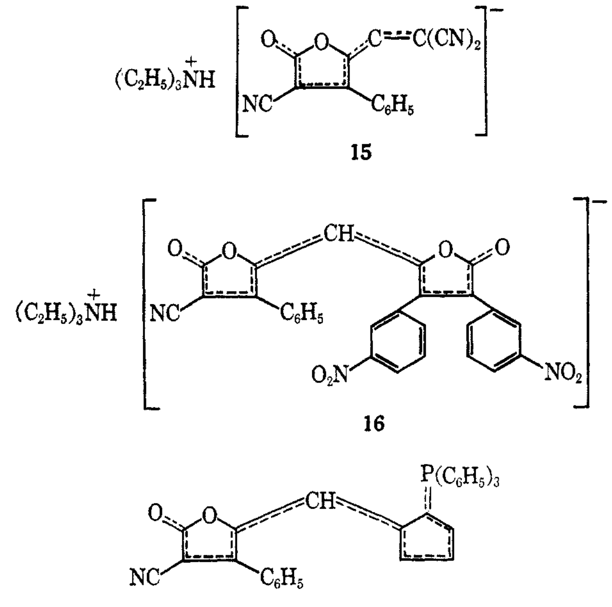
Chart II



15

16

17

chlorobenzene to give 20.8 g (47.8%) of green crystals, mp 258–261°, with sintering at 234°.

Bis[3-cyano-4-phenyl-2(5H)-furanone-(5)]monomethinoxonol, Pyridine Salt (9). A.—A mixture of 37.0 g (0.200 mole) of **1**, 14.8 g (0.100 mole) of triethyl orthoformate, and 250 ml of pyridine was refluxed for 1 hr and then cooled in an ice bath. The separated solid was recrystallized from 300 ml of pyridine to give 15.1 g (32.8%) of green crystals, mp 276–277°.

B.—Refluxing a mixture of 12.0 g (0.0652 mole) of **1**, 13.9 g (0.0652 mole) of 3-cyano-5-hydroxymethylene-4-phenyl-2(5H)-furanone, and 150 ml of pyridine for 3 hr, cooling, collection of the solid, and recrystallization from pyridine gave 8.4 g (28%) of **9**, mp 275–276°.

[3-Cyano-4-phenyl-2(5H)-furanone-(5)]-[3,4-di-*p*-nitrophenyl-2(5H)-furanone-(5)]monomethinoxonol, Triethylamine Salt (16).—Reaction of equimolar amounts of 3,4-di-*p*-nitrophenyl-2(5H)-furanone, triethylamine, and **13** in pyridine according to procedure B used to make **9** gave a 43% yield of shiny green crystals, mp 275–276°.

3-Cyano-5-dimethylaminomethylene-4-phenyl-2(5H)-furanone (13).—To 400 ml of dimethylformamide, there was added slowly (temperature being kept below 30°), with stirring and cooling, 61.2 g (0.400 mole) of phosphoryl chloride and then in one portion 74.0 g (0.400 mole) of **1**. The mixture was stirred for 2 hr (exotherm to 49°), cooled, and diluted with 300 ml of ice water. Collection of the solid and recrystallization from 900 ml of acetonitrile gave 83.2 g (86.6%) of yellow needles, mp 222–223°. The mass spectrum gave a parent peak of 240 mass units.

3-Cyano-5-hydroxymethylene-4-phenyl-2(5H)-furanone.—A mixture of 24.0 g (0.100 mole) of **13**, 300 ml of methanol, 4.0 g (0.10 mole) of sodium hydroxide, and 10 ml of distilled water was refluxed for 4 hr and then steam-distilled into a solution of 10 ml of concentrated hydrochloric acid and 100 ml of ethanol until the distillate was no longer basic. Evaporation of the distillate (800 ml) at room temperature and vacuum drying of the residue over anhydrous calcium sulfate gave 1.1 g of dimethylamine hydrochloride (mass spectrum identical with authentic sample). The cooled residue from the steam distillation was diluted with 500 ml of water and filtered. Acidification of the filtrate caused the separation of a solid which was washed with water and dried to give 20.2 g (94.7%): mp 218–221° (not raised by recrystallization from acetonitrile); λ_{OH}^{KBr} 3.22 μ; λ_{CN}^{KBr} 4.43 μ; $\lambda_{C=O}^{KBr}$ 5.75 μ; nmr spectrum (dimethyl sulfoxide) 7.36 (singlet, 1), 7.62 (singlet, 5), and 12.9 (singlet, 1) (exchangeable with deuterium oxide); 2,4-dinitrophenylhydrazone, yellow crystals from acetonitrile, mp 212–214°.

Anal. Calcd for $C_{12}H_7NO_3$: C, 67.6; H, 3.29; N, 6.57. Found: C, 67.4; H, 3.0; N, 6.5.

3-Cyano-5-[3-ethyl-2-benzothiazolylideneethylidene]-4-phenyl-2(5H)-furanone (14).—A stirred mixture of 12.7 g (0.0416 mole) of 3-ethyl-2-methylbenzothiazolium iodide, 10.0 g (0.0416 mole) of **13**, 1 ml of piperidine, and 200 ml of methanol was refluxed for 4 hr and allowed to cool overnight to room temperature. The separated solid was recrystallized twice from pyridine to give 8.9 g (58%) of shiny green crystals, mp 279–281°.

3-Cyano-5-(2-dicyanoethylidene)-4-phenyl-2(5H)-furanone, Triethylamine Salt (15).—A solution of 24.0 g (0.100 mole) of **13**, 6.6 g (0.10 mole) of malononitrile, 15 ml of triethylamine, and 150 ml of ethanol was refluxed for 3 hr and then cooled overnight in the refrigerator. The separated solid was recrystallized three times from ethyl acetate to give 18.4 g (50.8%) of orange-red crystals, mp 149–151°.

2-(3-Cyano-2,5-dihydro-2-oxo-4-phenyl-5-furylidenemethyl)-cyclopentadienylidenetriphenylphosphorane (17).—A stirred solution of 12.0 g (0.0500 mole) of **13**, 16.3 g (0.0500 mole) of cyclopentadienylidenetriphenylphosphorane, 1 ml of glacial acetic acid, and 200 ml of pyridine was refluxed for 1 hr, diluted with 200 ml of methanol, and cooled overnight in the refrigerator. Recrystallization of the separated solid from 100 ml of chlorobenzene gave 18.0 g (69.1%) of shiny gray crystals, mp 241–242°.

Acknowledgments.—The authors are indebted to Dr. T. H. Regan and Mr. R. L. Young, for running and interpreting nmr spectra; to Messrs. G. P. Happ and D. P. Maier, for running and interpreting mass spectra; to Miss Thelma J. Davis, for running infrared spectra; and to Mr. J. J. DePalma, for obtaining visible and ultraviolet spectra.

A Total Synthesis of Phytol[1]

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A total synthesis of phytol from acetone is described. The synthesis has shorter stages than previously reported methods. Triethyl phosphonocrotonate anion could be condensed with carbonyl compounds to give the corresponding dienoic esters. The products were converted to β-keto sulfoxides by reaction with methylsulfinyl carbanion and the sulfoxides were reduced with aluminum amalgam to give methyl ketones. Phytone, one of the compounds prepared in this manner, was converted to phytol by two methods.

In an earlier paper[2] a six-step synthesis of isophytol from pseudoionone and propargyl alcohol was described. Recently, Nazarov,[3] Lukes,[4] and Maurit[5] succeeded in the total synthesis of phytol from laevulinic acid or acetylene; however, these syntheses are unfit for a large scale operation because of the number of steps involved.

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(1) Presented in part at the 18th Annual Meeting of the Chemical Society of Japan, Osaka, April 1965.

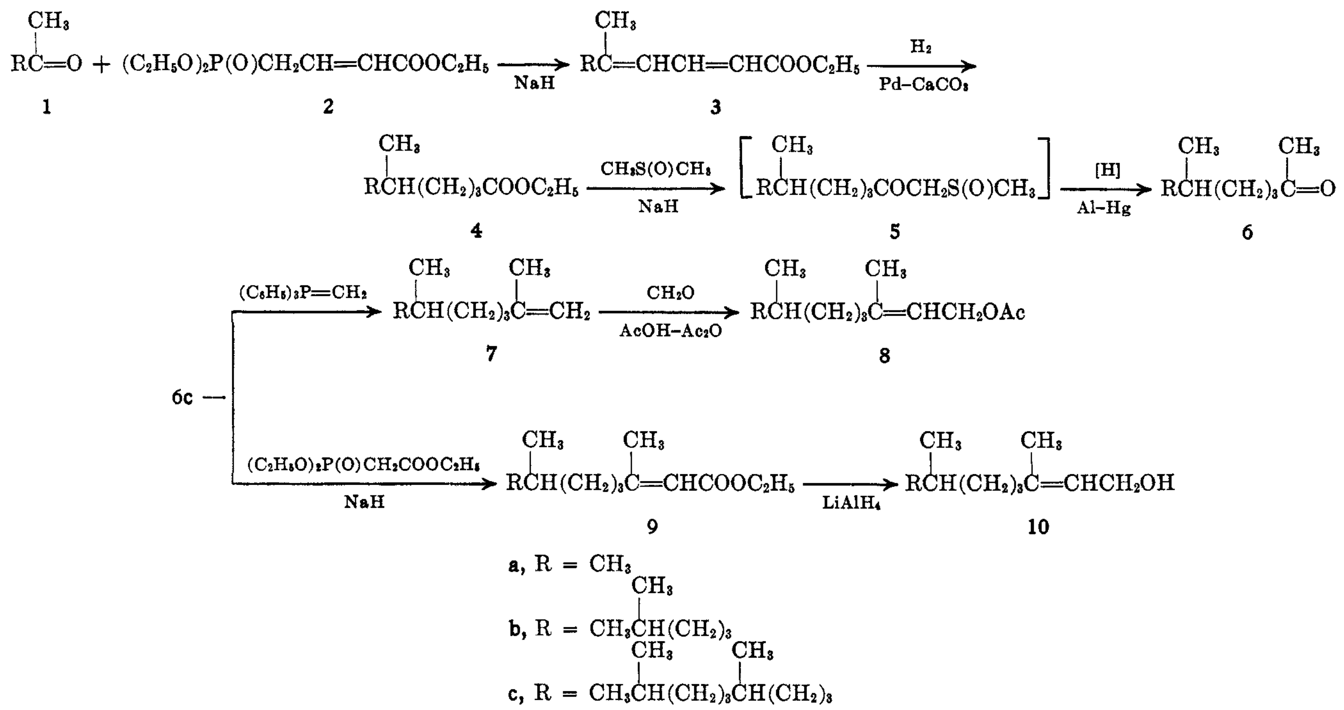
(2) K. Sato, Y. Kurihara, and S. Abe, *J. Org. Chem.*, **28**, 45 (1963).

(3) I. N. Nazarov, B. P. Gusev, and V. I. Gunar, *Zh. Obshch. Khim.*, **28**, 1444 (1958).

(4) R. Lukes and A. Zobácová, *Chem. Listy*, **51**, 330 (1957).

(5) M. E. Maurit, G. V. Smirnova, E. A. Parfenov, T. M. Vinkovskaya, and N. A. Preobrazhenskii, *Zh. Obshch. Khim.*, **32**, 2483 (1962).

SCHEME I



We have found that phytone can be obtained from acetone by application of two reactions developed by Wadsworth[6] and Corey;[7] phytone was readily converted to phytols. The total synthesis of phytol by Scheme I can be more readily accomplished than by other methods previously described.

Triethyl phosphonocrotonate[8] (2) was prepared in 86% yield by the reaction of triethyl phosphite with ethyl 4-bromocrotonate. Compound 2 was characterized by its elemental analysis and infrared and nmr spectra.

Wadsworth and Emmons[6] have recently reported that the reaction of phosphonate carbanions with ketones and aldehydes produces olefins. Since their study has suggested that 2 may react with carbonyl compounds in the presence of sodium hydride to give α,β-, γ,δ-conjugated dienoic ethyl esters, triethyl phosphonocrotonate anion was condensed in model experiments with typical carbonyl compounds (*e.g.*, 1, 2, 3 in Table I) and the dienoic esters were obtained in 41–52% yield. These results were successfully applied to the synthesis of phytol; that is, 2 reacted with methyl ketones **1a–c** to give the intermediates **3a–c** in the synthesis of phytol in 39–47% yield. These α,β-, γ,δ-conjugated dienoic ethyl esters were identified by elemental analyses and infrared spectra, which showed conjugated double-bond absorption in addition to the typical absorptions of the functional groups present. The results summarized in Table I show that 2 is less reactive to carbonyl compounds than triethyl phosphonoacetate.[6]

Saturated ethyl esters **4a–c** were obtained, in high yield, by catalytic hydrogenation of compounds **3a–c** in the presence of Pd-$CaCO_3$. The results are summarized in Table II.

Using the reaction developed by Corey, methyl ketones **6a–c** were prepared from compounds **4a–c**. Specifically, compounds **4a–c** reacted with methylsulfinyl carbanion for about 2 hr at room temperature under nitrogen to give the corresponding β-keto sulfoxides (**5a–c**). Attempts to crystallize the sulfoxides from the brown, oily products after removing the solvent were unsuccessful, but infrared spectra of the crude products showed characteristic absorption peaks of S→O at 1040–1025 cm^{-1}. Therefore, the crude products **5a–c** were directly reduced with aluminum amalgam in 10% aqueous tetrahydrofuran to the methyl ketones **6a–c**. Compounds **6a–c** were identified from elemental analyses, refractive indices, semicarbazone melting points, and infrared spectra. The results are summarized in Table III.

Phytone (**6c**) was converted to phytol or its derivatives by two procedures as shown previously. One synthesis proceeded *via* 2,6,10,14-tetramethyl-1-pentadecene (**7**) prepared by the reaction of phytone with methylenetriphenylphosphorane. Compound **7** reacted with paraformaldehyde at room temperature in the presence of acetic anhydride–acetic acid and sulfuric acid as catalyst to give a mixture of phytyl acetate and by-products. The phytyl acetate (**8**) could not be isolated by fractional distillation, but it was identified by gas chromatographic comparison with authentic phytyl acetate.

Phytol (**10**) was readily prepared by the reduction of ethyl phytenoate (**9**) obtained in 73% yield by the reaction of phytone with triethyl phosphonoacetate carbanion. Compound **9** was smoothly reduced with lithium aluminium hydride to phytol in 83% yield. Racemic phytol was identified from its elemental analysis, refractive index, and infrared spectrum.

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[6] W. S. Wadsworth, Jr., and W. D. Emmons, *J. Am. Chem. Soc.*, **83**, 1733 (1961).

[7] E. J. Corey and M. Chaykovsky, *ibid.*, **86**, 1639 (1964); *ibid.*, **87**, 1345 (1965).

[8] Independently P. J. van den Tempel and H. O. Huisman [*Tetrahedron*, **22**, 293 (1966)] have synthesized the Me ester.

TABLE I

α,β- AND γ,δ-UNSATURATED ESTERS

No.	Aldehyde or ketone	Product	Bp (mm), °C	Yield, %	n^{20}D	Infrared, cm^{-1} (C=C)		C, %		H, %	
								Calcd	Found	Calcd	Found
1	C_6H_5CHO	$C_6H_5CH{=}CHCH{=}CHCOOC_2H_5$[a]	130–132 (1)	41	1.6120	1625	1600	77.20	77.47	6.98	7.27
2	$CH_3CH(CH_3)CHO$	$CH_3CH(CH_3)CH{=}CHCH{=}CHCOOC_2H_5$	80–81 (4)	52	1.4916	1640	1620	71.39	71.14	9.59	9.58
3	$C_6H_5C(CH_3){=}O$	$C_6H_5C(CH_3){=}CHCH{=}CHCOOC_2H_5$[b]	156 (3)	52	1.5950	1625	1605	77.75	77.88	7.46	7.42
4	**1a**	**3a**[c]	81 (6)	47	1.5069	1640	1620	70.10	69.92	9.15	9.07
5	**1b**	**3b**	109–110 (0.8)	39	1.4911	1632	1615	74.95	74.60	10.75	10.65
6	**1c**	**3c**[d]	156–157 (2)	44	1.4910	1635	1610	77.49	77.50	11.64	11.63

[a] K. v. Auwers [*J. Prakt. Chem.*, **105,** 361 (1923)] reported $n^{42.2}_{\mathrm{HE}}$ 1.6135, mp 25–26°. [b] E. R. H. Jones, D. G. O'Sullivan, and M. C. Whiting [*J. Chem. Soc.*, 1415 (1949)] reported the Me ester, bp 130° (0.01 mm), n^{17}D 1.6225. [c] I. N. Nazarov, Zh. A. Krasnaya, and V. P. Vinogradov [*Zh. Obshch. Khim.*, **28,** 460 (1958)] reported bp 49–52° (0.05 mm), n^{20}D 1.4980. [d] J. Weichet, J. Hodrová, and V. Kvita [*Chem. Listy*, **51,** 568 (1957)] reported no physical constants for compound **3c**.

TABLE II

SATURATED ETHYL ESTERS **4a–c**

Compd	Bp (mm), °C	Yield, %	n^{20}D
4a[a]	76–77 (18)	93	1.4116
4b[b]	100–101 (2.5)	95	1.4314
4c[c]	148–150 (2)	93	1.4590

[a] W. Poetsch [*Ann.*, **218,** 69 (1883)] reported bp 181.5–182.5°. R. Kuhn, W. Badstübner, and C. Grundmann [*Ber.*, **69B,** 98 (1936)] reported the acid. [c] R. Lukes and A. Zobácová [*Chem. Listy*, **51,** 330 (1957)] reported no physical constants for compound **4c**.

TABLE III

METHYL KETONES **6a–c**

Compd	Bp (mm), °C	Yield, %	n^{20}D	infrared, cm^{-1} (C=O)	Semicarbazone mp, °C Obsd	Semicarbazone mp, °C Lit
6a	163–164 (760)	69	1.4151	1720	152–152.2	153–154[a]
6b	118–120 (14)	64	1.4368	1720	95–96	95–96[b]
6c	136 (2)	54	1.4489	1728	67–68	66–67[c]

[a] A. Windraus and C. Resau, *Ber.*, **46,** 1246 (1913). [b] N. Ishizaka, *ibid.*, **47,** 2453 (1914). [c] F. G. Fischer, *Ann.*, **464,** 69 (1928).

Experimental Section[9]

Starting Materials.—Triethyl phosphite was obtained by the method of Ford-Moore and Perry,[10] and ethyl 4-bromocrotonate was prepared by the reaction of N-bromosuccinimide[11] with ethyl crotonate in carbon tetrachloride in the presence of Bz_2O_2.[12] Triethyl phosphonoacetate was prepared by means of the Michaelis–Arbusov reaction.[13] The other chemicals were supplied from commercial sources.

Triethyl Phosphonocrotonate (2).—Freshly distilled ethyl 4-bromocrotonate (98.0 g, 0.51 mole) was added slowly to triethyl phosphite (95.0 g, 0.57 mole) at such a rate that the temperature of the stirred reaction mixture maintained at 120–130° for 2 hr. After the addition was completed and the evolution of ethyl bromide ceased, the mixture was stirred at the same temperature for 1 hr. The mixture was cooled and the small amount of unreacted triethyl phosphite was removed at reduced pressure. The residue was distilled at 121–123° (0.4 mm), yield 110.0 g (86%), n^{20}D 1.4539. The infrared spectrum showed a strong absorption at 1260 (P=O) along with absorptions at 1725 (ester, C=O), 1655 (C=C), 1030 (P—O), and 965 cm^{-1} (*trans* double bond). The nmr spectrum consisted of the following bands: (1) a triplet centered at τ 8.75 (methyl protons) and a quartet at 6.02 (methylene protons) for the carbethoxy group; (2) a triplet at 8.72 (methyl protons) and a quartet at 5.86 (methylene protons) for two ethoxy groups; (3) a multiplet at 7.28 for methylene protons adjacent to phosphorus; (4) a multiplet at 4.08 for the olefinic proton adjacent to the carbonyl group and a multiplet at 3.22 for the other olefinic proton.

Anal. Calcd for $C_{10}H_{19}O_5P$: C, 47.99; H, 7.65. Found: C, 47.40; H, 7.60.

Ethyl Cinnamylideneacetate. Typical Procedure for α,β- and γ,δ-Unsaturated Esters.—Sodium hydride (50% in mineral oil, 2.4 g, 0.05 mole) was placed in 100 ml of dry tetrahydrofuran (N,N-dimethylformamide was used in the case of **3c**). The slurry was cooled to 0°, triethyl phosphonocrotonate (12.5 g, 0.05 mole) was added dropwise with stirring, and gas evolution was observed. After the addition, the solution was stirred at 0° for 10 hr. To the brown solution, maintained below 0°, benzaldehyde (5.3 g, 0.05 mole) was added dropwise. The solution was stirred at room temperature for 7 hr. After evaporation of the tetrahydrofuran at reduced pressure, a gummy precipitate appeared. A large excess of water was added to this precipitate and the product was extracted with ether. The ether, after being dried over magnesium sulfate, was removed. The residue was distilled, giving 4.1 g (41% yield) of pale yellow liquid, bp 130–132° (1 mm), n^{20}D 1.6120. The infrared spectrum of the product contained strong bands at 1625 and 1600 cm^{-1}.

Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.47; H, 7.27.

Ethyl 5-Methylcaproate (4a). Typical Procedure for Saturated Ethyl Esters 4a–c.—Ethyl 5-methylsorbate (9.0 g, 0.058 mole) in 30 ml of ethanol was hydrogenated in an autoclave with 1.7 g of Pd-$CaCO_3$ (5%) catalyst under a pressure of about 100 atm of hydrogen at room temperature by the usual method. Reduction was completed in 1 hr. The catalyst was separated by filtration and after removal of the ethanol the saturated ester was distilled at 76–77° (18 mm), yield 8.6 g (93%), n^{20}D 1.4116.

6-Methylheptan-2-one (6a). Typical Procedure for Methyl Ketones 6a–c.—Dimethyl sulfoxide (60 ml) and sodium hydride (50% in mineral oil, 4.5 g, 0.094 mole) were placed in a flask under dry nitrogen. The mixture was heated with stirring to 65–70° for 45 min until the evolution of hydrogen ceased. An equal volume of dry tetrahydrofuran (60 ml) was added and the solution was cooled in an ice bath during the addition, with stirring, of ethyl 5-methylcaproate (7.2 g, 0.0455 mole). The ice bath was removed and stirring was continued for 2 hr. The reaction mixture was then poured into three times its volume of water, acidified with aqueous hydrochloric acid (to a pH of about

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(9) All boiling points and melting points are uncorrected. Infrared spectra were recorded on a Hitachi Model EPI-S2 spectrophotometer. The nmr spectrum was determined on a Varian Model A-60 spectrometer in carbon tetrachloride solution with tetramethylsilane as an internal reference. Gas chromatography was carried out on a Shimazu Model GC-1C gas chromatography using a 338-cm column of 15% polyethylene glycol succinate ester on Neosorb NC with helium as the carrier gas.

(10) A. H. Ford-Moore and B. J. Perry, "Organic Syntheses," Coll. Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1963, p 955.

(11) K. Ziegler, A. Späth, E. Schaaf, W. Schumann, and E. Winkelmann, *Ann.*, **551,** 80 (1942).

(12) H. Schmid and P. Karrer, *Helv. Chim. Acta*, **29,** 573 (1946).

(13) G. M. Kosolapoff, "Organophosphorus Compounds," 1st ed, John Wiley and Sons, Inc., New York, N. Y., 1950, Chapter 7.

3-4), and thoroughly extracted with chloroform. The combined extracts were washed three times with water and dried over anhydrous sodium sulfate. After the chloroform was evaporated, the residue was a brown liquid which did not yield crystalline β-keto sulfoxide. The infrared spectrum contained strong bands at 1710 and 1040 cm^{-1}.

The residue was dissolved in 10% aqueous tetrahydrofuran (450 ml). Aluminum amalgam (19.6 g of aluminum) was then freshly prepared as follows. Aluminum foil was cut into approximately 1-cm^2 pieces and immersed, all at once, in a 2% aqueous solution of mercuric chloride for 15 sec. The pieces were rinsed with absolute alcohol, then with ether, and directly put into the reaction vessel. The reaction mixture was heated at 65° for 2.5 hr after addition of the amalgam. The reaction mixture was then filtered and the filtered solid was washed with tetrahydrofuran. The filtrate was concentrated to remove most of the tetrahydrofuran, ether was added, and the ether phase was separated from the water, dried over anhydrous sodium sulfate, and evaporated. The residue was distilled, giving 4.0 g of clear liquid, bp 163-164°, 69% yield, $n^{20}\text{D}$ 1.4151. The infrared spectrum showed a strong band at 1720 cm^{-1}. The semicarbazone had mp 152-152.2°.

Anal. Calcd for $C_9H_{19}N_3O$: C, 58.34; H, 10.34; N, 22.68. Found: C, 58.55; H, 10.35; N, 22.68.

2,6,10,14-Tetramethyl-1-pentadecene (7).—Compound **7** was prepared according to the procedure of Burrell and co-workers.[14] When **6c** (17.7 g, 0.066 mole) was treated with methylenetriphenylphosphorane prepared from triphenylmethylphosphonium bromide[15] (21.4 g, 0.06 mole) in an ethereal solution of phenyllithium[16] (180 ml, 0.06 mole), 13.2 g (83% yield) of **7** was obtained, bp 113° (0.5 mm), $n^{20}\text{D}$ 1.4487. The infrared spectrum of the product contained bands at 1650 and 890 cm^{-1}.

Anal. Calcd for $C_{19}H_{38}$: C, 85.63; H, 14.37. Found: C, 85.83; H, 14.18.

Phytyl Acetate (8).—Paraformaldehyde (2.7 g), glacial acetic acid (7.8 g), acetic anhydride (6.6 g), and concentrated sulfuric acid (1 ml) were placed in a flask. The mixture was heated (80-90°) until the paraformaldehyde depolymerized. The solution was allowed to cool to room temperature and 8.0 g (0.03 mole) of freshly distilled **7** was added dropwise. After completion of addition, the mixture was stirred for 1.5 hr at room temperature. Three hundred cubic centimeters of water was then added to the mixture and the solution was extracted with ether. The ether was washed with water and saturated sodium bicarbonate solution until it became neutral and was then washed with water again. The ether extract was dried over magnesium sulfate and evaporated. The residue was distilled, giving 7.7 g of liquid, bp 140-165° (0.6 mm). The crude product was examined by gas chromatography, which showed four peaks. One peak coincided with that of authentic phytyl acetate and product yield was 28% (indicated by gas chromatography).

Ethyl Phytenoate (9).—Triethyl phosphonoacetate (11.2 g, 0.05 mole) was added dropwise at room temperature to a slurry of sodium hydride (50% in mineral oil, 2.4 g, 0.05 mole) in 100 ml of dry tetrahydrofuran. After the addition, the reaction mixture was stirred for 3 hr at room temperature until gas evolution had ceased. To the solution was added phytone (13.4 g, 0.05 mole) dropwise with stirring, then the solution was heated and refluxed with stirring for 4 hr. After cooling a large excess of water was added and the aqueous solution was extracted with ether. The residue, obtained after drying over magnesium sulfate and evaporating, was distilled giving 12.4 g (73%) of liquid, bp 143-145° (0.3 mm), $n^{20}\text{D}$ 1.4590 (lit.[17] $n^{20}\text{D}$ 1.4588). The product showed the expected infrared spectrum with strong bands at 1710 and 1640 cm^{-1}.

Anal. Calcd for $C_{22}H_{42}O_2$: C, 78.04; H, 12.50. Found: C, 78.01; H, 12.51.

Phytol (10).—Ethyl phytenoate (10.2 g, 0.03 mole) was reduced with lithium aluminium hydride (1.2 g, 0.025 mole) in dry ether (100 ml) according to the procedure of Burrell and coworkers[14] to yield 7.4 g (83% yield) of phytol, bp 153° (0.6 mm), $n^{20}\text{D}$ 1.4633 (lit.[18] $n^{25}\text{D}$ 1.4595). The infrared spectrum of the product contained strong bands at 3300 and 1670 cm^{-1}.

Anal. Calcd for $C_{20}H_{40}O$: C, 81.00; H, 13.60. Found: C, 81.11; H, 13.62.

Acknowledgment.—The authors wish to express their gratitude to Mr. S. Moriya and Mr. Y. Sakuma for their help in carrying out the study presented in this report. The authors are also indebted to Professor S. Abe for his kind advice.

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[18] F. G. Fischer and K. Löwenberg, *Ann.*, **475**, 183 (1929).

A Total Synthesis of Astaxanthin Dimethyl Ether

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4-Methoxy-β-ionone, which was prepared in good yield from 3-dehydro-β-ionone, served as the intermediate for a total synthesis of astaxanthin dimethyl ether (XV).

Kuhn and Sörensen[1] isolated a new pigment named astaxanthin from the eggs of lobster. They established the constitution of astaxanthin and its close relationship to astacin. In 1960, Davis and Weedon[2] reported a synthesis of astacin by an oxidation of canthaxanthin. Astaxanthin dimethyl ether (XV) has now been prepared by a total synthesis.

Henbest[3] reported the preparation of 3-substituted β-ionones III and IV from 3-bromo-β-ionone (II). The 4-substituted β-ionones which would find application for the synthesis of substituted carotenoids are not available by known methods of synthesis. We have now found that 4-methoxy-β-ionone (VI) can be prepared in good yield by addition of methyl alcohol to 3-dehydro-β-ionone (V) and used it as the basis for the synthesis of astaxanthin dimethyl ether (see Chart I).

3-Dehydro-β-ionone (V) was prepared by a modification of the procedure of Henbest.[3] β-Ionone (I) was brominated with N-bromosuccinimide in the presence of calcium oxide and sodium bicarbonate in carbon tetrachloride. Dehydrobromination with dimethylaniline and pyridine resulted in a 55% yield of V. When V was stirred in a solution of methyl alcohol and sulfuric acid at 5° for 24 hr, VI was obtained in 50% yield of fractionated product.

The methoxy C_{19}-aldehyde (IX) was prepared from 4-methoxy-β-ionone by the same sequence of reactions already described[4,5] (see Chart II).

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[3] H. B. Henbest, *J. Chem. Soc.*, 1074 (1951).

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