TABLE I

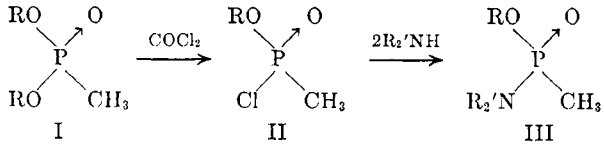
ALKYL *N,N*-DIALKYL METHYLPHOSPHONAMIDATES

Formula	°C./mm.	n_D/t°C.	Yield, %	Carbon		Hydrogen	
				Calcd.	Found	Calcd.	Found
$CH_3P(O)(OC_2H_5)N(CH_3)_2$	55/1.0	1.4303/24	70	39.7	39.4	9.3	9.0
$CH_3P(O)(n\text{-}C_3H_7)N(CH_3)_2$	62/1.0	1.4320/25	60	43.6	43.4	9.8	9.6
$CH_3P(O)(Oi\text{-}C_3H_7)N(CH_3)_2$	43/0.04	1.4300/22	56	43.6	43.5	9.8	9.7
$CH_3P(O)(On\text{-}C_4H_9)N(CH_3)_2$	64/0.5	1.4341/26	59	46.9	46.6	10.0	9.9
$CH_3P(O)(On\text{-}C_5H_{11})N(CH_3)_2$	91/1.0	1.4362/21	63	49.7	49.6	10.4	10.1
$CH_3P(O)(OC_2H_5)N(C_2H_5)_2$	54/1.0	1.4360/21	62	46.9	46.7	10.0	9.9
$CH_3P(O)(Oi\text{-}C_3H_7)(NC_5H_{10})$[a]	90/1.0	1.4590/16	63	53.0	53.2	9.8	9.5
$CH_3P(O)(Oi\text{-}C_3H_7)(NC_4H_8O)$[b]	86/1.0	1.4596/18	62	46.3	46.1	8.7	8.7

Derived from [a] piperidine and [b] morpholine.

a number of alkyl *N,N*-dialkyl ethylphosphonamidates. We have synthesized a number of similar compounds based on methylphosphonamidic acid by a different and apparently more convenient route.

Dialkyl methylphosphonates (I) were treated with phosgene by the procedure of Coe *et al.*[4] to give the alkyl methylphosphonochloridates (II). These compounds which are thermally unstable were obtained sufficiently pure by this method to be used without distillation. Reaction of the chloridates with two equivalents of the appropriate amine gave the corresponding alkyl *N,N*-dialkyl methylphosphonamidate (III) in yields ranging from 60–70% after distillation. Similarly by using piperidine and morpholine, with isopropyl methylphosphonochloridate, the isopropyl methyl phosphonopiperidate and morpholidate were obtained respectively.



These compounds, the data for which are given in Table I, were tested as insecticides and found to have pronounced systemic activity but very low mammalian toxicity.[5]

EXPERIMENTAL

n-Propyl N,N-dimethyl methylphosphonamidate. Dry phosgene was bubbled slowly through 60 g. (0.33 mole) of di-*n*-propyl methylphosphonate for 18 hr. with water cooling during the first 3 hr. Volatile products were removed by degassing at 30° and 10 mm. On analysis it was found that the chlorine content of the residue was within 0.5% of that required for $CH_3PO(OC_3H_7)Cl$. The chloridate was dissolved in 250 ml. of dry ether, and into it passed 30 g. (0.7 mole) of anhydrous dimethylamine, with continuous stirring and ice cooling. After standing for 3 hr. at room temperature the mixture was filtered and the ether removed under reduced pressure. The residue was fractionally distilled to yield 33 g. (60%) of *n*-propyl *N*-dimethyl methylphosphonamidate, b.p. 62° at 1 mm.; n_D^{25} 1.4320.

Anal. Calcd. for $C_6H_{16}O_2NP$: C, 43.61; H, 9.75. Found: C, 43.38; H, 9.60.

SUFFIELD EXPERIMENTAL STATION
RALSTON, ALBERTA

(4) D. G. Coe, B. J. Perry, and R. K. Brown, *J. Chem. Soc.*, 3604 (1957).

(5) D. G. Coe, H. Hurtig, B. J. Perry, and E. S. Sherlock, *J. Agr. Food Chem.*, **7**, 251 (1959).

Diosmetin Triacetate from 3-Bromohesperetin Triacetate and Silver Acetate-Acetic Anhydride[1,2]

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In an investigation of hesperetin (I) as a potential synthetic precursor of quercetin 4′-monomethyl ether, the reaction of the 3-bromohesperetin triacetate (II) of Zemplen and Bognar[4] with silver acetate in acetic anhydride, reported to give 3-acetoxyhesperetin triacetate,[4] was investigated. The present note reports that this reaction leads to diosmetin triacetate (III).

3-Bromohesperetin triacetate (II) was prepared by the general method of Zemplen and Bognar.[4] The quality of the absolute chloroform used in their procedure was found to be extraordinarily critical. Repeated attempts were made to carry out the reported synthesis of 3-acetoxyhesperetin triacetate by reaction of II with silver acetate in acetic anhydride. There was obtained, however, in yields up to 75%, III, identical with a product obtained from

(1) From the M.S. thesis (1956) of Myron James Holm.

(2) This investigation was supported in part by a research grant (E-1703) from the National Institute of Allergic and Infectious Diseases, Public Health Service.

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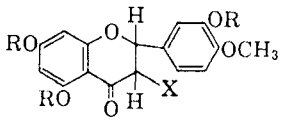
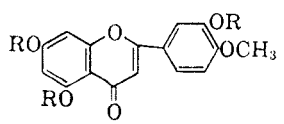
(4) G. Zemplen and R. Bognar, *Ber.*, **76B**, 454 (1943).

the action of NBS on hesperetin triacetate.[5] Characterization of III involved both acidic and basic hydrolysis to give diosmetin (IV), in turn characterized by reacetylation to III, and demethylation followed by acetylation to give luteolin tetraacetate. The IV thus obtained had an ultraviolet absorption spectrum identical with that previously reported.[6]

Our observation is similar to that of Robertson, Cavill and co-workers,[7] who attempted to prepare 3-acetoxy-7-methoxyflavanone by reaction of silver acetate with 3-bromo-7-methoxyflavanone. 7-Methoxyflavone was the sole reaction product.



I. X = H; R = H
II. X = Br; R = $COCH_3$



III. R = $COCH_3$
IV. R = H

EXPERIMENTAL

3-Bromohesperetin triacetate. Numerous experiments proved the quality of the absolute chloroform to be critical. Reagent grade chloroform was washed twice with conc. sulfuric acid, and then five or six times with water (at least twice after the chloroform layer becomes clear). The chloroform was shaken with anhydrous calcium chloride, decanted onto fresh calcium chloride, and allowed to stand for several hours. The chloroform was then distilled, and the first distillate fraction tested for phosgene by addition of silver nitrate. If any cloudiness whatsoever appeared, all of the chloroform, both distillate and residue, was discarded. If no cloudiness appeared, approximately 1/4 of the chloroform was distilled and discarded. The middle portion was then collected, and usually distilled over a 0.2° boiling range. If the boiling range was greater than 0.4°, all of the chloroform was discarded. The chloroform thus purified was used within a few hours.

A 1-g. quantity of hesperetin triacetate, m.p. 143.5–144.5°,[8] was brominated in absolute chloroform solution in a Vycor flask under irradiation with a Hanovia Model 30600 quartz mercury vapor lamp under the general conditions of Zemplen and Bognar. A total quantity of 720 mg. of crude, crystalline bromination product (two crops, second by crystallization of residual oil from ether) was obtained. Recrystallization of the total crude from 4 ml. of chloroform and 12 ml. of absolute ethanol gave 510 mg. of product, m.p. 170–190°. Three additional crystallizations from chloroform-ethanol gave 270 mg. of 3-bromohesperetin triacetate, m.p. 196–198° (lit.[4] m.p. 190–191°). The high loss upon recrystallization necessitated reworking of the mother liquors.

Anal.[9] Calcd for $C_{22}H_{19}BrO_9$: Br, 15.7. Found: Br, 15.6.

An alcoholic solution of 3-bromohesperetin triacetate gave no turbidity with aqueous silver nitrate at room temperature, but slowly became turbid at the boiling point. In acetonitrile, no silver bromide was obtained with silver nitrate in two weeks.

Reaction of 3-bromohesperetin triacetate with silver acetate. A 0.6 g. quantity of 3-bromohesperetin triacetate, 800 mg. of silver acetate, and 8 ml. of anhydrous acetic anhydride were heated on a steam bath for 2 hr., then for 1 hr. at 130° in an oil bath. The reaction mixture then was poured into water and allowed to stand overnight. The resulting solid was collected, extracted with three 20 ml. portions of chloroform, and the solvent subsequently evaporated. The residual oil was crystallized twice from acetone-alcohol, to give 320 mg. (75%) (two crops), of diosmetin triacetate, m.p. 195–197° (lit.[10] m.p. 195–196°). The infrared spectrum (KBr pellet) was identical with that of diosmetin triacetate obtained by NBS dehydrogenation of hesperetin triacetate, and contained strong or medium absorption bands at 1767, 1645, 1631, 1613, 1520, 1434, 1373, 1343, 1284, 1262, 1199, 1147, 1103, 1091, 1038, 1024, and 910 $cm.^{-1}$

In view of the previous report[4,11] that this substance is 3-acetoxyhesperetin triacetate, additional characterization was carried out. Basic hydrolysis of 50 mg. of product (diosmetin triacetate) in 2.5 ml. of 95% ethanol was effected by addition of 0.3 ml. of 3% aqueous sodium hydroxide, heating 5 min. on a steam bath, diluting with water, and acidifying to *p*H *ca.* 4.5. Further dilution gave a precipitate, m.p. 185–187° (positive test with magnesium–hydrochloric acid). This product was redissolved in 2.5 ml. of 95% ethanol and 0.3 ml. of 3% sodium hydroxide added. Immediate precipitation of yellow solid ensued, and solution was effected by addition of water. After warming 10 min., the solution was diluted and acidified to give diosmetin, m.p. 252° (lit.[10] m.p. 253–254°).

Acid hydrolysis was carried out by dissolving 200 mg. of diosmetin triacetate in 16 ml. of 97.5% ethanol, adding 0.4 ml. of concentrated hydrochloric acid and heating the resulting mixture under reflux 1 hr. under nitrogen. Dilution with 24 ml. of water, and cooling overnight gave a flocculent precipitate of diosmetin, which became orange colored during collection by filtration, even under nitrogen; yield, 140 mg., m.p. 255–258°. Acetylation of 50 mg. of this product in 3 ml. of acetic anhydride containing 250 mg. of anhydrous sodium acetate by heating under reflux for 3 hr. gave diosmetin triacetate, m.p. 196–197°. Demethylation of the crude diosmetin was effected by dissolving 50 mg. in 1 ml. of glacial acetic acid, adding 0.5 ml. of hydriodic acid (d. 1.7), and heating under reflux for 3 hr. The crude luteolin (*ca.* 40 mg.) was isolated by pouring the reaction mixture into ice water, collecting the precipitate by filtration and air drying; m.p. 326° (lit.[12] m.p. 327–329°). The luteolin thus obtained was acetylated by boiling 1 hr. with 40 mg. of anhydrous sodium acetate and 2 ml. of acetic anhydride. The mixture was poured into water, and the precipitated solid collected and recrystallized from 95% ethanol; m.p. 230° (lit.[13] m.p. 226–227°).

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(8) This m.p. is in reasonable agreement with the value of 139–141° reported for racemic hesperetin triacetate by H. R. Arthur, W. H. Hui, and C. N. Ma, *J. Chem. Soc.*, 632 (1956).

(9) Previous analytical characterization (ref. 4) was restricted to methoxyl determination.

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(11) Zemplen and Bognar (ref. 4) reported m.p. 193–194°, and observed OCH_3 = 6.84 for 3-acetoxyhesperetin triacetate (calcd. OCH_3 = 6.40). M.p. of diosmetin triacetate is 195–196°, and theoretical OCH_3 = 7.28.

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