purified dianilide (158 mg.) was dissolved in 1 ml. of pyridine and 1.5 ml. of acetic anhydride and allowed to stand overnight at room temperature. Addition of water, neutralization, and extraction with ether gave 181 mg. of a gum which slowly crystallized. Repeated crystallization from various solvents gave 45 mg. of needles, m.p. 125.4-126.4°, which were identified by elementary analyses, mixed melting point, and X-ray diffraction pattern as the methyl ether of zymonanilide (VII).

Anal. Calcd. for $C_{13}H_{13}NO_4$: C, 63.2; H, 5.30; N, 5.67; OCH_3, 12.6. Found: C, 63.4; H, 5.28; N, 5.50; OCH_3, 12.5.

Permanganate Oxidation of Methyl Ether of Zymonic Acid.—The acid hydrate (653 mg.) was dissolved in 36 ml. of ice-cold sodium bicarbonate solution (2.5%). Over a period of 40 minutes a potassium permanganate solution (733 mg. in 28 ml. of water) was added dropwise with shaking. After dilution with water, the solution was heated to coagulate the manganese dioxide which was then removed by filtration. The *p*H of the filtrate was adjusted to 6 and a calcium chloride solution (1 g. in 5 ml. of water) added. The calcium oxalate (289 mg.) was separated, treated with hydrochloric acid, and the oxalic acid removed by ether extraction (227 mg. anhydrous acid or 73% of theory). The oxalic acid was converted to the dibenzylamine salt, m.p. 205–206°, which showed no depression in melting point on admixture with an authentic sample.

Methyl Ether of Tetrinic Acid (X).—Tetrinic acid (XI), prepared by the method of Wolff,[5] was converted with diazomethane into the methyl ether which has been reported as a liquid by Conrad and Gast.[6] By fractionation we obtained one of the isomers, presumably the *trans* form, as a crystalline solid, m.p. 84–85° (long needles from acetone-petroleum ether).

Anal. Calcd. for $C_6H_8O_3$: C, 56.2; H, 6.29; OCH_3, 24.2. Found: C, 55.9; H, 6.00; OCH_3, 24.5.

In 95% alcohol the compound showed a single band at 2670 Å. ($E^{1\%}_{1\text{cm}}$ 1436, ϵ 18,380). It was completely hydrolyzed by water on the steam-bath in five minutes or at room temperature overnight. Correct methoxyl values were obtained only when the hydriodic acid was cooled in ice before the sample was added.

Methyl Ether of Zymonamide from ***Hansenula subpelliculosa.***—A fermentation using this organism (NRRL Y-1009) was conducted in the same manner as with *Trichosporon capitatum*, except that "Medium B" was used (same as Medium D only the urea was replaced by 2.5 g. $(NH_4)_2SO_4$). This yielded a methyl ester fraction (b.p. 117–118° at 1 mm., n^{28}D 1.4651) which gave a crystalline amide in good yield. This product (m.p. 208–209°) analyzed as follows.

Anal. Calcd. for $C_7H_9O_4N$: C, 49.1; H, 5.30; N, 8.19; OCH_3, 17.9. Found: C, 49.4; H, 5.18; N, 8.30; OCH_3, 18.5.

This sample was shown by mixed melting point and by comparison of X-ray patterns to be identical with the amide from *Trichosporon capitatum*.

Methyl Ether of Zymonamide from ***Kloeckera brevis.***—From a fermentation using this organism (NRRL Y-915) on Medium B, 5.74 g. of methyl ester (b.p. 112–117° at 1 mm., n^{28}D 1.4650) was obtained from 56 g. of glucose (10.3% weight yield). The ester gave in good yield an amide shown by mixed melting point to be identical with the *Trichosporon* derivative.

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[5] L. Wolff, *Ann.*, **288**, 16 (1895).

[6] M. Conrad and R. Gast, *Ber.*, **31**, 2731 (1898).

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF TEMPLE UNIVERSITY]

Di-*n*-alkylphosphine Oxides. I. Synthesis

BY ROBERT H. WILLIAMS[1a] AND LYLE A. HAMILTON[1b]

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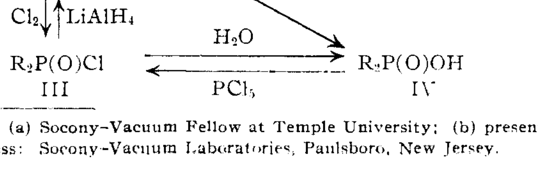
The preparation of the di-*n*-hexyl-, di-*n*-octyl- and di-*n*-octadecylphosphine oxides, *i.e.*, compounds of the type $R_2P(O)H$, by the reaction of the appropriate Grignard reagent with di-*n*-butyl phosphite is reported. The di-*n*-octylphosphine oxide has also been prepared by the reaction of di-*n*-octylphosphinyl chloride, $(n\text{-}C_8H_{17})_2P(O)Cl$ with lithium aluminum hydride. These higher di-*n*-alkylphosphine oxides are white solids and are stable, neutral entities. Chemical evidence suggests that they exist as the phosphine oxides rather than the isomeric phosphinous acids, R_2POH.

A review of the chemical literature has revealed no description of the di-*n*-alkylphosphine oxides (phosphinous acids). We have been able to prepare the di-*n*-hexyl-, di-*n*-octyl- and di-*n*-octadecylphosphine oxides. This preparation is most conveniently accomplished by treating the appropriate Grignard reagent with di-*n*-butyl phosphite or other dialkyl phosphite, II, although the replacement of the halogen in a dialkylphosphinyl chloride (R_2P-$P(O)Cl$), III, with hydrogen, using lithium aluminum hydride, has also been successful. We have been unable to isolate either dimethylphosphine oxide or diphenylphosphine oxide from the reaction of the appropriate Grignard reagent on di-*n*-butyl phosphite, probably because of the greater instability of these phosphine oxides.



As proof of structure of the dialkylphosphine oxides, the di-*n*-octylphosphine oxide was chlorinated to the phosphinyl chloride and the latter hydrolyzed to the phosphinic acid. This acid was identical with di-*n*-octylphosphinic acid prepared by the addition of *n*-1-octene to hypophosphorous acid.[2] Direct oxidation of the di-*n*-octylphosphine oxide with hydrogen peroxide gave the same di-*n*-octylphosphinic acid. The conversion of dialkyl phosphites, II, to dialkylphosphinic acids, IV, by reaction with Grignard reagent and oxidation with hydrogen peroxide but without isolation of intermediates, has been reported by Kosolapoff.[3] The method of synthesis of di-*n*-octylphosphine oxide from the phosphinic acid by conversion of the latter to the phosphinyl chloride and replacement of the chlorine with hydrogen by means of lithium

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[2] British Patent 660,918.

[3] G. M. Kosolapoff and R. M. Watson, THIS JOURNAL, **73**, 4101 (1951).

aluminum hydride, offers support to our contention that these compounds are described better as phosphine oxides rather than as phosphinous acids. Unequivocal proof that much of the material has the phosphine oxide structure has been furnished by infrared absorption studies which are now being prepared for publication.[4]

The di-*n*-alkylphosphine oxides from C-6 to C-18 are white solids, the higher members being stable at room temperature. The melting points increase with molecular weight. The *n*-hexyl derivative developed a slight phosphine-like odor in about two weeks but its melting point was not affected nor was any titratable acidity developed. A sample of di-*n*-octylphosphine oxide has remained perfectly stable for over two years. The di-*n*-octadecyl derivative also shows no evidence of instability on storage at laboratory temperature.

Work is now in progress to synthesize other dialkylphosphine oxides and to extend the scope of the two preparative methods described. We plan to study the rate of decomposition of some of the less stable phosphine oxides.

Experimental Part

Di-*n*-hexylphosphine Oxide.—A solution of Grignard reagent was prepared, under nitrogen atmosphere, from 175 g. (0.827 mole) of *n*-hexyl iodide and 18 g. (0.75 mole) of magnesium in 550 ml. of dry ether. To this reagent there was added, with stirring, in the course of 50 minutes, a solution of 48.5 g. (0.25 mole) of di-*n*-butyl phosphite in 150 ml. of dry ether. The temperature in the reaction flask was maintained at 15° during the addition and was subsequently raised to the reflux point to complete the reaction. The mixture was then cooled to 10° and 300 ml. of 25% sulfuric acid solution was added during a one-hour period. The ether layer was separated and washed successively with three 200-ml. portions of distilled water, three 100-ml. portions of 15% potassium carbonate solution and five 300-ml. portions of distilled water. The ether solution was dried over anhydrous sodium sulfate, filtered, and the ether removed on the steam-bath. Recrystallization of the crude product from *n*-hexane gave 21 g. of white crystals, m.p. 76.5°. The yield was 29% based on the di-*n*-butyl phosphite.

Anal. Calcd. for $(C_6H_{13})_2P(O)H$: P, 14.22. Found: P, 14.17.

A potentiometric titration showed that the compound was neutral.

Di-*n*-octylphosphine Oxide.—The procedure used closely followed that for di-*n*-hexylphosphine oxide, the same molar amounts being used throughout. Upon evaporation of the ether solution 77 g. of crude product was obtained. Recrystallization from hexane gave 48 g. (70% of theory) of the pure compound, m.p. 85°.

Anal. Calcd. for $(C_8H_{17})_2P(O)H$: P, 11.3; mol. wt., 274. Found: P, 11.3; mol. wt., 305 (b.p. in benzene).

The compound showed no acidity by potentiometric titration.

Di-*n*-octadecylphosphine Oxide.—The procedure for preparing di-*n*-octadecylphosphine oxide was modified from that described for the hexyl homolog because of the insolubility of the *n*-octadecyl derivative in ether. A Grignard reagent was prepared by treating 12.2 g. (0.5 mole) of magnesium and 177.6 g. (0.53 mole) of *n*-octadecyl bromide (activated with a few ml. of *n*-butylmagnesium bromide solution) in 800 ml. of dry ether. To this reagent was added a solution of 32.3 g. (0.166 mole) of di-*n*-butyl phosphite in 150 ml. of dry ether. The temperature was maintained at 15° during the addition, which required about 50 minutes, and then was raised to reflux for a few minutes to complete the reaction. The solution was cooled to 15° and hydrolyzed at 15–20° with 300 ml. of 25% sulfuric acid solution. The di-*n*-octadecylphosphine oxide came out of solution and formed a thick gelatinous mass. The entire contents of the reaction flask were transferred to a large buchner funnel and filtered under vacuum. The filter cake was dissolved in 2 l. of hot benzene and the solution filtered to remove water and magnesium sulfate. Upon cooling the benzene solution in an ice-bath and filtering, 42 g. of a tan solid was obtained. Recrystallization from equal parts of benzene and *n*-hexane, using Super-Filtrol clay as a decolorizing agent, gave 24 g. (26% yield) of the pure compound, m.p. 107°.

Anal. Calcd. for $(C_{18}H_{37})_2P(O)H$: P, 5.59. Found: P, 5.61.

Di-*n*-octylphosphine Oxide from Di-*n*-octylphosphinic Acid.—Di-*n*-octylphosphinic acid, prepared by the addition of *n*-1-octene to hypophosphorous acid,[2] was converted to the acid chloride by treating 15.2 g. (0.054 mole) of the acid with 11.3 g. (0.054 mole) of PCl_5 in 210 ml. of dry benzene for one hour under gentle reflux. After the removal of benzene and $POCl_3$ by distillation, the phosphinyl chloride residue was dissolved in 100 ml. of dry ether and added during one hour to a well-stirred suspension of 7.0 g. (0.18 mole) of finely ground lithium aluminum hydride in 200 ml. of dry ether. The reaction was carried out in a nitrogen atmosphere and the temperature was maintained at −2° during the addition and for an additional reaction period of one hour. Decomposition of excess lithium aluminum hydride was accomplished at 10° by the cautious addition of excess water followed by 500 ml. of 15% sulfuric acid solution. The ether layer was separated and thoroughly washed with 6% potassium carbonate solution and then with water. A crude residue of 13.5 g. was recovered from evaporation of the ether solution. Recrystallization from *n*-hexane, after decolorizing with carbon, yielded 8.0 g. (53.9% yield) of white crystals which melted at 85° and which did not depress the melting point of a sample of di-*n*-octylphosphine oxide prepared from di-*n*-butyl phosphite and *n*-octylmagnesium iodide. The melting point of a sample of di-*n*-octylphosphinic acid was depressed by 6°.

Anal. Calcd. for $(C_8H_{17})_2P(O)H$: P, 11.3; mol. wt., 274. Found: P, 11.35; mol. wt., 315 (b.p. in benzene).

X-Ray diffraction patterns obtained on samples of di-*n*-octylphosphine oxide made by the Grignard method and by the lithium aluminum hydride method were compared. They were found to be identical.

Di-*n*-octylphosphinic Acid from Di-*n*-octylphosphine Oxide.—Chlorine gas was bubbled slowly into a solution of 6.0 g. (0.022 mole) of di-*n*-octylphosphine oxide in 130 ml. of carbon tetrachloride, maintained at 0–9°, until the greenish-yellow color of excess chlorine persisted. The solution of the phosphinyl chloride was then treated with a solution of 15 g. of potassium carbonate in 200 ml. of distilled water, followed by acidification with 15% sulfuric acid solution. After washing with water and removing the solvent, the crude acid was recrystallized from *n*-hexane giving 5.5 g. (86.6% yield) of di-*n*-octylphosphinic acid, m.p. 85°, which did not depress the melting point of an authentic sample of di-*n*-octylphosphinic acid.

Anal. Calcd. for $(C_8H_{17})_2P(O)OH$: P, 10.7; neut. equiv., 290.4. Found: P, 10.69; neut. equiv., 290.1.

Direct oxidation of a sample of di-*n*-octylphosphine oxide with excess 30% hydrogen peroxide[3] at 60–70° also yielded di-*n*-octylphosphinic acid, m.p. 85°, which did not depress the melting point of an authentic sample of di-*n*-octylphosphinic acid, but which did depress the melting point of a sample of the original di-*n*-octylphosphine oxide by 6°.

Di-*n*-hexylphosphinic Acid from Di-*n*-hexylphosphine Oxide.—Oxidation of a sample of di-*n*-hexylphosphine oxide with excess 30% hydrogen peroxide[3] at 60–70° yielded di-*n*-hexylphosphinic acid, m.p. 77.0–78.5°. This acid depressed the melting point of a sample of the original di-*n*-hexylphosphine oxide by 10°.

Anal. Calcd. for $(C_6H_{13})_2P(O)OH$: neut. equiv., 234.3. Found: neut. equiv., 235.3.

The literature[5] reports a m.p. of 78–79° for this compound under the name di-*n*-hexylphosphonous acid.

Di-*n*-octadecylphosphinic Acid from Di-*n*-octadecylphosphine Oxide.—Di-*n*-octadecylphosphine oxide was converted to the acid by treatment of a sample with excess PCl_5 followed by hydrolysis. The crude product was decolorized

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(4) C. D. Miller, M. A. Thesis, Temple University.

(5) G. M. Kosolapoff and J. S. Powell, *J. Chem. Soc.*, 3535 (1950).

with charcoal and recrystallized four times from benzene. The final product was a white powder which melted at 105–105.5°. It did not depress the melting point of an authentic sample of di-*n*-octadecylphosphinic acid prepared from *n*-1-octadecene and hypophosphorous acid[2] (m.p. 105.3–106°), but did depress the melting point of the original di-*n*-octadecylphosphine oxide by 10°.

Anal. Calcd. for $(C_{18}H_{37})_2P(O)OH$: neut. equiv., 571. Found: neut. equiv., for the sample from the phosphine oxide 560, for the sample from hypophosphorous acid 583.

X-Ray diffraction patterns indicated that the two acid samples were essentially identical.

It was noted in taking the mixed melting point of di-*n*-octadecylphosphine oxide with di-*n*-octadecylphosphinic acid that no depression was obtained unless the samples were very intimately mixed.

After normal mixing of the samples melting points of 105–106° were obtained, but when these melts were solidified and again heated they melted 10° lower.

Attempts to oxidize di-*n*-octadecylphosphine oxide with 30% hydrogen peroxide resulted in little or no reaction.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AT THE OHIO STATE UNIVERSITY]

Perfluorinated Cyclic Ethers

BY ALBERT L. HENNE AND SIDNEY B. RICHTER

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$CF_2CF_2\text{-}O\text{-}CF_2CF_2$ and $CF_2CF_2CF_2\text{-}O\text{-}CF_2CF_2$ were synthesized and found incapable of dissolving Lewis acids. The lack of basic properties already shown in perfluorinated open chain ethers is therefore not due to steric hindrance, and is attributed to electronegative induction.

Perfluorinated ethers do not dissolve in sulfuric acid, nor are they colored by ferric chloride, and this loss of basic character has been attributed to electronegative induction[1]; but since tetrahydrofuran is known to be more basic than open chain ethers,[2] the loss might have been caused by steric factors. Perfluorinated cyclic ethers were therefore prepared, in which the steric factor would be absent; they were found to be non-basic.

The syntheses follow. A perfluorinated dibasic ester $RO_2CCF_2(CF_2)CF_2CO_2R$ (formulated with one of its CF_2 groups in parentheses to denote either a succinate or a glutarate) was reduced to a diol $HOCH_2CF_2(CF_2)CF_2CH_2OH$ and the latter cyclized to an ether $(CF_2)CF_2CH_2\text{-}O\text{-}CH_2CF_2$. Chlorination yielded a perhalogenated cyclic ether $(CF_2)CF_2CCl_2\text{-}O\text{-}CCl_2CF_2$, which fluorination transformed into the desired perfluorinated cyclic ether $(CF_2)CF_2CF_2\text{-}O\text{-}CF_2CF_2$. Alternate routes, through a perfluorinated cyclic anhydride, failed. The last step of the sequence, halogen exchange, proved much easier with the smaller, five-membered ring which did not break than with the larger six-membered ring, where completion of the halogen exchange was almost prevented by decomposition. Resisted halogen exchange by the larger, fluorine-richer ring rather than weakness in ring size is regarded as the cause of the difference.

The resistance to solvolysis of the CF_2 groups next to the oxygen bridge was tested by heating cyclo-C_4F_8O with an alcohol solution of sodium alcoholate for a week at 100°, without effect. This behavior parallels that reported for "protected" CF_2 groups in open chain ethers.[1]

The infrared spectrum of cyclo-C_4F_8O is shown as Fig. 1, with the spectrum of the open chain $C_4F_9\text{-}O\text{-}C_4F_9$ for comparison.

Experimental Syntheses

Perfluorosuccinic Acid.—$CF_2{=}CCl_2$ was obtained by perchlorination[3] of commercial CF_2HCH_3 (quantitative) followed by zinc dechlorination (95% yield). Its dimerization[4] at 220° gave, in 24 hours, an 85% yield of cyclo-$CF_2CF_2CCl_2CCl_2$, quantitatively dechlorinated to cyclo-$CF_2CF_2CCl\text{-}CCl$, the oxidation[5] of which gave a 74% yield of diethyl perfluorosuccinate.

Perfluorosuccinic Anhydride.—This anhydride could not be obtained by heating the diacid with concentrated sulfuric acid at 140° for three hours; it was, however, obtained in 62% yield by heating a mixture of perfluorosuccinic acid (19 g. or 0.1 mole) with P_2O_5 (28.4 g. or 0.2 mole) to 185° in a Claisen flask, and the balance of the acid was recovered. The anhydride $CF_2CO\text{-}O\text{-}COCF_2$, b.p. 54–55°, n^{20}_D 1.3240, d^{20}_4 1.6209, MR 21.30, AR_F 1.40, had properties which agreed with those shown in a recent patent.[6] Attempts to transform it to $CF_2CCl_2\text{-}O\text{-}CCl_2CF_2$ with PCl_5 failed, and attempts to reduce it to a lactone $CF_2CO\text{-}O\text{-}CH_2CF_2$ gave only the diol described hereunder.

Tetrafluorobutanediol $HOCH_2CF_2CF_2CH_2OH$.—Diethyl perfluorosuccinate (102 g. or 0.414 mole) was reduced with $LiAlH_4$ (17.3 g. or 0.45 mole) in dry ether to give $HOCH_2CF_2CF_2CH_2OH$ (57.6 g. or 0.355 mole) in 86% yield. This diol, b.p. 110–112° at 13 mm., melted at 80–80.6° after recrystallization from benzene, agreeing with McBee's description.[7] Its first and second ionization constants were determined by Glasstone's method[8] as 1.2×10^{-11} and 4.1×10^{-12}, the correct order of magnitude.[7,9]

Cyclization.—A mixture of the glycol (81 g. or 0.5 mole) and concentrated sulfuric acid (10 g. or 0.1 mole) was kept in an oil-bath at 185°. The cyclic ether which distilled over was dried with Drierite and redistilled, to give $CF_2CH_2\text{-}O\text{-}CH_2CF_2$ (71 g. or 0.49 mole), b.p. 68° in 97% yield.

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[1] A. L. Henne and M. A. Smook, THIS JOURNAL, **72**, 4378 (1950).

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[3] E. T. McBee, A. L. Henne, H. B. Hass and N. H. Elmore, *ibid.*, **62**, 3340 (1940).

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[9] A. L. Henne and R. L. Pelley, THIS JOURNAL, **74**, 1426 (1952).