platinum black and the mixture was filtered. The filtrate was evaporated to give 362 mg of nearly pure (−)-argemonine N-oxide. A portion was purified by preparative tlc to yield the pure N-oxide, mp 140–160° (effervescence), $[\alpha]^{25}D$ −152° (*c* 10.71, $CHCl_3$). The ir, nmr, and mass spectra of the prepared sample were identical with those of the isolated alkaloid (see above).

Synthesis of (−)-Argemonine Methohydroxide.—(−)-Argemonine (30 mg) which had been isolated from *A. gracilenta* (see above) was dissolved in a few drops of methanol. Methyl iodide (10 ml) was added and the solution was heated at reflux for 1 hr. The solution was evaporated to dryness, the residue was dissolved in water, and the iodide ion was precipitated with $AgNO_3$. The mixture was filtered and 30 ml of 40% aqueous NaOH was added. The resulting mixture was filtered and the filtrate was extracted with $CHCl_3$. The $CHCl_3$ solution was dried and evaporated to yield 25 mg of a semisolid whose properties were essentially identical with those of the isolated (−)-argemonine methohydroxide (see above).

Synthesis of (−)-Platycerine.—(−)-Munitagine (50 mg) which had been isolated[6] from *A. munita* was dissolved in 10 ml of methanol and a 1.5 molar equiv of diazomethane (generated from Diazald) in ether solution was added, while the solutions were kept cold in ice. The resulting solution was allowed to come to room temperature slowly and then allowed to stand for 12 hr. The solution was evaporated to dryness on a steam bath, and the residue was dissolved in 1 *M* HCl and then basified and extracted with $CHCl_3$ successively at pH 12.5 and 8.4. From the pH 12.5 extract was isolated O,O-dimethylmunitagine.[8] The residue from the pH 8.4 extract was purified by preparative tlc and yielded 13 mg of (−)-platycerine, mp 120–140° (effervescence), $[\alpha]^{25}D$ −224° (*c* 0.80, $CHCl_3$). The ir, nmr, and mass spectra were identical with those of the isolated (−)-platycerine (see above) and an authentic sample.[6]

Registry No.—(−)-Ic, 18826-67-0; (−)-IIc, 18826-68-1; (−)-IV, 18841-61-7; (−)-V, 18826-69-2.

The Synthesis of trans-β-Carotene from Retinyl Phosphonate by the Michaelis–Arbuzov Reaction

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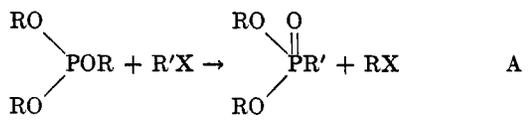
Retinyl phosphonate, which was synthesized for the first time, was condensed with vitamin A aldehyde to afford β-carotene in good yield.

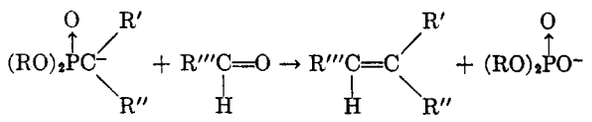
The Michaelis–Arbuzov reaction[1] provides a versatile method for the formation of carbon–phosphorus bonds by the reaction of a phosphite ester with an alkyl halide.



A

The characteristic of this reaction is the formation of a P=O bond. The mechanism involves an expansion of the valence shell of phosphorus from eight to ten electrons, made possible by the vacant 3d orbitals.

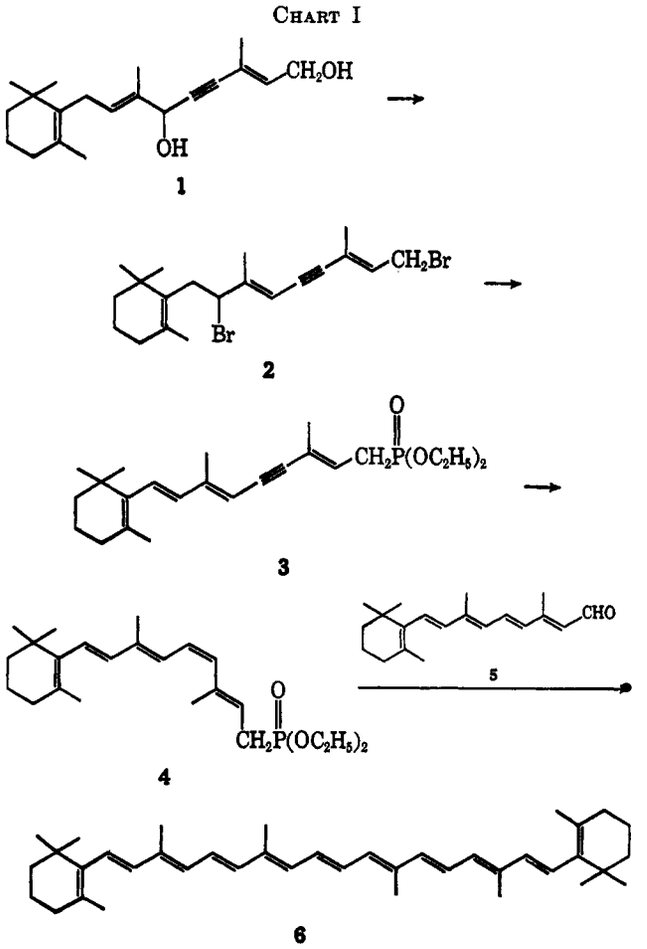
It has been demonstrated by earlier workers[2,3] that the alkyl diethyl phosphonates form carbanions which react with carbonyl compounds to afford olefins.



Since the phosphite esters have the advantage of being less expensive than triarylphosphines, the so-called Wittig reagents, it occurred to us that the Michaelis–Arbuzov reaction may be used favorably for preparing β-carotene. However, as there is no known procedure for preparing the halide from vitamin A as required by eq A, retinyl halide was eliminated as a possible precursor to retinyl phosphonate. This problem has been resolved by following the synthetic route shown in Chart I.

The C-20 diol (1), which is an intermediate of an industrial vitamin A synthesis,[4,5] was treated with phosphorus tribromide to yield the rearranged dibromide **2.**

Chart I



(1) R. G. Harvey and E. R. De Sombre, *Topics of Phosphorous Chemistry*, Vol. 1, Interscience, New York, 1964, p 57.

(2) L. Horner, H. Hoffmann, H. G. Wippel, and G. Klohre, *Chem. Ber.*, **92**, 2499 (1959).

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

(4) O. Isler, A. Ronco, W. Guex, N. C. Hindley, W. Huber, K. Dialer, and M. Kofler, *Helv. Chim. Acta*, **32**, 489 (1949).

(5) J. D. Surmatis, U. S. Patent 2,610,208 (1952).

The rearrangement which took place in the preparation of **2** is known.[4-6] The dibromide **2**, on treatment with triethyl phosphite, gave the phosphonate **3** in 70% yield based on the C_{20} diol. Selective reduction of **3** with Lindlar catalyst[7] resulted in retinyl phosphonate (**4**). The nmr spectra and the analytical data of **2–4** were compatible with the assigned structures.

The phosphonate **4** and vitamin A aldehyde **5** were stirred with sodium methoxide in pyridine at 0° to yield β-carotene. The reduction of an ethynyl function with Lindlar catalyst leads to the *cis* configuration. Since phosphonate reactions in general give *trans* couplings, the reaction of **4** and **5** was expected to lead to 11-*cis*-β-carotene. The uv spectrum of the product contained a "*cis* peak"[8] at 338 mμ; however, attempts to prepare an analytical sample of 11-*cis*-β-carotene by column chromatography or recrystallization led to a *cis–trans* mixture because of the mild condition at which isomerization took place.

Isomerization of the crude β-carotene by heating in heptane,[8] followed by recrystallization from methylene chloride, afforded *trans*-β-carotene (**6**) in 61% yield based on **5**.

Experimental Section[9]

1,8-Dibromo-3,7-dimethyl-9-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2,6-nonadien-4-yne (**2**).—3,7-Dimethyl-9-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2,7-nonadien-4-yne-1,6-diol (**1**, 100 g) was placed in a 2-l. flask with ethyl ether (500 ml) and pyridine (1 ml). Phosphorous tribromide (32 ml) dissolved in hexane (200 ml) was added dropwise to the stirred solution at −5° in 3 hr. The reaction mixture was poured onto crushed ice in a separator and extracted with ethyl ether. The combined extracts were washed with water, saturated sodium bicarbonate solution, and, finally, water. The solvent was removed under vacuum after drying over anhydrous sodium sulfate. The dibromide **2** which was obtained as an orange syrup (125 g) and was used without further purification for the next step had uv max (EtOH) 285 mμ. The nmr spectrum showed signals for a *gem*-dimethyl group at δ 0.98 and 1.05 (singlets), a singlet at 1.65 (>C=C< CH_3), multiplet at 1.97 ($J \cong 1$ cps) (≡C(CH_3)C=), a doublet at 2.13 (J = 1.2 cps) (>CCH_3), a multiplet at 1.40 and 2.10 (-$CH_2CH_2CH_2$-), a signal at 2.78 (C=CCH_2-), a doublet at 4.20 (J = 8 cps) (CH_2Br), C*H*Br at 4.78, a singlet at 5.78 (=C*H*C≡C-), a triplet at 5.97 (J = 8 cps) (=C*H*-). *Anal.* Calcd for $C_{20}H_{28}Br_2$: Br, 37.32. Found: Br, 37.30.

3,7-Dimethyl-9-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2,6,8-nonatrien-4-yn-1-ylphosphonic Acid Diethyl Ester (**3**).—The dibromide **2** (107 g), toluene (100 ml), and triethyl phosphite (83 g) were placed in a distillation flask and heated to 145° in 4 hr. The solvent was removed and the resulting residue was distilled through a centrifugal molecular still (Type CMS, Consolidated Vacuum Corp.) to yield 80.9 g (70%) of **3**, $n^{25}D$ 1.567, mp 28°, $E^{1\%}_{1\,cm}$ (318 mμ) 834 (in ethyl alcohol). *Anal.* Calcd for $C_{24}H_{37}O_3P$: C, 71.25; H, 9.22. Found: C, 71.23; H, 9.16.

3,7-Dimethyl-9-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2,4,6,8-nonatetraen-1-ylphosphonic Acid Diethyl Ester (**4**).—A solution of **3** (50 g) in toluene (1.5 l.) was hydrogenated in the presence of Lindlar catalyst.[7] The catalyst was filtered off and washed with toluene. On removal of the solvent under vacuum, **4** was obtained as a yellow syrup: 49 g (98%); $n^{25}D$ 1.555; nmr ($CDCl_3$), δ 5.15–6.70 (*m*, 6, olefin H), 4.10 (quintet, 4, OCH_2), 2.56 (*d* of *d* J = 7.5 and 21.5 cps, CH_2P), 1.96 (s, 6, two on-chain CH_3 groups), 1.78 (s, 3, terminal CH_3), 1.30 (t, 3, CH_3CH_2), 1.02 (s, 6, C(CH_3)$_2$). *Anal.* Calcd for $C_{24}H_{39}O_3P$: C, 70.70; H, 9.66. Found: C, 71.02; H, 9.84.

***trans*-β-Carotene** (**5**).—Retinyl phosphonate (**4**, 36 g) and vitamin A aldehyde (20 g) were dissolved in pyridine (280 ml) and the solution was cooled to 0°. Sodium methoxide (19 g) was added in portions to the stirred reaction over a period of 2 hr, while the temperature was maintained at 0–5°. After stirring for 3 hr, the reaction mixture was diluted with water and extracted with benzene. The combined extracts were washed with cold (5%) sulfuric acid and then with water until neutral. The solvent was removed under vacuum to yield 53 g of crude β-carotene: uv max (cyclohexane) 285, 338, 425, 448 ($E^{1\%}_{1\,cm}$ 834), and 475 mμ. A sample, after two recrystallizations from methylene chloride–methyl alcohol (methylene chloride washed with sodium bicarbonate) melted at 128°; uv max ($E^{1\%}_{1\,cm}$ 1300). Continued recrystallization resulted in a gradual increase in melting point with a loss of uv absorption at 338 mμ.

The crude β-carotene was isomerized by heating in heptane (100 ml) at reflux for 20 hr under an atmosphere of nitrogen. The reaction mixture was cooled to 20°, diluted with additional heptane (50 ml), and filtered. After two recrystallizations from methylene chloride, 23 g (61%) of *trans*-β-carotene was obtained (mp 181°), $E^{1\%}_{1cm}$ (454 mμ) 2500.

Registry No.—**2**, 18793-78-7; **3**, 18793-79-8; **4**, 18793-80-1; **6**, 116-32-5.

Acknowledgment.—We wish to thank Dr. A. Steyermark and his staff for the microanalyses, Dr. F. Forrester and Mr. J. Volpe for the ultraviolet spectra, and Dr. F. Vane and Dr. T. Williams for the nmr spectra.

(6) J. D. Surmatis, U. S. Patent 2,760,998 (1956).
(7) H. Lindlar, *Helv. Chim. Acta*, **35**, 446 (1952).
(8) J. D. Surmatis, J. Maricq, and A. Ofner, *J. Org. Chem.*, **23**, 157 (1958).
(9) Melting points were determined in vacuum capillaries and are uncorrected. The nuclear magnetic resonance (nmr) spectrum was obtained with a Varian A-60 spectrometer using deuteriochloroform as solvent and tetramethylsilane as the internal reference.

The Synthesis of Derivatives of 2,3-Diamino-2,3-dideoxy-D-galactose

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Aminations of methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-β-D-*threo*-hex-2-enopyranoside (**2**) with aqueous ammonia or, better, with a molten mixture of dry ammonium acetate and acetamide furnished methyl 4,6-*O*-benzylidene-2-*N*-benzylideneamino-2,3-dideoxy-3-nitro-β-D-galactopyranoside (**4**). In this reaction, one part of intermediate methyl 2-amino-4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-β-D-galactopyranoside (**3**) evidently was *N*-benzylidenated by benzaldehyde lost from another part. Acetic anhydride converted **4** into methyl 2-acetamido-4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-β-D-galactopyranoside (**5**) which by acidic de-*O*-benzylidenation yielded methyl 2-acetamido-2,3-dideoxy-3-nitro-β-D-galactopyranoside (**6**) (4,6-diacetate, **7**). Catalytic hydrogenation of **6** followed by *N*-acetylation and *N,O*-acetylation, respectively, gave methyl 2-acetamido-3-amino-2,3-dideoxy-β-D-galactopyranoside hydrochloride (**8**), methyl 2,3-diacetamido-2,3-dideoxy-β-D-galactopyranoside (**9**), and methyl 2,3-diacetamido-4,6-di-*O*-acetyl-2,3-dideoxy-β-D-galactopyranoside (**10**).

A recent paper from this laboratory commented upon the significance of diamino sugars in the chemistry of antibiotics and reported a new synthesis of 2,3-diamino-2,3-dideoxy-D-glucose.[2] The principle consisted of the

(1) Taken from the Ph.D. thesis of K. S. O., University of Ottawa, 1968.
(2) H. H. Baer and T. Neilson, *J. Org. Chem.*, **32**, 1068 (1967).