The volume of hydrogen evolved was noted with 5-min. intervals. After 5 hr., when the calculated volume of hydrogen (330 ml.) corresponding to the reaction of two hydroxyl groups with sodium had been evolved, the rate of hydrogen evolution became negligible. The reaction mixture was filtered with suction through a column (2-cm. diameter), packed with glass wool (5 cm.) and Hyflo Super Cel (3 cm.) under anhydrous conditions. The apparatus was washed with anhydrous dioxane and the washings collected with the filtrate (210 ml.). The amount of alkoxide was determined in an aliquot of the filtrate.[8]

The dioxane filtrate (approximately 200 ml. containing 0.0114 mole of alkoxide) was slowly added over a period of 15 min. under anhydrous conditions, with the aid of a dropping funnel, to a mechanically stirred solution of N,N-bis-(β-chloroethyl)phosphamido dichloride[5] (V) (3.0 g., 0.0116 mole) in 50 ml. of anhydrous dioxane in a dried 500-ml. three-necked flask. The reaction mixture was cooled in an ice bath during the addition of the alkoxide. The mixture was left at room temperature under exclusion of aerial moisture.

After 60 hr. a fine white precipitate was collected by centrifugation and shown to consist of sodium chloride (1.55 g., calculated 1.30 g.). The supernatant was concentrated in vacuum at 50°. A light yellow oil, which could not be crystallized, was obtained. The oil was dissolved in anhydrous ether, a small, yellow, insoluble fraction being rejected. The ethereal extract was concentrated in vacuum and the product precipitated with petroleum ether (50–70°). Repeated precipitations from ether–petroleum ether yielded an analytically pure colorless oil (4.8 g.) which could not be crystallized.

Anal. Calcd. for $C_{18}H_{26}O_7NPCl_2$: C, 45.96; H, 5.57; N, 2.97. Nitrogen mustard hydrochloride, 37.95. Found: C, 45.86; H, 5.51; N, 2.47; nitrogen mustard hydrochloride after acid hydrolysis, 38.58.

N,N-Bis-(β-chloroethyl-3,5-cyclophosphamido-D-ribose Dimethyl Acetal (II).—A solution of N,N-bis(β-chloroethyl)-2,4-*O*-benzylidene-3,5-cyclophosphamido-D-ribose dimethyl acetal (I, 4.8 g.) in absolute methanol (50 ml.) was hydrogenated in the presence of 10% palladized charcoal (1.6 g.). Hydrogen was consumed at an initial rate of approximately 3 ml. per min.

After 6 hr., when the calculated volume of hydrogen (458 ml. corrected to S.T.P.) had been taken up, the catalyst was filtered off and the filtrate concentrated in vacuum. The resulting oil could not be obtained analytically pure by precipitation procedures or column chromatography on cellulose. Paper chromatography (butanol–water) revealed that the material consisted of a fast moving (R_f: 0.85) main fraction which could be revealed on paper, after acid hydrolysis, as a single well defined spot by appropriate coloration procedures for reducing sugars, phosphorus, and nitrogen mustard. A slower moving (R_f: 0.38) sugar contaminant, which did not contain phosphorus or nitrogen mustard, could thus far only be removed by means of preparative paper chromatography on a small scale. The purified material obtained in this manner was shown to contain an acetal grouping and to be free of benzylidene groups (ultraviolet spectrum).

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[8] A 10-ml. aliquot was diluted with 25 ml. of water and the liberated alkali determined by titration with 0.100 *N* hydrochloric acid (phenolphthalein), 12.6 ml. being required. (Calcd. 11.7 ml.). On the basis of these titration figures and the volume of hydrogen evolved we concluded that both unsubstituted hydroxyl groups in the 2,4-*O*-benzylidene-D-ribose dimethyl acetal had reacted with sodium.

Formation of 1,4-Diphenylcyclohexadiene-1,4 in an Attempted Internal Wittig Reaction

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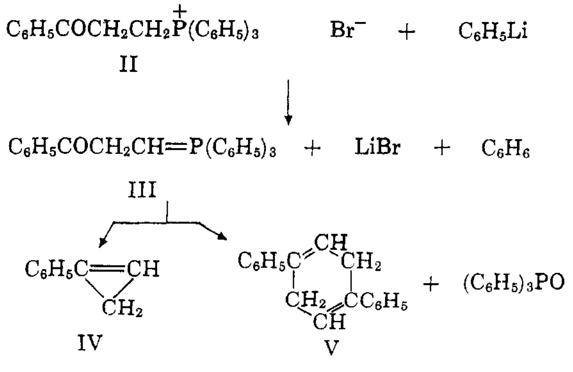
The extremely versatile Wittig reaction[1] between alkylidene phosphoranes and aldehydes and ketones to yield alkenes and phosphine oxides has been applied to the synthesis of a number of cyclic olefins by intermolecular processes.[2] However, only one successful intramolecular Wittig reaction leading to a cyclic product has been recorded; Bieber and Eisman recently reported the formation of 1-phenylcyclopentene by ring closure of the phosphorane derived from triphenyl(4-benzoyl-1-butyl)phosphonium bromide (I).[3] We now wish to report the results of a similar reaction of a lower homolog of I.[4] Triphenyl(2-benzoylethyl)phosphonium bromide (II) prepared by quaternization of β-bromopropiophenone with triphenylphosphine, yielded upon reaction with phenyllithium in benzene an olefin of empirical formula C_9H_8 as the sole isolable product. This olefin showed typical styrene absorption in the ultraviolet (λ_{max} 246 mμ) and infrared bands characteristic of a trisubstituted olefin (786 cm.$^{-1}$) and a phenyl conjugated double bond (1605 cm.$^{-1}$).[5] Two courses for the reaction appeared feasible: intramolecular closure of the phosphorane (III) to yield 1-phenylcyclopropene (IV) or ring formation involving two molecules of III to yield 1,4-diphenylcyclohexadiene-1,4 (V).



On the basis of the well established probability

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[1] S. Trippett in "Advances in Organic Chemistry; Methods and Results," Vol. I, edited by R. A. Raphael, E. C. Taylor, and H. Wynberg, Interscience Press, New York, 1960, pp. 83–102.

[2] G. Wittig, H. Eggers, and P. Duffner, *Ann.*, **619**, 10 (1958); K. Dimroth and G. Pohl, *Angew. Chem.*, **73**, 436 (1961); C. E. Griffin, K. R. Martin, and B. E. Douglas, *J. Org. Chem.*, **27**, 1627 (1962).

[3] T. I. Bieber and E. H. Eisman, *ibid.*, **27**, 678 (1962).

[4] This study was undertaken, in part, to develop new methods for the synthesis of 1,2-disubstituted cyclopropenes, N. T. Castellucci and C. E. Griffin, *J. Am. Chem. Soc.*, **82**, 4107 (1960).

[5] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed., John Wiley and Sons, Inc., New York, 1958, pp. 34–52.

and ring size factors in cyclization reactions, the latter course appeared to be inherently more probable. Although analytical and spectral (ultraviolet, infrared) data did not allow a differentiation between structures IV and V for the olefin, it was unequivocally identified as V by catalytic reduction to 1,4-diphenylcyclohexane. When sodium ethoxide in ethanol was employed for the generation of the phosphorane (III), only unchanged II, triphenylphosphine were detected; no olefinic materials were isolated or detected. These findings differ from those of Bieber and Eisman[8] who obtained a significantly higher yield of 1-phenylcyclopentene from I with lithium ethoxide than with phenyllithium.

The formation of 1,4-diphenylcyclohexadiene-1,4 (V) and not the conjugated isomer, 1,4-diphenylcyclohexadiene-1,3 (VI), provides a further example of the specific double bond placement and lack of isomerization generally observed in the Wittig reaction. The assignment of the nonconjugated structure to the product follows from the similarity of its spectrum (λ_{max} 246 mμ) to those of model styryl systems: styrene (244 mμ)[6a]; *cis*-2-phenylbutene-2 (243 mμ)[7]; 1-phenylcyclohexene (246, 247 mμ).[8] Additionally the molar absorptivity (23,800) is, as expected for two isolated styryl systems, double that observed (11,700–12,000) in the model systems. The conjugated isomer (VI) would be expected to show a spectrum similar to that of 1,4-diphenylbutadiene (λ_{max} 328, 350 mμ; ϵ 25,000, 41,000)[6b] and markedly different from the observed styrene absorption.

While cyclopropenes might be formed by this procedure in a structurally more favorable case, this study does indicate an effective limitation to the synthesis of simple cyclic olefins by intramolecular Wittig processes.

Experimental[9]

Triphenyl(2-benzoylethyl)phosphonium Bromide (II).—A mixture of 40.0 g. (0.188 mole) of β-bromopropiophenone,[10] 49.6 g. (0.188 mole) of triphenylphosphine and 200 ml. of anhydrous benzene was refluxed with constant stirring for 3 hr., allowed to cool to room temperature and filtered to remove the precipitated phosphonium salt, 61.3 g. (69%). Recrystallization from chloroform gave a material melting at 180–181°.

Anal. Calcd. for $C_{27}H_{24}BrOP$: C, 68.22; H, 5.09; P, 6.52. Found: C, 66.64, 66.35; H, 5.31, 5.20; P, 6.54.

1,4-Diphenylcyclohexadiene-1,4 (V).—A solution of 0.11 mole of phenyllithium in anhydrous ether was added to a suspension of 31.7 g. (0.067 mole) of the phosphonium salt (II) in anhydrous benzene (total volume 200 ml.). An initial vigorous exothermic reaction occurred to give a dark red reaction mixture, which turned to orange after being refluxed for 1 hr. After a total reflux period of 30 hr., the reaction mixture was allowed to cool to room temperature, filtered, and concentrated under reduced pressure. Distillation of the residue gave a fraction, b.p. 90° (1 mm.), which solidified in the condenser and receiver to give 950 mg. (12%) of a waxy, colorless solid, m.p. 63.5–67.0°. This solid decolorized bromine in carbon tetrachloride and potassium permanganate in acetone. After two sublimations at 30 mm. and drying under vacuum over phosphorus pentoxide, the solid (V) melted at 67.5–68.5°.

Anal. Calcd. for C_9H_8 or $C_{18}H_{16}$: C, 93.06; H, 6.94. Found: C, 92.89; H, 6.78.

Examination of the infrared spectrum of the distillation residue showed the presence of unchanged II, triphenylphosphine, and triphenylphosphine oxide.

The ultraviolet spectrum of V in 95% ethanol showed a maximum at 246 mμ (ϵ 23,800). The infrared spectrum was recorded in chloroform (5000–840 cm.$^{-1}$) and in acetonitrile (840–650 cm.$^{-1}$) and showed bands at the following frequencies (cm.$^{-1}$): 3077 m-s, 3030 m-s, 1605 s, 1577 m, 1488 s, 1462 w, 1435 s. 1387 w 1340 w, 1323 w, 1271 w, 11.76 w, 11.57 w, 1075 s, 1045 m, 1011 s, 992 s, 969 s, 920 w, 907 m, 840 w, 786 m, 741 s, 702 s.

A 370-mg. (0.0016 mole) sample of V in 50 ml. of ethanol was hydrogenated over a platinum catalyst at room temperature and at a pressure of 3.1 atm. Hydrogen uptake (70.4 ml., 0.0031 mole) ceased after 3 hr. The catalyst was removed by filtration and the solvent was evaporated to give a colorless oil which crystallized from 95% ethanol to give colorless crystals, m.p. 167–169°. Recrystallization from 95% ethanol gave 280 mg. (75%) of 1,4-diphenylcyclohexane, m.p. 169–170° (lit.,[11] m.p. 170°).

The 1,4-diphenylcyclohexane was treated with 355 mg. (0.0045 mole) of selenium at 325° until the evolution of hydrogen selenide ceased (3 hr.). The reaction mixture was cooled and extracted with benzene; the benzene extracts were filtered and concentrated to dryness at 50°. The solid residue was recrystallized twice from benzene to give 208 mg. of *p*-terphenyl, m.p. 209–210°. This material was identical with an authentic sample of *p*-terphenyl in all respects (mixture melting point, infrared and ultraviolet spectra).

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(6) (a) A. E. Gillam and E. S. Stern, "An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry," 2nd ed., Edward Arnold Ltd., London, 1957, p. 141; (b) p. 123.

(7) D. J. Cram, *J. Am. Chem. Soc.*, **71**, 3884 (1949).

(8) A. C. Cope, F. S. Fawcett, and G. Munn, *ibid.*, **72**, 3401 (1950); R. B. Carlin and H. P. Landerl, *ibid.*, **75**, 3973 (1953).

(9) Melting points are uncorrected. Microanalyses were performed by Galbraith Laboratories, Knoxville, Tennessee.

(10) W. J. Hale and E. C. Britton, *J. Am. Chem. Soc.*, **41**, 845 (1919).

(11) C. Nenitzescu, *Ber.*, **70**, 347 (1937).

New Synthesis of 3,5-Diiodothyroacetic Acid

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Known methods of preparation of 3,5-diiodothyroacetic acid are based on 3,4,5-triiodonitrobenzene (requiring eight steps),[1] 4-hydroxyphenyl-

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(1) (a) C. R. Harington, *Biochem. J.*, **21**, 169 (1927). (b) C. R. Harington and R. Pitt-Rivers, *ibid.*, **50**, 438 (1952).