TABLE I

CONDUCTIVITY OF IRRADIATED LIQUID AMMONIA

Volume NH_3, 8.3 ml.

Exposure, sec.	Dark time, sec.	Target current, μa.	Roentgens[a] × 10^{-7}	Sp. resist × 10^6	r./μa.-sec. × 10^{-5}
Sample 3, temperature −74°; 2 Mev. cathode rays					
0	..	..		1.50	
65	..	3.4	1.8	1.50[b]	0.68
...	30	..	...	1.50	..
...	65	..	...	1.50	..
30	..	10.0	2.4	...	.80
150	..	3.5	4.3	1.45[b]	.82
120	..	3.6	3.5	...	.81

Total exposure time, min.	Current, μa.	Roentgens total	Sp. resist × 10^3
Sample 4, temperature −75° to −72°; 2 Mev. X-rays			
0	...	0	510
2	100	6×10^3	490[b]
5	100	1.5×10^4	450[b]
Off 5	...	....	450
6	100	1.8×10^4	460[b]
8	100	2.5×10^4	...
8′20″	...	....	460
Off 4	...	....	460

[a] Dose calculated assuming only one-half ammonia irradiated. [b] Measurement made during irradiation.

tion of about 3×10^{-9} mole per liter of alkali metal or free electron in liquid ammonia could have been detected. On the basis of the data, no evidence was obtained for the formation of stabilized free electrons during the irradiation of liquid ammonia under the experimental conditions used.

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The Effect of Esterification on Anticholinesterases as Determined by Three Different Enzymes

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The preparation of 50 phosphonic and phosphinic acids has been described recently from our laboratory.[1] These compounds were examined for their anti-plasma cholinesterase activity.[2] Several of the compounds were found to be quite active. A few of the acids were esterified. Most of the esters were much more active against human plasma cholinesterase than the free acids. It is desirable for the development of insecticides to examine the action of anticholinesterases on enzymes of different species. In the present experiments we subjected our most active compounds to a comparative study using three different enzymes, human plasma cholinesterase, pig brain acetylcholinesterase and fly brain acetylcholinesterase. The effect of the esters on the cholinesterase activity of the three different soluble enzyme preparations has also been tested.

Methods and Materials.—The human plasma cholinesterase was the same as in our previous work.[2] The method for the preparation of soluble pig brain acetylcholinesterase has been described recently.[3] A similar procedure was employed for the preparation of acetylcholinesterase from the heads of the house fly (*Musca domestica* L.). An activator buffer–salt solution[3] was used in conjunction with the pig brain and fly brain acetylcholinesterase but not with the human plasma cholinesterase. Details concerning the enzyme inhibitor experiments have been described previously.[2,3] Residual acetylcholine was analyzed by Hestrin's[4] method using Klett–Summerson photoelectric colorimeter.

Inhibition of Three Different Cholinesterases.—It may be seen in Table I that our most active compounds are all *ortho*-halogen derivatives. The *m*-halogen derivatives were less active, while the *p*-substituted compounds had no activity. The meta and para compounds are not included in Table I. It may be seen that esterification considerably increased the inhibitory power of the free acids in most instances. The isopropyl ester of (*o*-bromophenyl)-phenylphosphinic acid was more inhibitory than its ethyl ester and methyl ester. Concerning the plasma enzyme the ethyl ester of bis-(*o*-bromophenyl)-phosphinic acid was about 33 times more inhibitory than the free acid and the ethyl ester of *o*-bromobenzenephosphonic acid was 400 times more active than the free acid. When the pig brain enzyme was employed the ethyl ester of bis-(*o*-bromophenyl)-phosphinic acid was 200 times more inhibitory than the free acid and when the fly brain enzyme was tested the ester was at least 250 times more active than the free acid.

TABLE I

THE EFFECT OF ESTERIFICATION ON ANTICHOLINESTERASES AS MEASURED BY THREE DIFFERENT ENZYMES

Compound	Plasma ChE (I_{50},[a] moles/l.)	Brain AChE	Fly AChE
$(o\text{-BrC}_6H_4)C_6H_5PO_2H$	6×10^{-5}	7×10^{-3}	$>5 \times 10^{-3}$
$(o\text{-BrC}_6H_4)C_6H_5PO_2CH(CH_3)_2$	1×10^{-6}	2.5×10^{-4}	2.5×10^{-6}
$(o\text{-BrC}_6H_4)C_6H_5PO_2C_2H_5$	1×10^{-5}	2×10^{-4}	5×10^{-6}
$(o\text{-BrC}_6H_4)C_6H_5PO_2CH_3$	8×10^{-5}	3.1×10^{-3}	$>1 \times 10^{-3}$
$(o\text{-BrC}_6H_4)_2PO_2H$	1×10^{-4}	5×10^{-3}	$>5 \times 10^{-3}$
$(o\text{-BrC}_6H_4)_2PO_2C_2H_5$	3×10^{-6}	2.5×10^{-5}	2×10^{-5}
$o\text{-BrC}_6H_4PO_3H_2$	4×10^{-3}	$>5 \times 10^{-3}$	$>5 \times 10^{-3}$
$o\text{-BrC}_6H_4PO(OC_2H_5)_2$	1×10^{-5}	1.25×10^{-3}	1×10^{-3}

[a] The I_{50} values (concentrations required for 50% inhibition) in this table were obtained from graphs in which % inhibition was plotted against the logarithm of the molar concentration of the compounds.

Among the 3 enzymes human plasma cholinesterase is much more readily inhibited by all compounds with the exception of ethyl ester of (*o*-bromophenyl)-phenylphosphinic acid, than the pig brain and fly brain acetylcholinesterase. This is not surprising since the plasma cholinesterase and the two brain enzymes belong to 2 different groups of enzymes.

Acknowledgments.—The authors are grateful to Drs. G. O. Doak and L. D. Freedman for the phosphorus compounds.

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Preparation of a Cyclopentenone by the Stobbe Condensation

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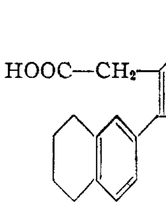
The Stobbe condensation with two δ-keto-esters has been shown to give substituted cyclohexenones.[1,2] A similar reaction has now been observed with a γ-keto-ester. The crude Stobbe half-ester mixture from methyl β-(5,6,7,8-tetrahydro-2-naphthoyl)-propionate could not be purified because there was decomposition in an attempted vacuum distillation. It was hydrolyzed with alcoholic potash to give the cyclized product, 3-(5,6,7,8-tetrahydro-2-naphthyl)-2-cyclopenten-1-one-2-acetic acid (I), in 40% yield.

The structure of this cyclopentenone was easily demonstrated by preparing the same product from 2-acetyl-5,6,7,8-tetrahydronaphthalene by an established method.[3,4] The initial product of the Stobbe condensation was probably a 2-carbomethoxycyclopenten-1-one which lost its carbomethoxy group on hydrolysis.

The Stobbe condensation is the better of the two methods of preparation described.



I

Experimental

Furfurylidene-2-acetyl-5,6,7,8-tetrahydronaphthalene.—To 260 g. of 2-acetyltetrahydronaphthalene[5] in 600 ml. of ethanol and 124 ml. of furfural, was added 10 ml. of 45% aqueous potassium hydroxide solution. After standing overnight, the product was filtered; yield 350 g., m.p. 65–68°. A sample was recrystallized from ethanol, m.p. 65–66°.

Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39. Found: C, 80.87; H, 6.30.

ε-(5,6,7,8-Tetrahydro-2-naphthoyl)-homolevulinic Acid.—Treatment of 600 g. of the preceding with 7200 ml. of ethanol and 1800 ml. of concentrated hydrochloric acid followed by repeated extraction with a mixture of 3600 ml. of concentrated hydrochloric acid, 3600 ml. of acetic acid and 7200 ml. of water in the usual manner[3,4] gave 187 g. of the diketo acid (25%). A sample was recrystallized from ether-pentane, m.p. 114.5–115°.

Anal. Calcd. for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.95; H, 6.99.

3-(5,6,7,8-Tetrahydro-2-naphthyl)-2-cyclopenten-1-one-2-acetic Acid.—(a) This was prepared in the usual manner[3,4] from the preceding in 95% yield. The product was recrystallized from chloroform and then from ether, m.p. 129–130°.

Anal. Calcd. for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.32; H, 6.65.

The oxime of this keto-acid was prepared in pyridine–ethanol and recrystallized from ethyl acetate, m.p. 160–161° (dec.).

Anal. Calcd. for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71. Found: C, 71.55; H, 6.70.

The methyl ester made with diazomethane in ether was crystallized from ethanol, m.p. 88–89°.

Anal. Calcd. for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 75.72; H, 7.00.

(b) Methyl β-(5,6,7,8-tetrahydro-2-naphthoyl)-propionate was prepared by the esterification of the acid[6] using the method of Clinton and Laskowski.[7] The ester has been described by Newman and Zahm.[5] The ester (246 g.) dissolved in 292 g. of dimethyl succinate was added to a refluxing solution of 52 g. of potassium in 900 ml. of dry *t*-butyl alcohol in an atmosphere of nitrogen. A solid potassium salt separated immediately. The mixture was kept in an oil-bath at 110–130° for 30 minutes, cooled, and worked up by the usual method.[8] The acidic fraction weighed 325 g. (90%).

A 14-g. sample was dissolved in 100 ml. of ethanol containing 15 ml. of 45% aqueous potassium hydroxide. The solution was heated on the steam-bath. Water was added (50 ml.) to dissolve the precipitated salt and heating was continued for 30 minutes. The solution was cooled, acidified with dilute hydrochloric acid and extracted with ether. The ethereal solution was treated in the usual manner and the ether was removed. The residue was crystallized from chloroform–pentane giving 4.7 g. (45%), m.p. 129–130° undepressed on admixture with the preparation of (a) above. A repetition of the hydrolysis on a larger scale (116 g.) gave 36 g. of crude product and 25 g. of recrystallized material (m.p. 129–130°). An additional 14 g. (m.p. 128–130°) was recovered by treatment of the mother liquor with Girard Reagent T, followed by recrystallization of the ketonic fraction from chloroform.

Anal. Calcd. for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.51, 75.44; H, 6.63, 6.65.

The oxime, made as in (a) and crystallized from ethyl acetate had m.p. 161–162° (dec.) undepressed on admixture with the oxime of (a).

Anal. Calcd. for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71. Found: C, 71.63; H, 6.81.

The methyl ester was made with diazomethane and crystallized from ethanol, m.p. 87–89° undepressed on admixture with the ester of (a).

Anal. Calcd. for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 76.02; H, 7.05.

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Methylpentaerythrityl Ether

By S. Wawzonek and J. P. Henry[1]

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In the formation of the methyl and dimethyl ethers of pentaerythritol by the Tollens condensation of acetaldehyde and formaldehyde in 50% methanol, β-methoxypropionaldehyde has been postulated as an intermediate.[2] This assumption has now been verified by the preparation of the methyl ether of pentaerythritol using β-methoxypropionaldehyde in the Tollens condensation in place of the acetaldehyde. The similar yield of this ether (13.4%) to that (11.4%) obtained from the condensation using acetaldehyde indicates that β-methoxypropionaldehyde is partly dissociated into acrolein and methanol in the Tollens condensation. This behavior is consistent with the mechanism proposed.[2]

Experimental[3]

β-Methoxypropionaldehyde[4] was prepared by adding acrolein (56.0 g.) to a solution of sodium methoxide (from 0.4 g. of sodium) in absolute methanol (150 ml.) at 0° in the course of three hours and allowing the resulting solution to

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