A solution of 1.42 g. (5.0 mmoles) of benzoyl-L-phenylalanine hydrazide in 25 ml. of 1 *N* hydrochloric acid and 7.5 ml. of glacial acetic acid was cooled in an ice–salt-bath and a cold solution of 350 mg. (5.0 mmoles) of sodium nitrite in 2 ml. of water was added and the mixture was shaken. The azide precipitated and was extracted with two 50-ml. portions of cold ether. The ethereal solution was washed at 0° with 25 ml. of water and twice with 50 ml. of 5% sodium bicarbonate solution (final wash was basic to litmus). The ethereal solution was dried over anhydrous sodium sulfate at 0° for 5 min.

The ethereal solution of L-leucine methyl ester was filtered through a cotton plug, and the solution of the azide was poured through the same plug. A small amount of solid, presumably azide, which had separated in the ethereal solution during the sodium bicarbonate washes was dissolved from the cotton by the addition of 1 ml. of dimethylforma mide. The resulting solution was evaporated *in vacuo* to approximately 50 ml. and was left at 0° overnight and then at room temperature for 24 hours.

The solution was washed with 1 *N* hydrochloric acid, water and 5% sodium bicarbonate solution, and was dried over anhydrous sodium sulfate. The solution was evaporated to dryness *in vacuo;* weight 1.52 g. (77%), m.p. 130–165°. The product was recrystallized from 20 ml. of 95% ethanol and 20 ml. of water (cooled to room temperature only); weight 1.25 g. (63%), m.p. 163–166°. It was recrystallized for analysis.

Anal. Calcd. for $C_{23}H_{28}N_2O_4$: N, 7.1. Found: N, 7.2.

Benzoyl-L-phenylalanyl-L-leucine Hydrazide.—A mixture of 1.10 g. (2.8 mmoles) of benzoyl-L-phenylalanyl-L-leucine methyl ester, 2.6 ml. of absolute ethanol and 1.3 ml. of hydrazine hydrate was heated at 75° for 4 hr. The mixture was cooled, 6 ml. of water was added, and the solid was collected by filtration, washed with water, and dried *in vacuo* to constant weight; 1.07 g. (97%); m.p. 208–212°.

Anal. Calcd. for $C_{22}H_{28}N_4O_3$: N, 14.1. Found: N, 14.0.

Benzoyl-L-phenylalanyl-L-leucyl-L-leucine Methyl Ester.—A solution of L-leucine methyl ester was prepared from 3.0 mmoles of the hydrochloride, as in the above preparation of benzoyl-L-phenylalanyl-L-leucine methyl ester.

A solution of 990 mg. (2.5 mmoles) of benzoyl-L-phenylalanyl-L-leucine hydrazide in 20 ml. of 1 *N* hydrochloric acid and 20 ml. of glacial acetic acid was used in the preparation of the azide. The procedure was the same as in the preparation of benzoyl-L-phenylalanine azide, except that a total of 110 ml. of sodium bicarbonate solution was necessary for the last wash to be basic, and 2 ml. of dimethylformamide was added after the azide and ester solutions were combined. The product crystallized out at 0° and the reaction mixture was solid after 20 hr. at 0°. The mixture was left 24 hr. at room temperature. The mixture was cooled, mixed with 5 ml. of 1 *N* hydrochloric acid, and was filtered. The solid was washed on the funnel with water, 1 *N* hydrochloric acid, water, 5% sodium bicarbonate solution and water. It was dried in the air, and finally *in vacuo;* 1.03 g. m.p. 165–200°. The product was recrystallized from 10 ml. 95% ethanol and 5 ml. of water; 772 mg. (61%); m.p. 199–202°. It was recrystallized for analysis, m.p. 200–203°.

Anal. Calcd. for $C_{29}H_{39}N_3O_5$: N, 8.25. Found: N, 8.1.

For comparison, benzoyl-L-phenylalanyl-L-leucyl-L-leucine methyl ester was also prepared from L-leucyl-L-leucine methyl ester. A solution of 392 mg. of carbobenzoxy-L-leucyl-L-leucine methyl ester in 4.0 ml. of dimethylformamide was mixed with 200 mg. of palladium black, and hydrogen was bubbled through, with shaking, for one-half hour. The catalyst was filtered off, and to the cold solution was added a solution of benzoyl-L-phenylalanine azide prepared as described above. Once recrystallized product (248 mg.) had the same melting point and mixed melting point as the benzoyl-L-phenylalanyl-L-leucyl-L-leucine methyl ester described above.

Benzoyl-L-phenylalanyl-L-leucyl-L-leucine.—A mixture of 637 mg. (1.25 millimoles) of benzoyl-L-phenylalanyl-L-leucyl-L-leucine methyl ester, 5.0 ml. of methanol and 1.25 ml. of 1.12 *N* sodium hydroxide was heated in a bath at 75° five minutes to dissolve all the solid, and the solution was left at room temperature one-half hour. The excess alkali was neutralized by the addition of 0.15 ml. of 1.00 *N* hydrochloric acid and the methanol was evaporated *in vacuo*. The residue was dissolved in 8 ml. of water, and the solution was extracted with four 5-ml. portions of ether. The aqueous solution was acidified with 0.4 ml. of 5 *N* hydrochloric acid, and was extracted with four 5-ml. portions of ether. This ethereal solution was washed with 2 ml. of water, dried over magnesium sulfate and evaporated to dryness *in vacuo*. The product was a glass, 580 mg. (90% yield, based on a neutralization equivalent of 515 (theory 496)).

L-Leucyl-L-leucine.—To a solution of 535 mg. (1.04 mmoles) of benzoyl-L-phenylalanyl-L-leucyl-L-leucine in 8.2 ml. (1.09 mequiv.) of 0.133 *N* sodium hydroxide solution was added 28 mg. of chymotrypsin (Armour, salt-free crystalline) and 33.5 ml. of water. The *p*H of the solution was 7.3. The solution was left at room temperature for 8 hr. The solution was acidified with 1.06 ml. of 1.03 *N* hydrochloric acid and the benzoyl-L-phenylalanine was extracted with three 50-ml. portions of ether (278 mg., m.p. 134–141°, neut. equiv. 287 (authentic benzoyl-L-phenylalanine, m.p. 141–143°, neut. equiv. 269)). The aqueous solution, containing L-leucyl-L-leucine, chymotrypsin and sodium chloride, was evaporated to dryness *in vacuo* over phosphorus pentoxide. The residue, 350 mg., was extracted with 10 and 3 ml. of boiling 95% ethanol. L-Leucyl-L-leucine hydrate crystallized as the solution cooled; 229 mg. (84%). Analyses indicated that this still contained approximately 2% sodium chloride. The sodium chloride was removed by another recrystallization (80% recovery) from 95% ethanol; m.p. 258–263°, $[\alpha]^{23}D$ −13.4° (*c* 1, *N* sodium hydroxide).[5]

Anal. Calcd. for $C_{12}H_{24}N_2O_3H_2O$: N, 10.7; Cl, 0.0. Found: N, 10.7; Cl, 0.0.

Paper chromatograms (butanol–acetic acid–water (4:1:5)) of samples taken at various stages in the preparation, as well as chromatograms of the isolated crystalline L-leucyl-L-leucine, indicated that L-leucyl-L-leucine (R_f 0.85) was the only compound which reacted with ninhydrin that was formed in the reactions. (As little as 1% of L-leucine or L-phenylalanine would have been detected on the chromatograms.)

L-Leucyl-L-leucine hydrate prepared from carbobenzoxy-L-leucyl-L-leucine had properties identical with those of the above material.

(5) Calculated rotation for the anhydrous material: E. Fischer (*Ber.*, **39**, 2893 (1906)) reported m.p. 270° and $[\alpha]^{20}D$ −13.4° (*c* 8.1, *N* sodium hydroxide). F. H. Carpenter and D. T. Gish (THIS JOURNAL, **74**, 3818 (1952)) reported m.p. 252–254° (uncor.) and $[\alpha]^{22}D$ −13.7° (*c* 0.95, *N* sodium hydroxide).

NEW YORK STATE AGRICULTURAL EXPERIMENT STATION
CORNELL UNIVERSITY
GENEVA, NEW YORK

The Methoxymercuration of 1,3-Butadiene

BY K. H. MCNEELY AND GEORGE F WRIGHT

RECEIVED DECEMBER 17, 1954

In order to evaluate an hypothesis that oxymercuration of alkenes proceeds *via* an alkanemercurinium salt[1] we have studied the reaction of 1,3-butadiene with one equivalent of mercuric acetate in methanol. This addition ought to be analogous with that of bromine which is thought by some to proceed *via* an alkanebromonium ion intermediate.

A good yield of 4-chloromercuri-3-methoxy-1-butene is obtained when the rapidly reacting system is finally poured into aqueous sodium chloride. The structure of this product has been demonstrated by ozonization, which yields formaldehyde, and by conversion to the known 1,4-diacetoxymercuri-2,3-dimethoxybutane.[2] None of the 1,4-addition product can be found, although it might have

(1) H. J. Lucas, F. R. Hepner and S. Winstein, THIS JOURNAL, **61**, 3102 (1939).

(2) J. R. Johnson, W. H. Jobling and G. W. Bodamer, *ibid.*, **63**, 131 (1941).

been expected if a 1,4-butanemercurinium salt had been an intermediate in the reaction. It is unfortunate that 4-methoxycrotylmercuric salt could not be found since its geoisomeric configuration should have been significant.[3] The only contaminant which can be isolated is 1,4-dichloromercuri-2,3-dimethoxybutane (estimated as 0.5% of theoretical yield).

Experimental[4]

4-Chloromercuri-3-methoxy-1-butene. A. Preparation.—To a solution of 31.8 g. (0.1 mole) of mercuric acetate in 300 ml. of methanol at 0° was added 16.3 g. (0.3 mole) of 1,3-butadiene in 50 ml. of methanol. After 5 minutes at this temperature the system gave a negative test for mercuric ion so it was filtered into 100 ml. of 10% aqueous sodium chloride. The precipitated oil was taken up in 100 ml. of chloroform. This extract was twice washed with water and then was evaporated at room temperature leaving 29.1 g. (91%) of product, m.p. 40–44°. This was extracted with 60 ml. of hot methanol leaving 30 mg., m.p. 140–150°. After two hours at room temperature 90 mg., m.p. 146–156°, was precipitated. The two crops (0.14%) of 1,4-dichloromercuri-2,3-dimethoxybutane, combined and crystallized from 24 ml. of methanol, were thus purified to melt at 163–165°. A mixture melting point with an authentic sample was not depressed.

Evaporation of the extract from which the dichloromercurial had been partly removed yielded successive crops of the monochloromercurial, the first and major crop of which melted at 49.2–50° (unchanged by crystallization from methanol, 2 ml. per g.). The less-pure crops, as well as the evaporated mother liquor, could be purified by solution in aqueous alkali followed by acidification with gaseous carbon dioxide after 5 hours; the precipitate ultimately was crystallized from methanol, m.p. 49–50°.

Anal. Calcd. for C_5H_9ClHgO: C, 18.7; H, 2.82. Found: C, 18.9; H, 2.95.

B. Ozonization.—A solution of 0.337 g. (0.001 mole) of 4-chloromercuri-3-methoxy-1-butene in 10 ml. of dry chloroform (pre-ozonized, sulfuric acid and water washed) was ozonized for 1 hour at 0°. After vacuum evaporation of the solvent the ozonide was hydrolyzed overnight by 200 mg. of zinc dust in 10 ml. of water. The hydrolysate was distilled and the distillate diluted with an equal volume of ethanol. A drop of piperidine and 0.3 g. of dimedone were added and the system was warmed for 5 minutes on the steam-bath. Water was then added until precipitation occurred and the system cooled to 0° was filtered. The vacuum dried formaldehyde–dimedone derivative, 0.096 g. (31%), melted at 189.5–191.5° and was identified by mixture melting point.

1,4-Dichloromercuri-2,3-dimethoxybutane.—A solution of 0.78 g. (0.0024 mole) of 4-chloromercuri-3-methoxy-1-butene in 5 ml. of methanol was treated with 0.76 g. (0.0024 mole) of mercuric acetate in 10 ml. of methanol. After 2 hours the system was added to 10 ml. of 10% aqueous sodium chloride solution. The precipitate, 0.83 g. (59%), m.p. 132–138°, was twice crystallized from ethanol (200 ml. per g.), m.p. 165–166°.

Anal. Calcd. for $C_6H_{12}Cl_2Hg_2O_2$: C, 12.2; H, 2.05. Found: C, 12.2; H, 2.31.

This compound was also accessible from 1,3-butadiene by utilization of 2 equivalents of mercuric acetate in the procedure outlined for the monomercurial.

1,4-Diacetoxymercuri-2,3-dimethoxybutane.—To a solution of 2.67 g. (0.005 mole) of 1,4-dichloromercuri-2,3-dimethoxybutane in 125 ml. of methanol was added 1.67 g. (0.01 mole) of silver acetate. After 30 minutes shaking the silver chloride was filtered off, 1.33 g. (92%). The filtrate, partially vacuum evaporated, yielded 2.35 g. (74%), m.p. 150–153°. Crystallization from ethanol (10 ml. per g.) gave a product, m.p. 153–154°, which was identical according to mixture melting point with that previously prepared.[2]

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF TORONTO
TORONTO, ONTARIO, CANADA

(3) K. Mislow and H. M. Hellman, THIS JOURNAL, **73**, 244 (1951).

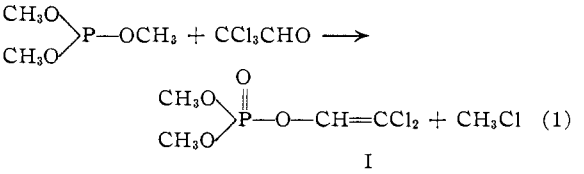
(4) Melting points have been corrected against reliable standards.

The New Insecticide O,O-Dimethyl 2,2,2-Trichloro-1-hydroxyethylphosphonate

BY W. LORENZ, A. HENGLEIN AND G. SCHRADER

RECEIVED NOVEMBER 18, 1954

The condensation of chloral and trialkyl phosphite[1] yields O,O-dialkyl O-(2,2-dichloroethenyl)-phosphate in an interesting reaction with the elimination of alkyl chloride

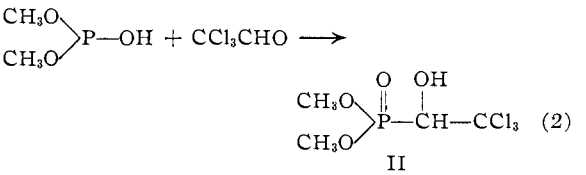


(1)

I

This new group of phosphoric esters shows high insecticidal activity associated with a high degree of toxicity toward mammals.[2]

The condensation of chloral and dimethyl phosphite proceeds quite differently to yield O,O-dimethyl 2,2,2-trichloro-1-hydroxyethylphosphonate (II)[3,4]



(2)

II

The ester II is a solid readily soluble in water. The determination of its molecular weight revealed that it is present in the bimolecular state.[6] It is relatively non-toxic to mammals. The following LD-50 values were found: rat oral 450 mg./kg., rat (male) intraperitoneal[7] 225 mg./kg., mouse subcutaneous 400 mg./kg., mouse intraperitoneal 500 mg./kg.[7] 100% mortality of houseflies was obtained in 11 minutes at a concentration of 0.01%, in 24 minutes at 0.001%, and in 280 minutes at 0.0001%.

The ester II is relatively stable at room temperature in aqueous solution. In an alkaline medium, however, a very interesting rearrangement takes place.

TABLE I

Time, hr.	Alkaline dec. at room temperature: Ml. of 0.1 *N* NaOH[a] used/g.	Dec., %	Dec by boiling in water at 100°; determination of acid liberated: Ml. of 0.1 *N* NaOH used/g.	Dec., %
1	152.5	78	22.3	11.5
2	174.5	90	45.5	23.3
3	178.5	91	63.8	33.0
4	183.2	94	88.5	45.6
8	192.0	99	92.0	47.5

[a] 1 equivalent = 19.4 ml. of 0.1 *N* NaOH.

(1) W. Perkow, *et al.*, *Chem. Ber.*, **87**, 755 (1954).

(2) W. Perkow, K. Ullerich and F. R. Meyer, *Naturwissenschaften*, **39**, 353 (1952).

(3) W. Lorenz, U. S. Patent 2,701,225.

(4) This compound has been made available as an insecticide in 1952 under the code number Bayer L 13/59. It has been later described by Barthel, Giang and Hall.[5] It is currently being marketed under the trade name Dipterex.

(5) W. F. Barthel, P. A. Giang and S. A. Hall, THIS JOURNAL, **76**, 4186 (1954).

(6) V. S. Abramow, *Doklady Acad. Nauk. (U.S.S.R.)*, **73**, 487 (1950); *J. Gen. Chem. (U.S.S.R.)*, **22**, 547 (1952).

(7) K. P. DuBois and G. J. Cotter, A.M.A. Archives of Industrial Hygiene and Occupational Medicine, in press.