

material had b.p. 98.5° (770 mm.) and  $n_D^{25}$  1.4050. Our final experiments were carried out with 2-heptene which was prepared by a method similar to that used by Wibaut and Gitsels<sup>12</sup> for the preparation of 3-octene. The alkene was distilled through the Fenske column and had b.p. 98.5° (766 mm.) and  $n_D^{25}$  1.4043. The infrared spectrograms of the two samples of 2-heptene were identical except for minor differences in intensity of absorption. Carbon tetrachloride was purified according to Fieser.<sup>13</sup> N-Bromosuccinimide (Arapahoe Chemicals, Inc., Boulder, Colo.) was used as purchased.

**4-Bromo-2-heptene.**—The influence of the following factors on the reaction was studied: ratio of reactants, time of refluxing, light and benzoyl peroxide. The procedure described below gave consistently good results. In a 500-ml., three-necked flask fitted with a stirrer, reflux condenser and nitrogen inlet tube were placed 40 g. (0.41 mole) of synthetic 2-heptene, 48.1 g. (0.27 mole) of NBS, 250 ml. of carbon tetrachloride and 0.2 g. of benzoyl peroxide (Distillation Products, Rochester, N. Y.). The mixture was stirred and refluxed in a nitrogen atmosphere for two hours. The reaction mixture was cooled, the succinimide removed by filtration and washed with two 15-ml. portions of carbon tetrachloride. The succinimide weighed 26.5 g. (99%). The volatile material was removed from the carbon tetrachloride solution by distillation *in vacuo* through a 20-cm. column filled with glass helices. The residue was then distilled from a Claisen flask. Both distillations were carried out in a nitrogen atmosphere. There was a forerun of 1.2 g., b.p. 31–71.5° (37 mm.),  $n_D^{25}$  1.4650; then 36.3 g. (76%) of 4-bromo-2-heptene was collected, b.p. 71.5–72° (37 mm.),  $n_D^{25}$  1.4712,  $d_4^{25}$  1.151; 6.6 g. of high boiling material,  $n_D^{25}$  1.5174, remained in the distilling flask. This represents our best yield; the yield was usually 60–70%.

*Anal.* Calcd. for C<sub>7</sub>H<sub>13</sub>Br: C, 47.5; H, 7.2; Br, 45.2. Found<sup>14</sup>: C, 47.3; H, 7.4; Br, 45.3; active bromine (determined by a five-minute reflux of the compound with alcoholic silver nitrate), 44.9.

The infrared spectrogram of the 4-bromo-2-heptene had absorption maxima at the same wave lengths as the 2-heptene, and one additional peak at 8.5  $\mu$ . In neither curve was there any evidence of terminal carbon-carbon unsaturation.

**Ozonation of 4-Bromo-2-heptene.**—A solution of 17.5 g. (0.1 mole) of 4-bromo-2-heptene in 150 ml. of purified *n*-pentane<sup>15</sup> was ozonized in an apparatus which has been described elsewhere.<sup>15</sup> The reaction mixture was kept at –45 to –38° during the ozonation. The ozonizer was producing 395 mg. of ozone per hour (gas flow, 11.4 l. per hour; 1.64 volume % of ozone). The ozone-oxygen solution was led into the reaction flask for 12.15 hours in order to introduce 0.1 mole of ozone. The effluent gas from the reaction flask first contained ozone 9.79 hours after the start of the ozonation, but between this time and the conclusion of the reaction only 4 mg. of ozone was unabsorbed by the reaction mixture.

**Decomposition of Ozonide and Identification of Products.**—The ozonide-pentane solution was transferred to a one-liter, three-necked flask which was in an ice-bath. The flask was kept in the ice-bath and the pentane removed *in vacuo*. The flask was then fitted with a stirrer, dropping funnel, reflux condenser and thermometer well. The ice-bath was replaced by a salt-ice-bath, and 250 ml. of aqueous hydrogen peroxide (2.76% hydrogen peroxide) was added dropwise to the reaction flask during 1.25 hours. The addition of the hydrogen peroxide was regulated such that the temperature of the reaction mixture never rose above 0°. The mixture was allowed to stand at room temperature for two days, stirred at room temperature for 12 hours, refluxed for one hour, cooled, a spatula tip of Adams platinum oxide added and the mixture allowed to stand overnight. After refluxing for one hour the reaction mixture gave a negative test for peroxide with potassium iodide. The platinum oxide was removed by filtration, and the

aqueous layer extracted with five 25-ml. portions of ether. The combined ether extracts were dried over freshly heated sodium sulfate.

The aqueous layer was neutralized to a phenolphthalein end-point with 1 *N* sodium hydroxide. The solution was evaporated to dryness *in vacuo*, and after drying in a vacuum desiccator over phosphorus pentoxide the residue weighed 7.8 g. The theoretical amount of sodium acetate would be 8.2 g. Fusion of a portion of the residue with sodium and subsequent testing for bromide gave a negative result. Were  $\alpha$ -bromoacetic acid or  $\alpha$ -bromopropionic acid formed during the ozonolysis procedure, one might expect some of these acids to remain in the aqueous layer. Two-tenths of a gram of the residue gave 0.38 g. of *p*-bromophenacyl ester, m.p. 83–84.5°; the same amount of residue also gave 0.16 g. of *p*-nitrobenzyl ester, m.p. 75–77°. Authentic sodium acetate (0.20 g.) gave 0.41 g. of *p*-bromophenacyl ester, m.p. 83.5–84°, and 0.19 g. of *p*-nitrobenzyl ester, m.p. 76–77°; mixed m.p. 83–84° and 76–77°, respectively.

The ether layer was filtered from the sodium sulfate and the ether removed through a column filled with glass helices. The lachrymatory residue was vacuum distilled to give a forerun and then three fractions (combined weight 5.4 g.) having  $n_D^{25}$  1.4467, 1.4578 and 1.4580 were collected at 70–80° (9 mm.). Two-tenths of a gram of this material gave 0.20 g. of *p*-bromophenacyl ester, m.p. 71–73°, mixed m.p. 72–73°. Authentic  $\alpha$ -bromovaleric acid was prepared according to Marvel<sup>16</sup> and had b.p. 132–136° (28 mm.) and  $n_D^{25}$  1.4592. The authentic bromoacid (0.20 g.) gave 0.23 g. of *p*-bromophenacyl ester, m.p. 72–73°.

**Acknowledgments.**—We are indebted to Samuel P. Sadtler and Son, Inc., and to Dr. Gordon Evans for the infrared spectrograms. For a Frederick Gardner Cottrell grant that made this work possible we wish to express our gratitude to the Research Corporation of New York.

(16) C. S. Marvel, *Org. Syntheses*, **21**, 74 (1941).

DEPARTMENT OF CHEMISTRY  
TUFTS COLLEGE  
MEDFORD 55, MASSACHUSETTS

## Some Nitro- and Aminodibenzofurans

BY HENRY GILMAN AND ROBERT K. INGHAM

RECEIVED MAY 13, 1953

The announcement by Barry<sup>1</sup> of the high antituberculous activity of 2-chloro-7-aminodibenzofuran emphasized the desirability of additional research upon dibenzofuran derivatives. Since dibenzofuran may be regarded as a "closed model" of diphenyl ether, information concerning the activity of the diphenyl ether series was reviewed.

One of the more active diphenyl ethers is 2-chloro-4'-aminodiphenyl ether.<sup>1</sup> Evidence indicates that for high activity the chlorine atom must be either ortho or para to the ether linkage and that additional halogen substitution in either ring results in a marked increase in activity. Barry also found the brominated derivative to be equally as active as the chloro compound. These findings indicated that the preparation and testing of an aminodihalodibenzofuran would be valuable. 2,8-Dibromo-3-aminodibenzofuran was synthesized by the bromination and subsequent hydrolysis of 2-bromo-7-acetaminodibenzofuran. The positions of the bromine atoms were verified by deamination to yield 2,8-dibromodibenzofuran. The results of pharmacological tests will be reported elsewhere.

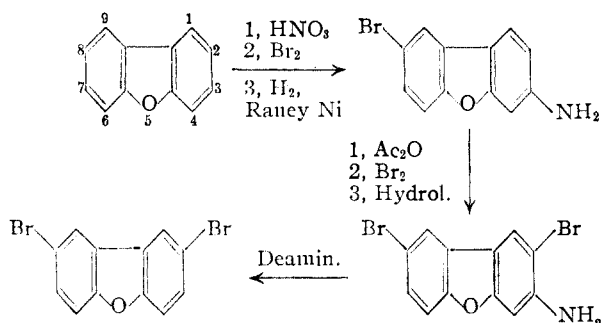
(1) V. C. Barry, L. O'Rourke and D. Twomey, *Nature*, **160**, 800 (1947).

(12) J. P. Wibaut and H. L. Gitsels, *Rec. trav. chim.*, **59**, 947 (1940).

(13) L. F. Fieser, "Experiments in Organic Chemistry," 2nd edition, D. C. Heath and Company, New York, N. Y., 1941, p. 365.

(14) Analysis by Dr. Carol K. Fitz, Needham Heights 94, Mass.

(15) F. L. Greenwood and M. G. Wolkowich, *J. Org. Chem.*, **17**, 1551 (1952).



2-Nitro-3-aminodibenzofuran was prepared by the previously reported method<sup>2</sup> and deaminated according to the procedure of Bigelow and co-workers<sup>3</sup> to give 2-nitrodibenzofuran. Bromination of the 2-nitro derivative gave 2-bromo-8-nitrodibenzofuran. This compound was not reduced to the amino analog because of the small quantity available.

4-Aminodibenzofuran was prepared by the reaction of *O*-methylhydroxylamine with 4-dibenzofuryllithium. A similar preparation of 4-aminodibenzothiophene has been reported.<sup>4</sup>

Many cases of replacement of the diazonium by the nitro group have appeared in the literature; a general review of the reaction through 1935 is available.<sup>5</sup> All of the earlier methods are of limited application. A report of a procedure of general application employing the diazonium cobaltinitrites has been published<sup>6</sup> and was applied to dibenzofuran derivatives. Since 3-aminodibenzofuran is more accessible than the 4-isomer, the method was first run with the 3-amino compound. The method seems to be generally applicable for the preparation of nitrodibenzofurans and may be valuable for the preparation of difficultly obtainable nitro compounds of similar systems.

#### Experimental<sup>7</sup>

**2-Bromo-7-aminodibenzofuran.**—Bromination of 3-nitrodibenzofuran and nitration of 2-bromodibenzofuran have been shown to yield the same product,<sup>8</sup> which has been proved to be the 2-bromo-7-nitro derivative<sup>2</sup>; the former reaction is preferable. The 2-bromo-7-nitrodibenzofuran was prepared by the procedure of Cullinane.<sup>8</sup>

2-Bromo-7-nitrodibenzofuran has been reduced by zinc and alcoholic hydrochloric acid (33% yield), and by tin and concentrated hydrochloric acid (56% yield).<sup>2</sup> The following catalytic reduction was found more practical and gave better yields.

A suspension of 10 g. (0.034 mole) of 2-bromo-7-nitrodibenzofuran and about 1.5 g. of Raney nickel catalyst in 100 ml. of absolute ethanol was placed in the hydrogenation bottle. The reaction container was steam heated and the hydrogen pressure maintained between 50 and 30 lb./in.<sup>2</sup>. After 15 minutes the pressure dropped to a constant reading. The hot solution was filtered free from catalyst and the filtrate diluted with water, giving 7.7 g. (87%) of the amine, m.p. 126–130.5°. One recrystallization from dilute eth-

anol yielded 7.2 g. (81%) of white crystals melting at 131.5–133°; the reported m.p.<sup>2</sup> is 133–134°.

**2-Bromo-7-acetaminodibenzofuran.**—Seventeen grams (0.065 mole) of 2-bromo-7-aminodibenzofuran was placed in 225 ml. of benzene. The flask was warmed slightly to complete dissolution of the compound. To this solution was added 7 ml. of acetic anhydride. Within 2 minutes a flocculent white precipitate appeared. After standing for 3 hours to complete precipitation, the solid was filtered and washed with petroleum ether (b.p. 23–30°). There was thus obtained 16.2 g. (81.7%) of white crystals, melting at 215–218°. Recrystallization from benzene raised the melting point to 220–220.5°.

**Bromination of 2-Bromo-7-acetaminodibenzofuran.**—To a partial solution of 10 g. (0.03 mole) of 2-bromo-7-acetaminodibenzofuran in 60 ml. of glacial acetic acid was added dropwise 5 g. (0.03 mole) of bromine. An immediate change in the crystalline form of the solid occurred and an additional 25 ml. of acetic acid was added to facilitate stirring. The mixture was warmed to 50° and stirred for 3 hours. Subsequent to cooling and filtering, there was obtained 10 g. (80%) of a light yellow solid, melting over the range 220–229°. One recrystallization from absolute ethanol gave 9.1 g. (73%) of white needles melting at 235–236°.

**2,8-Dibromo-3-aminodibenzofuran.**—Eight grams of the dibromoacetamino derivative described in the preceding experiment was refluxed for 2 hours with 150 ml. of 95% ethanol and 150 ml. of concentrated hydrochloric acid. After cooling, the precipitated hydrochloride was filtered, suspended in water and decomposed with ammonium hydroxide. Filtration of the ammoniacal mixture gave 7.2 g. (93%) of a white solid, melting over the range 179–182°. Recrystallization from absolute ethanol yielded 7 g. (90%) of white needles, melting at 182–183°.

*Anal.* Calcd. for C<sub>12</sub>H<sub>7</sub>ONBr<sub>2</sub>: Br, 46.87. Found: Br, 47.02, 47.05.

**Deamination of 2,8-Dibromo-3-aminodibenzofuran.**—To a cold mixture of 9 ml. of ethanol and 2.5 ml. of concentrated sulfuric acid was added 0.5 g. (0.0015 mole) of 2,8-dibromo-3-aminodibenzofuran. The mixture was cooled to 10° and a solution of 1.5 g. of sodium nitrite in 3 ml. of water was added. The temperature was not allowed to rise above 10° during this addition; the mixture was stirred for 20 minutes after the addition to complete the reaction. The flask was then warmed cautiously until a vigorous evolution of gas began. When this reaction had moderated, the mixture was heated for 10 minutes on a steam-bath. The solution was then diluted, filtered and the resulting tan solid washed well with water. This solid material melted over the range 183–193°. One recrystallization from toluene brought the m.p. to 192–193°. A mixed m.p. with authentic 2,8-dibromodibenzofuran showed no depression. The yield was 0.3 g. (55%).

**2-Nitrodibenzofuran.**—2-Nitro-3-acetaminodibenzofuran was prepared by the previously published procedure<sup>2</sup>; the nitroacetamino compound melted at 198–199°. Hydrolysis gave the 2-nitro-3-aminodibenzofuran, m.p. 227–228°. An attempt to prepare the 2-nitrodibenzofuran by the reported method was not successful. The deamination procedure of Bigelow and co-workers<sup>3</sup> was employed.

To a cold mixture of 25 ml. of 25% ethanol and 5 ml. of concentrated sulfuric acid was added 6.5 g. (0.03 mole) of 2-nitro-3-aminodibenzofuran. The mixture was maintained below 10° while 3 g. of sodium nitrite in 4 ml. of water was added slowly, with stirring. This mixture was then stirred for an additional 20 minutes to complete the reaction. The flask was warmed cautiously until gas evolution had begun. When this evolution had moderated the mixture was heated for 1 hour on a steam-bath. The solution was diluted and filtered, giving an orange solid melting over the range 175–195°. Two recrystallizations from methanol gave 3.5 g. (56%) of yellow needles, m.p. range 135–143°. Recrystallization from glacial acetic acid did not improve the m.p. The compound was vacuum distilled (b.p. 160–170° at 0.6 mm.) and the distillation product crystallized from methanol to yield 1.5 g. (24%) of yellow needles melting at 151–152°. A mixed m.p. with the 2-nitro derivative of Kirkpatrick<sup>3</sup> (m.p. 149°) was not depressed.

**2-Bromo-8-nitrodibenzofuran.**—To 1 g. (0.0047 mole) of 2-nitrodibenzofuran in 20 ml. of glacial acetic acid was added dropwise 1 ml. of bromine. The solution was then refluxed for 6 hours. After cooling, the solution was di-

(2) H. Gilman, G. E. Brown, W. G. Bywater and W. H. Kirkpatrick, *THIS JOURNAL*, **56**, 2473 (1934).

(3) L. A. Bigelow, J. R. Johnson and L. T. Sandborn, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 133.

(4) H. Gilman and S. Avakian, *THIS JOURNAL*, **68**, 1514 (1946).

(5) K. H. Saunders, "The Aromatic Diazo Compounds and Their Technical Applications," E. Arnold and Company, London, 1936, p. 158.

(6) H. H. Hodgson and E. Marsden, *J. Chem. Soc.*, 22 (1944).

(7) All melting points are uncorrected.

(8) N. M. Cullinane, H. C. Davey and H. J. H. Padfield, *J. Chem. Soc.*, 716 (1934).

luted with water and the resulting solid filtered. This solid was recrystallized from acetone-water, giving 1.3 g. of yellow solid, melting over the range 185–203° (96% crude yield). A second recrystallization from this solvent did not improve the m.p. Recrystallization from a large amount of petroleum ether (b.p. 77–115°) gave 1 g. (74%) of yellow needles melting at 210–212°.

*Anal.* Calcd. for  $C_{12}H_8O_3NBr$ : Br, 27.38. Found: Br, 27.35, 27.30.

**4-Aminodibenzofuran.**—A procedure for the preparation of 2-aminodibenzofuran *via* metalation and reaction with O-methylhydroxylamine appears in the Doctoral Dissertation of Willis,<sup>9</sup> but has not been published elsewhere. The following is a modification of that procedure.

To a solution of 42 g. (0.25 mole) of dibenzofuran in 150 ml. of anhydrous ether was added 0.4 mole of *n*-butyllithium.<sup>10</sup> The solution was stirred at room temperature for 38 hours; at the end of this period, Color Test II<sup>11</sup> remained positive. To this solution (cooled in an ice-salt-bath) was added slowly 6.1 g. (0.13 mole) of O-methylhydroxylamine in 40 ml. of ether. The free amine was prepared from O-methylhydroxylamine hydrochloride<sup>12</sup> by treatment with 50% sodium hydroxide, the resulting vapors being passed over some pellets of potassium hydroxide in a heated U-tube and subsequently condensed. Soon after the addition of the base, Color Test I<sup>13</sup> became negative. The solution was stirred an additional 2 hours and then hydrolyzed slowly with ice water. The ethereal layer was separated and the aqueous solution extracted twice with ether. The combined extracts were dried over sodium sulfate and the ethereal solution subsequently treated with dry hydrogen chloride to precipitate the amine hydrochloride. The 4-aminodibenzofuran hydrochloride was dissolved in 1 liter of water and the solution made alkaline. The tan colored amine was collected by filtration; the yield was 12.9 g. (54%, based on the O-methylhydroxylamine or 79%, based on the amount of dibenzofuran used), melting at 83–84°.

**3-Nitrodibenzofuran from 3-Aminodibenzofuran.**—Thirteen milliliters of concentrated hydrochloric acid, 8 ml. of water and 9.2 g. (0.05 mole) of 3-aminodibenzofuran were placed in the reaction flask and cooled in a salt-ice-bath. To this mixture was slowly added 4 g. of sodium nitrite in 10 ml. of water. The solution was then carefully neutralized with calcium carbonate and filtered. Into the filtrate was stirred 8.0 g. of finely powdered sodium cobaltinitrite, and the resulting crystalline diazonium salt was filtered. The diazonium cobaltinitrite (still wet) was added portionwise, at room temperature, to a well stirred solution of 5 g. of sodium nitrite and 5 g. of cupric sulfate in 40 ml. of water in which 3 g. of cupric oxide was suspended. This mixture was stirred overnight and filtered. The residue was refluxed with portions of glacial acetic acid and filtered. The combined filtrates were concentrated to about 100 ml. and cooled to allow crystallization of the 3-nitrodibenzofuran. There was thus obtained 7.6 g. (71%) of crude product melting from 140–152°. Two recrystallizations from glacial acetic acid brought the m.p. range to 165–179°. An additional recrystallization from absolute ethanol and finally again from glacial acetic acid brought the m.p. to 181–182°; the final yield was 3.3 g. (31%). A mixed m.p. with authentic 3-nitrodibenzofuran was not depressed.

**4-Nitrodibenzofuran from 4-Aminodibenzofuran.**—Into the reaction flask were placed 9 ml. of hydrochloric acid, 5 ml. of water and 6.1 g. (0.0333 mole) of 4-aminodibenzofuran; this mixture was cooled in a salt-ice-bath. Sodium nitrite (2.5 g.) in 10 ml. of water was added slowly. The diazonium cobaltinitrite was prepared and decomposed as above. Recrystallization from dilute ethanol gave a yellow solid, melting from 60–90°; further recrystallization from this solvent did not improve the m.p. One recrystallization from petroleum ether (b.p. 77–115°) raised the m.p. range to 132–136°. Two additional recrystallizations gave tan needles melting at 138–139°; the same m.p. for 4-nitrodibenzofuran is reported by Yamashiro.<sup>14</sup> The final yield

(9) H. B. Willis, Doctoral Dissertation, Iowa State College, 1943.

(10) H. Gilman, J. A. Beel, C. G. Brannen, M. W. Bullock, G. E. Dunn and L. S. Miller, *THIS JOURNAL*, **71**, 1499 (1949).

(11) H. Gilman and J. Swiss, *ibid.*, **62**, 1847 (1940).

(12) Eastman Kodak Company, White Label.

(13) H. Gilman and F. Schulze, *THIS JOURNAL*, **47**, 2002 (1925).

(14) S. Yamashiro, *J. Chem. Soc. Japan*, **59**, 945 (1938) [*C. A.*, **33**, 603 (1939)].

was 1.5 g. (21%); in a second run, eliminating the ethanolic recrystallization, a 28% yield was obtained.

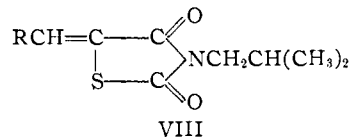
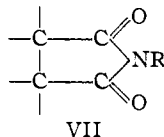
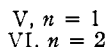
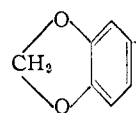
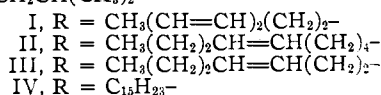
DEPARTMENT OF CHEMISTRY  
IOWA STATE COLLEGE  
AMES, IOWA

### 5-Aralkylidene-3-isobutyl-2,4-thiazolidinediones

BY CHIEN-PEN LO, ELWOOD Y. SHROPSHIRE AND  
W. J. CROXALL

RECEIVED MARCH 14, 1953

A number of isobutyramides of unsaturated acids, *e.g.*, affinin (I),<sup>1,2</sup> herculin (II),<sup>3,5</sup> pellitorine (III)<sup>4,5</sup> and scabrin (IV),<sup>6</sup> have been isolated from various plants and shown to have insecticidal properties comparable to pyrethrins. Many fagaramides (V)<sup>7</sup> and piperamides (VI)<sup>8,9</sup> are known to



have synergistic activity with pyrethrum. All these are derivatives of acrylamide. It is also known that some N-alkyl cyclic imides of the general structure VII<sup>10</sup> are synergists for pyrethrins. The present paper reports the synthesis of a few 5-aralkylidene-3-isobutyl-2,4-thiazolidinediones (VIII) which contain both the acrylamide and the cyclic imide structures for testing as fly toxicants. These compounds were prepared by the isobutylation of 5-aralkylidene-2,4-thiazolidinediones. The choice of the isobutyl group is based on the fact that all the aforementioned naturally occurring unsaturated acid amides are isobutylamides and that N-isobutylundecylenamide<sup>11</sup> is a synergist for

(1) (a) F. Acree, M. Jacobson and H. L. Haller, *J. Org. Chem.*, **10**, 237 (1945); (b) F. Acree, M. Jacobson and H. L. Haller, *ibid.*, **10**, 449 (1945); (c) M. Jacobson, F. Acree and H. L. Haller, *ibid.*, **12**, 731 (1947).

(2) For simplicity, the name affinin is used here despite the fact that the original authors proposed to discontinue the use of this name (ref. 1c).

(3) M. Jacobson, *THIS JOURNAL*, **70**, 4234 (1948).

(4) M. Jacobson, *ibid.*, **71**, 366 (1949).

(5) There is now some doubt as to the correctness of the gross structures originally assigned to natural herculin and pellitorine. See L. Crombie, *J. Chem. Soc.*, 2997, 4338 (1952); *Chem. and Ind.*, 1034 (1952). We are grateful to the referee for this information.

(6) M. Jacobson, *THIS JOURNAL*, **73**, 100 (1951).

(7) S. I. Gertler and H. L. Haller, U. S. Patent 2,326,350 (1943).

(8) E. K. Harvill, A. Hartzell and J. M. Arthur, *Contrib. Boyce Thompson Inst.*, **13**, 87 (1944).

(9) Piperine, the piperide of piperic acid, (VI, RR' =  $-(CH_2)_9-$ ) is highly toxic to houseflies either used alone or in combination with pyrethrum (ref. 8).

(10) (a) H. W. Arnold and N. E. Searle, U. S. Patent 2,462,835 (1949); (b) A. A. Schreiber, U. S. Patent 2,476,512 (1949).

(11) (a) A. Weed, *Soap*, **14**, 133 (1938); (b) E. W. Bousquet, U. S. Patent 2,166,119–20 (1939); (c) W. A. L. Davis and P. Bracey, *Nature*, **153**, 594 (1944).