Procedure B. 7-Amino-2-cyclohexyl-6-methylmerimine. A mixture of 22.2 g. (0.1 mole) of 7-amino-6-methylmerimine dihydrochloride, 25 ml. (0.24 mole) of cyclohexanone, 2 g. of 5% palladium on carbon catalyst, 2 g. of 10% platinum-on-carbon catalyst and 230 ml. of water was shaken in the Parr hydrogenator under hydrogen pressure of about 3 atmospheres until about 0.13 mole of hydrogen was absorbed. The catalyst was filtered off, and the filtrate was concentrated and then treated with 25 ml. of 50% potassium hydroxide. The crystals which separated were filtered, washed with water, and dried. The crude yield of 7-amino-2-cyclohexyl-6-methylmerimine, m.p. 178–180°, was 97%. On recrystallization from ethanol, a 79% yield of pure product, m.p. 181–182°, was obtained.

When the above base was treated with two equivalents of ethanolic hydrogen chloride, 7-amino-2-cyclohexyl-6-methylmerimine dihydrochloride, m.p. 300°, was obtained. This compound was purified by recrystallization from dilute ethanol.

7-Chloro-2,6-dimethylmerimine dihydrochloride. A solution of 7.25 g. of sodium nitrite in 60 ml. of water was added over 5 min. to a mixture of 23.6 g. (0.1 mole) of 7-amino-2,6-dimethylmerimine dihydrochloride, 100 ml. of 4*N* hydrochloric acid and 600 ml. of water. The reaction mixture was held at 0 to −2° during this addition and for 10 min. longer and then poured into a mixture of 10 g. of cuprous chloride and 150 ml. of 4*N* hydrochloric acid. The mixture was allowed to warm up to 30° over a 3-hr. period and was then treated with hydrogen sulfide. The precipitate was filtered off and the filtrate was treated with activated charcoal. The clear solution was concentrated to dryness and the product was washed onto a filter with ethanol. The yield of salt and crude product was 20.1 g. The estimated product was 14.3 g. (56%). This mixture was stirred with 6.2 g. of sodium methylate and 400 ml. of ethanol for 2 hr. The salt was filtered off and the filtrate was treated with activated carbon and then concentrated to dryness. On addition of alcoholic hydrogen chloride, a precipitate separated. This product was filtered off and recrystallized twice from 90% ethanol. The yield, including recoveries, of pure 7-chloro-2,6-dimethylmerimine dihydrochloride, m.p. 264° dec., was 8.1 g. (33%).

7-Bromo-2,6-dimethylmerimine dihydrochloride. A mixture of 23.6 g. (0.1 mole) of 7-amino-2,6-dimethylmerimine dihydrochloride, 11.2 g. of sodium methylate and 400 ml. of anhydrous ethanol was stirred at room temperature for 2 hr. and then filtered to remove the salt. The filtrate was concentrated under reduced pressure to a white solid. A mixture of 400 ml. of water and 50 ml. of 40% hydrobromic acid was added and the solution was cooled to −2°. A solution of 7.25 g. of sodium nitrite in 60 ml. of water was added over a 5-min. period at 0 to −2°. The reaction mixture was held at this temperature for 10 more min. and then poured into a cold mixture of 17.5 g. of cuprous bromide, 70 ml. of 40% hydrobromic acid and 40 ml. of water. After 19 hr., hydrogen sulfide was passed in and the dark precipitate was filtered off. The filtrate was treated with activated carbon, concentrated to dryness, and the product was washed onto a filter with ethanol. The dried filter cake was added to an excess of 5*N* sodium hydroxide and extracted with chloroform. After drying over magnesium sulfate, the chloroform layer was mixed with 37 ml. of 4*N* ethanolic hydrogen chloride and the product which separated was filtered off and recrystallized from 90% ethanol. The yield of 7-bromo-2,6-dimethylmerimine dihydrochloride, m.p. 269° dec., was 43%.

7-Dimethylamino-2,6-dimethylmerimine dihydrochloride. A mixture of 22.2 g. (0.1 mole) of 7-amino-6-methylmerimine dihydrochloride, 40.5 g. (0.5 mole) of 37% formaldehyde, 160 ml. of water and 2 g. of 10% palladium-on-carbon catalyst was shaken in the Parr hydrogenator under an initial hydrogen pressure of about 3 atmospheres. Hydrogen absorption was rapid at first and 0.1 mole was absorbed in 25 min. The reaction rate then dropped sharply and the absorption was only 0.23 moles at the end of 22 hr. An additional 2 g. of 10% palladium-on-carbon catalyst was added and the reduction was continued until the total hydrogen absorption was 0.3 moles. The total reaction time was 29 hr. The reaction mixture was filtered, concentrated, treated with aqueous sodium hydroxide, and extracted with chloroform. The chloroform layer was distilled and the portion which boiled at 102–108° (0.2 mm.), n_D^{23} 2.544, was collected. This oil was treated with ethanolic hydrogen chloride and ether, and the crystals which separated were recrystallized from ethanol by the addition of ether. The yield of pure 7-dimethylamino-2,6-dimethylmerimine dihydrochloride, m.p. 246° dec., was 19.7 g. (75%).

2-Cyclohexyl-7-hydroxy-6-methylmerimine. (A) *From 7-amino-2-cyclohexyl-6-methylmerimine.* A solution of 3.8 g. of sodium nitrite in 30 ml. of water was added over a 30-min. period at 93–97° to a rapidly stirred solution of 11.5 g. (0.05 mole) of 7-amino-2-cyclohexyl-6-methylmerimine in 600 ml. of 0.05*N* hydrochloric acid. The reddish solution was held at the same temperature for 20 min. longer and then treated with activated carbon. The filtrate was concentrated to about 100 ml. and treated with excess sodium carbonate. The tan product which separated was filtered and washed with water, and the moist cake was recrystallized twice from ethanol. The yield of 2-cyclohexyl-7-hydroxy-6-methylmerimine, m.p. 253–255°, was 3.7 g. (32%). Recoveries from the alcoholic filtrates increased the yield to 50%.

(B) *From 2-Cyclohexyl-7-methoxy-6-methylmerimine.* A solution of 2.0 g. of 2-cyclohexyl-7-methoxy-6-methylmerimine, m.p. 58–60° but not analyzed, in 20 ml. of 48% hydrobromic acid was heated on the steam bath for 30 hr. and then concentrated to dryness. The residue was washed onto a filter with ethanol and dried. The yield of 2-cyclohexyl-7-hydroxy-6-methylmerimine dihydrobromide, m.p. *ca.* 320° dec., was 3.2 g. (100%). Recrystallization from ethanol improved the color but did not change the decomposition point.

When the dihydrobromide was dissolved in water and treated with sodium carbonate, the base was obtained. After recrystallization from ethanol it was identical by melting point, mixture melting point, and infrared spectra to the 2-cyclohexyl-7-hydroxy-6-methylmerimine prepared by method A above.

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Alkyl *N,N*-Dialkyl Methylphosphonamidates[1]

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In a series of recent publications Razumov *et al.*[3] describe the preparation and biological properties of

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(3) A. I. Razumov, O. A. Mukhacheva, and E. A. Markovich, *Khim. i Primenie Fosfororgan. Soedinenii, Akad. Nauk S.S.S.R., Trudy l-oi Konferents.*, 194 (1955) (published 1957); and *Zhur. Obschei Khim.*, **27**, 2389 (1957); A. I. Razumov, *Trudy Kazan. Khim. Technol. Inst. im. S. M. Kirova*, **23**, 205 (1957).

TABLE I

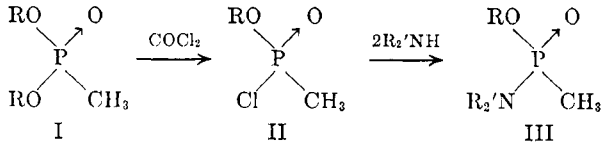
ALKYL *N,N*-DIALKYL METHYLPHOSPHONAMIDATES

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

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