene in an exothermic reaction that was kept at 20–25°. After 2 hr. the mixture was filtered and the filtrate was washed with water, dried, and distilled to give 21–30 g. (21–30%) of 2-cyanotetrahydropyran, b.p. 90–92°/18 mm.,  $n_D^{25}$  1.4430.

In a similar way, 40 g. (0.30 mole) of silver cyanide added over 30 min. to 51 g. (0.31 mole) of the bromopyran in 200 ml. of dry toluene at 25–30° gave 9.0 g. (27%) of 2-cyanotetrahydropyran, b.p. 77–83°/16 mm.,  $n_D^{25}$  1.4455.

*Anal.* Calcd. for  $C_6H_9ON$ : C, 64.85; H, 8.16; N, 12.60. Found: C, 65.15; H, 8.16; N, 12.63.

Reaction of equimolar amounts of 2-bromotetrahydropyran and cuprous cyanide in a similar manner at 20–25° gave 12% of product, b.p. 75–79°/15 mm.,  $n_D^{25}$  1.4422, provided the reaction mixture was washed with 10% ammonium hydroxide before distillation.

*2-Tetrahydropyrancarboxylic acid.* A mixture of 55.6 g. (0.50 mole) of 2-cyanotetrahydropyran was boiled for 7 hr. with 40.0 g. (1.00 mole) of sodium hydroxide in 200 ml. of water. The alkaline solution was extracted with three 50-ml. portions of ether and exactly neutralized with one equivalent of hydrochloric acid. Ether extraction in a liquid-liquid extractor and distillation of the ether extract gave 41 g. (63%) of 2-tetrahydropyrancarboxylic acid, b.p. 142–145°/20 mm.,  $n_D^{25}$  1.4620.

*Anal.* Calcd. for  $C_6H_{10}O_3$ : C, 55.37; H, 7.75; neut. equiv., 130. Found: C, 55.50; H, 7.82; neut. equiv. 129.

The acid was further characterized by conversion to phenacyl 2-tetrahydropyrancarboxylate, m.p. 74–76°.

*Anal.* Calcd. for  $C_{14}H_{16}O_4$ : C, 67.72; H, 6.50. Found: C, 67.92; H, 6.65.

*2-(Phenylacetyl)tetrahydropyran.* A solution of 16.8 g. (0.15 mole) of 2-cyanotetrahydropyran in 100 ml. of ether was added dropwise to the Grignard reagent prepared from 7.2 g. (0.30 mole) of magnesium and 38 g. (0.30 mole) of benzyl chloride in 400 ml. of anhydrous ether. One hour after addition was complete, hydrolysis with ice and dilute hydrochloric acid and distillation of the dried ether layer gave 13 g. (42%) of 2-(phenylacetyl)tetrahydropyran, b.p. 155–165°/3–4 mm.,  $n_D^{25}$  1.5241. An analytical sample was obtained as a fraction, b.p. 140–141°/3 mm.,  $n_D^{25}$  1.5218.

*Anal.* Calcd. for  $C_{13}H_{16}O_2$ : C, 76.44; H, 7.90. Found: C, 76.54; H, 8.00.

This product was further characterized as the 2,4-dinitrophenylhydrazone, m.p. 139–142°.

(7) R. Paul and S. Tchelitcheff, *Compt. rend.*, **232**, 2230 (1951).

(8) 2-Chlorotetrahydropyran made the same way can be distilled although occasionally rapid decomposition may occur.

(1) Abstracted from the senior thesis of Kenneth Yorka, De Paul University, 1955. Preliminary experiments were conducted by A. M. Laurinaitis.

(2) Present address: 1653 S. Elm Ave., Bartlesville, Okla.

(3) C. W. Smith, U. S. Patent 2,489,729 (Nov. 29, 1949).

(4) C. W. Smith, D. G. Norton, and S. A. Ballard, *J. Am. Chem. Soc.*, **73**, 5270 (1951).

(5) R. Paul, *Bull. soc. chim. France*, **5**, 1, 1397 (1937); *Compt. rend.*, **198**, 375, 1246 (1934).

(6) S. P. Lingo and H. R. Henze, *J. Am. Chem. Soc.*, **61**, 1574 (1939). Also, H. R. Henze, G. W. Benz, and G. L. Sutherland, *J. Am. Chem. Soc.*, **71**, 2122 (1949). The subject has been reviewed by D. T. Mowry, *Chem. Revs.*, **42**, 199 (1948).

Anal. Calcd. for  $C_{19}H_{20}O_5N_4$ : C, 59.36; H, 5.24; N, 14.59. Found: C, 59.23; H, 5.29; N, 14.60.

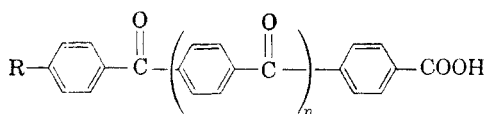
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### *p*-(*p*-Benzoylbenzoyl)benzoic Acid

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Information concerning the synthesis of linear polybenzoylbenzoic acids of type I is sparse. Koelsch and Bryan<sup>2</sup> prepared dibasic acids (Ia, n



Ia, R = COOH

Ib, R = H

= 1, 2, 3) by acylating toluene with acid chlorides such as those derived from terphthalic acid, *p,p'*-benzophenonedicarboxylic acid, etc., and subsequently oxidizing the end methyl groups to carboxylic acid groups. Acylation of benzene with *p,p'*-benzophenonedicarbonyl chloride gave *p*-(*p*-benzoylbenzoyl)benzoic acid as a by-product.<sup>3</sup> Finally, the acid catalyzed condensation of benzyl alcohol yields polymers which oxidized to a mixture of polyketones containing both ortho and para linkages.<sup>4</sup>

A possible route to compounds of type Ib is the Friedel-Crafts arylation of *p*-benzylbenzoic acid by halides such as benzoyl chloride and *p*-benzoylbenzoyl chloride. In this way the preparation of *p*-(*p*-benzoylbenzoyl)benzoic acid and its oxidation product, *p*-(*p*-benzoylbenzoyl)benzoic acid, was readily achieved. However, the few attempts to extend the synthesis were unsuccessful.

#### EXPERIMENTAL

*p*-(*p*-Benzoylbenzoyl)benzoic acid. A solution of 0.05 mole of benzoyl chloride in 30 ml. of carbon disulfide was added with stirring to 0.04 mole of *p*-benzylbenzoic acid<sup>5</sup> and 0.16 mole of aluminum chloride in 30 ml. of carbon disulfide. The mixture was stirred and heated under reflux for 3 hr. after which it was hydrolyzed with ice and hydrochloric

acid. The carbon disulfide was removed by steam distillation and the residue was dissolved in aqueous alkali and filtered. Acidification precipitated the crude acid which was twice recrystallized with decolorization from 150-ml. portions of methanol to give 6.6 g. (52%) of *p*-(*p*-benzoylbenzoyl)benzoic acid, m.p. 181.5–182.5°.

Anal. Calcd. for  $C_{21}H_{16}O_5$ : C, 79.73; H, 5.10; N.E. 316. Found: C, 79.50; H, 5.17; N.E. 316.

*p*-(*p*-Benzoylbenzoyl) benzoic acid. A solution of 3.5 g. of sodium dichromate in 5 cc. of water, 8 cc. of acetic acid, and 1.7 cc. of concentrated sulfuric acid was added dropwise over a 20-min. period to a boiling solution of 3.0 g. of *p*-(*p*-benzoylbenzoyl)benzoic acid in 25 ml. of acetic acid. After 45 min. it was poured into water and the precipitate was collected. This was difficultly soluble in dilute sodium hydroxide and methanol. Crystallization from 30 ml. of dioxane gave 2.0 g. (64%) of *p*-(*p*-benzoylbenzoyl)benzoic acid, m.p. 268.5–269.5° (lit., m.p. 268°).<sup>3</sup>

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### Estrogen Esters<sup>1</sup>

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In the steroid field the same acylating group can promote a desirable physiological response in more than one hormone category.<sup>2,3</sup>

This study extended our observations with the acylation of androgens<sup>4</sup> to the synthetic estrogens diethylstilbestrol (I) and hexestrol (II). More particularly, we were interested in varying the character of the acylating group so that the estrogenic activity inherent in I and II would be increased as well as decreased. This objective is an outgrowth of the provocative concept of Myers<sup>5</sup> and coworkers who have stressed the importance of the steroid sex

(1) Presented at the Meeting-in-Miniature, North Jersey Section, American Chemical Society, January 1958.

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(1) Present address: 1653 Elm Street, Bartlesville, Okla.

(2) C. F. Koelsch and C. E. Bryan, *J. Am. Chem. Soc.*, **67**, 2041 (1945).

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