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The Wittig Reaction of Stabalized Phosphonium Ylids with Derivatives of D-Ribose

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THE WITTIG REACTION OF STABILIZED PHOSPHONIUM YLIDS WITH DERIVATIVES OF D-RIBOSE

by

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George R. Wellman

TABLE OF CONTENTS

INTRODUCTION

The Wittig reaction is the reaction of a phosphonium ylid with an aldehyde or ketone to yield an olefin and a phosphine oxide.

$$R\text{-}\overset{O}{\overset{\|}{C}}\text{-}R' + R_3'''\text{-}P{=}CR_2''' \longrightarrow R\text{-}\underset{R'}{\overset{|}{C}}{=}C\text{-}R_2''' + R_3'''\text{-}P{\rightarrow}O$$

The purpose of this work was to investigate the Wittig reaction of certain resonance stabilized phosphonium ylids with carbohydrates serving as the aldehydes. The reaction of ylids derived from maleimides with D-ribose was of particular interest because the products might serve as possible intermediates in the total synthesis of the antibiotic Showdomycin.

HISTORICAL

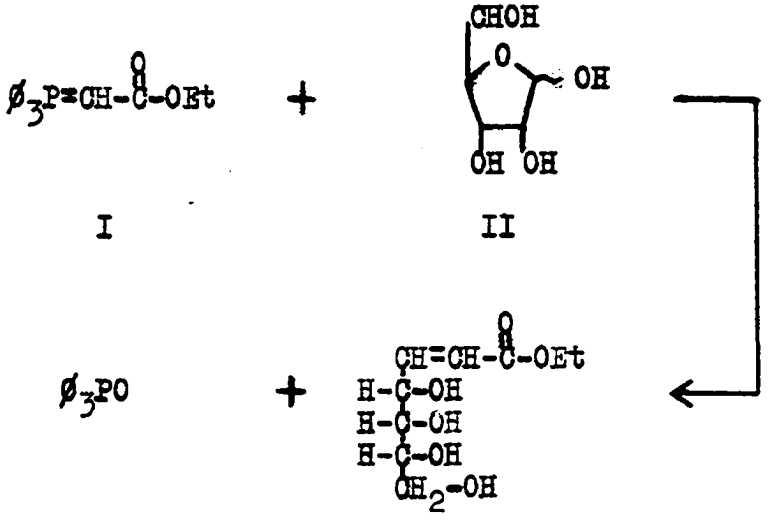
Stabilized Phosphonium Ylids and the Wittig Reaction with Carbohydrates

The reaction of a carbonyl compound with a phosphonium ylid to give an olefin and a phosphine oxide, was discovered by Staudinger[1] in 1919. However, the reaction was extensively studied much later in the 1940's and 1950's by the German chemist George Wittig[2], after whom the reaction was named. Since Wittig's work, the reaction has received much additional study by others who have broadened its scope, studied its mechanism, and extended its utility[2].

The stability and reactivity of the ylids toward carbonyl compounds and with respect to other agents has been the focus of much of this work. Ylids are conveniently classified according to their reactivity and stability. Ylid stability covers a broad spectrum and those which can be isolated, purified and stored are commonly termed "stabilized" ylids. The stabilizing factor is usually an electron withdrawing group bonded to the carbon atom bearing the negative charge which can assist in the delocalization of that charge by resonance or inductive effects.

One area that has received relatively little

attention has been the reaction of stabilized ylids with carbohydrates. It might have been expected that those carbohydrates which are hemiacetals, and thus presumably exist in equilibrium in solution with the aldehydo form, could undergo a Wittig reaction. Kochetkov and Dmitriev[3,4] first reported such a reaction in 1963 noting that the resonance stabilized ylid, triphenylmethylenecarbethoxyphosphorane (I) reacted with a variety of monosaccharides including D-ribose (II), to yield the expected Wittig product, ethyl-2,3-dehydro-2,3-dideoxy-D-ribo-heptanoate (III).

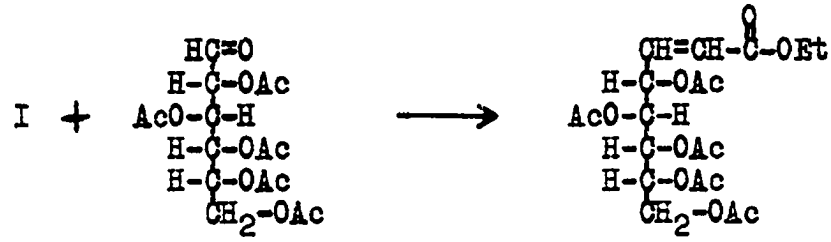


I II

III

The reactions were run in dimethylformamide (DMF) as a solvent. This solvent offers the important advantages of being non-hydroxylic (hydroxylic solvents can cause decomposition of the ylid) and it is polar

enough to act as a good solvent for the carbohydrate. It was further demonstrated that I would also react with acetylated aldehydo sugars like 2,3,4,5,6-penta-O-acetyl-aldehydo-D-glucose (IV) to give the expected ethyl-2,3-dehydro-2,3-dideoxy-4,5,6,7,8-penta-O-acetyl-D-gluco-octanoate (V).



IV V

Trans products have been suggested for these adducts by Kochetkov and Dmitriev. Work done by others has shown that generally the trans isomer predominates.[5]

Another group of Russian workers, Zhdanov, Dorofeenko and Uzlova[6,7] extended the work of Kochetkov and Dmitriev to include two other stabilized ylids. Thus, using triphenylfurfurylphosphorane, triphenylmethyleneacetylphosphorane, and also ylid I in DMF with various monosaccharides, they obtained the normal Wittig reaction products.[6] In a later paper, they reported the reaction of these ylids with aldehydo isopropylidene and benzylidene derivatives of monosaccharides.[7]

In 1967, Mirzayanova, Davydova and Samokhvalov[8] studied the reaction of ethoxymethylcarbethoxyphosphorane with 2,3-4,5-di-O-isopropylidene-D-arabinose and obtained the expected Wittig product, ethyl-2,3-dehydro-3-deoxy-2-ethoxy-4,5-6,7-di-O-isopropylidene-D-arabino-heptanoate.

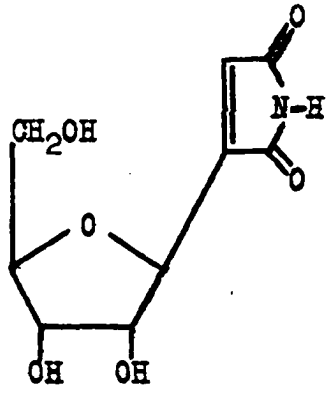
Dmitriev and coworkers[9] reported again in 1967 on a method for lengthening the carbon chain of a carbohydrate by three carbon atoms at a time. They reported that ylids derived from esters of bromopyruvic acid could be reacted with various sugars using their earlier procedures to obtain the expected products.

Showdomycin

Showdomycin is an antibiotic, active against both gram positive and gram negative bacteria. It was isolated from the growth medium of a new species of Streptomyces (Streptomyces showdoensis n. sp.) in 1964 by Nishimura and coworkers.[10] It showed exceptional activity against Streptococcus Hemolyticus and also showed good anticancer activity in both Ehrlich tumors *in vivo*, and HeLa cells *in vitro*.[11]

The structure of Showdomycin was apparently determined at about the same time by different workers. Nakagawa and workers[12] and also Robins and

coworkers[13] reported the structure of Showdomycin to be 2-(β-D-ribofuranosyl) maleimide (VI).

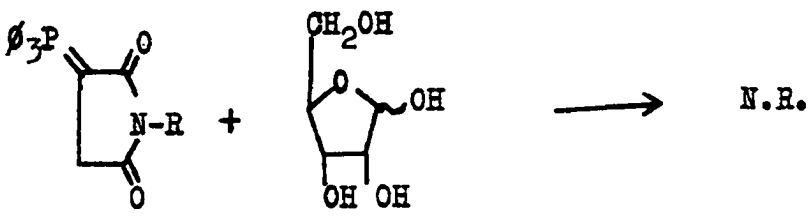


VI

DISCUSSION

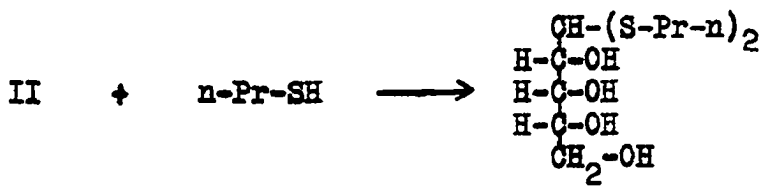
Heyda and Theodoropulos[14] observed in their work with ylids derived from maleimide (VII) and N-phenyl maleimide (VIII) and from maleic anhydride, that the former reacted smoothly to give high yields of the Wittig products, while the latter gave tars when reacted with normal aldehydes. Since the maleimide ylids VII and VIII appeared to react as normal stabilized ylids, and carbohydrates were known to react via a Wittig reaction with certain other stabilized ylids;[3,4,6-9] it appeared likely that D-ribose would react directly with ylids VII and VIII.

This reaction was tried using DMF as a solvent and the progress of the reaction was followed by thin-layer chromatography (tlc). After 10 to 20 hours, the ylid spot had disappeared and a number of new spots were observed, two of which were identified as triphenylphosphine and triphenylphosphine oxide. The triphenylphosphine oxide suggested a Wittig reaction but the ribose spot was unchanged in size. An identical tlc was obtained when the ribose was omitted from the reaction mixture, indicating that there was no reaction between the ylid and the ribose.

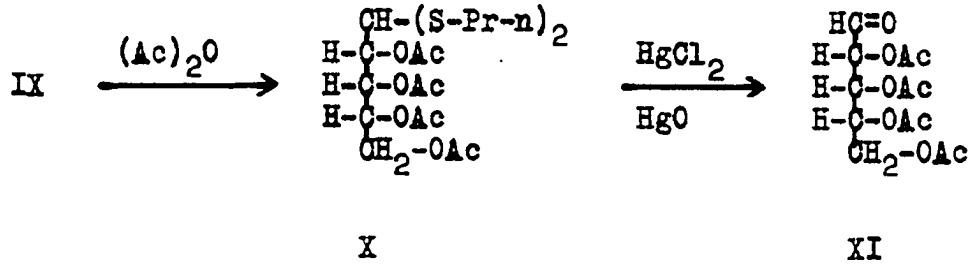


VII R=H
VIII R=phenyl II

In view of the failure of ylids VII and VIII to react directly with D-ribose, the acetylated aldehydo derivative of D-ribose was prepared according to Zinner's[15] procedure. The D-ribose (II) was converted to the di-n-propyl dithioacetal derivative, IX, using n-propyl mercaptan. In pyridine, IX was acetylated using acetic anhydride to give the acetylated mercaptal X, which was then demercaptalated using mercuric chloride and mercuric oxide to yield 2,3,4,5-tetra-O-acetyl-aldehydo-D-ribose (XI).

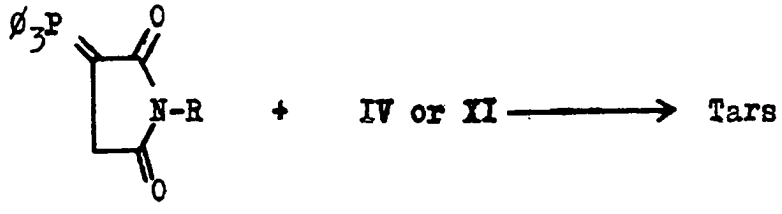


IX



X XI

Similarily, 2,3,4,5,6-penta-O-acetyl-aldehydo-D-glucose (IV) was prepared. In contrast to the successful reactions of aldehydo sugars with stabilized ylids previously discussed, attempts to react ylids VII and VIII with the aldehydo sugars XI and IV produced tars.



VII R=H
VIII R=phenyl

Attempts to moderate the reaction by reverse addition of the ylid were not successful nor did different solvents affect the results.

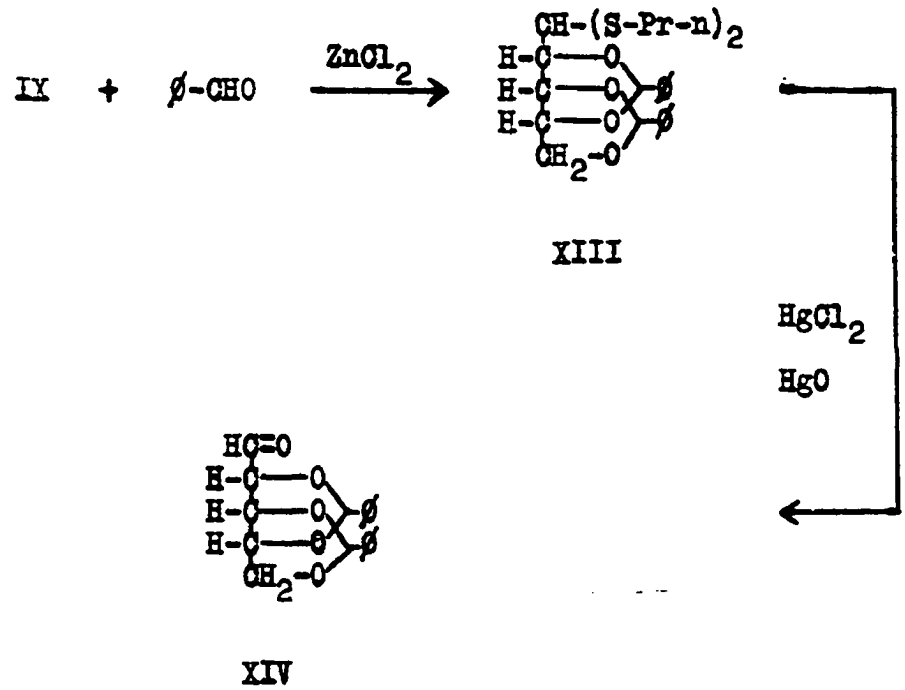
One possible explanation for the observed results was made by Johnson[16] who noted that ylids, especially unstabilized ylids, react with other groups such as esters. However, it seems unlikely that the less

reactive stabilized ylids VII and VIII would react with the less reactive carbonyl groups of an ester when the opportunity for reaction with an aldehyde was possible. Furthermore, it was shown that ylids VII and VIII were stable for 1 hour in refluxing ethyl acetate, which suggests a low reactivity towards esters.

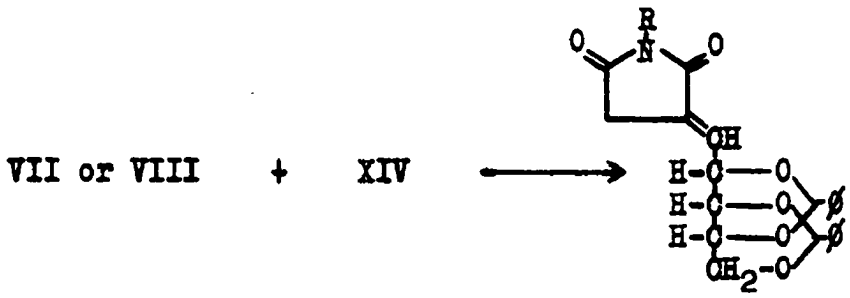
Another possible explanation for the observed results was indicated by the work of Hauser[17] who showed that ylids act as bases and therefore can catalyze aldol type condensations. To determine if such a condensation were likely, the comparative basicities of ylids I, VII and VIII were determined by the method of Speziale and Ratts.[18] The results of the titrations suggest that ylid I was more basic than ylids VII and VIII. Since ylid I does not cause aldol type side reactions with aldehydo acetylated carbohydrates, it seems unlikely that ylids VII and VIII, which are less basic, would cause this type of reaction.

Thus while the ester groups seem to cause the tar formation, the manner in which they interfere is not clear. To avoid the apparent complicating effect of the ester protecting groups, a di-O-benzylidene protected derivative of aldehydo-D-ribose was prepared.

The procedure given by Potgieter and MacDonald[19] was used for the preparation of the 2,4-3,5-di-O-benzylidene di-n-propyl dithioacetal of D-ribose (XIII) in which the mercaptal of D-ribose was treated with benzaldehyde and zinc chloride. The dibenzylidene mercaptal was then demercaptalated as described previously to yield 2,4-3,5-di-O-benzylidene-aldehydo-D-ribose (XIV).



The Wittig reaction of XIV with ylids VII and VIII proceeded as originally expected in high yields (85%) to give the Wittig product, 2,4-3,5-di-O-benzylidene-1-deoxy-1-(2,5-dioxo-3-pyrrolidinylidene)-D-ribitol (XV) or its N-phenyl derivative (XVI).

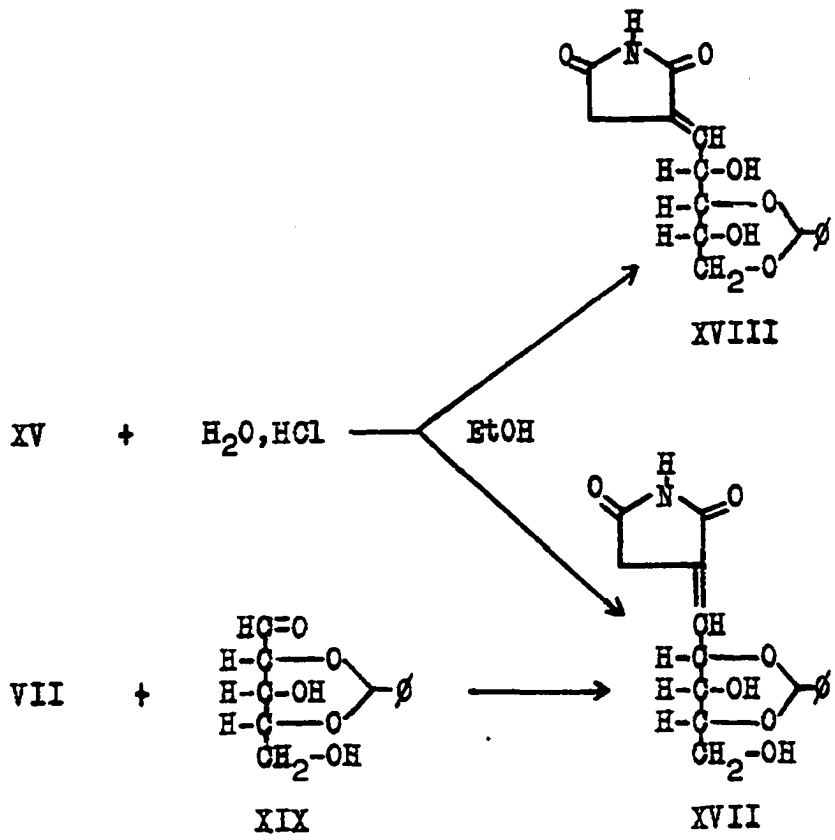


86% XV R=H
XVI R=phenyl

Mild treatment of XV with dilute hydrochloric acid in ethanol gave a product with an elemental analysis which suggested a compound resulting from the removal of only one of the two benzylidene groups. The nmr spectrum supported this conclusion, both from the relative integration of the aromatic protons, and from the fact that only a single benzyl proton peak was observed whereas XV had two. The nmr spectrum also demonstrated that the compound was still an open chain olefin since the olefinic proton resonance at ~6.6 ppm gave the proper integration and was similar in its splitting pattern (roughly a broadened doublet) to that observed in the spectrum of XV.

In order to determine which benzylidene group had been removed under the mild hydrolysis that yielded XVII or XVIII, the 2,4-isomer, XVII, was obtained by an alternate route. The 2,4-O-benzylidene-aldehydo-D-ribose (XIX) which was a known compound was prepared by the method of Potgieter and MacDonald.[19]

This involved controlling the conditions so that a monobenzylidene **ribose mercaptal** precipitated from the reaction mixture before it was converted to the di-O-benzylidene compound. The monobenzylidene mercaptal was then demercaptalated using mercuric chloride to yield a monobenzylidene aldehydo-D-ribose identified as the 2,4 isomer, XIX, by Potgieter and MacDonald.[19]



The product from the reaction of the known 2,4-O-benzylidene aldehydo-D-ribose (XIX) with ylid VII was identical with the product obtained by hydrolysis of XV. This demonstrated that the product of the

dibenzylidene hydrolysis was 2,4-O-benzylidene-1-deoxy-1-(2,5-dioxo-3-pyrrolidinylidene)-D-ribitol (XVII) and not the 3,5 isomer (XVIII).

More vigorous treatment of XV using more concentrated acid under elevated temperatures did not lead to the complete removal of both benzylidene groups. Rather the tlc evidence suggested that it led to a mixture of XVII and the compound where both groups were removed. This was demonstrated by following the progress of the reaction using tlc. After treatment of XV with acid in ethanol for 15 minutes, two spots were observed, one of which was identified as XVII and the other was presumed to be the compound with both benzylidene groups removed. The relative ratios of these spots remained constant over a period of hours suggesting that an equilibrium had been reached. The fact that one acetal was more readily removed than the other was not surprising since this behavior has been reported for isopropylidene acetals.[20] What was unexpected was that under more prolonged and severe hydrolysis conditions, both benzylidene groups could not be completely removed while the benzaldehyde remained in the reaction mixture.

EXPERIMENTAL

General

All melting points were taken on a Thomas-Hoover melting point apparatus and are corrected. The elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee. A Beckman IR-8 spectrophotometer was used to record the infrared spectra and the Beckman DU-2 with a Keston polarimeter used to determine the optical rotations. A Varian A-60 spectrometer was used to determine the nmr spectra. Where a reference is made to a literature melting point, the procedure used to prepare that compound is essentially that given in the cited reference. All starting materials are commercially available.

Preparation of Compounds

Preparations of Triphenylsuccinimidenephosphorane (VII)

Maleimide (20 g, 0.21 m) was dissolved in 250 ml of glacial acetic acid and the solution was heated on a steam bath. Triphenylphosphine (52 g, 0,21 m) was added in portions with stirring to the above solution. The solution was heated for 1 hr and cooled to 10-15° whereupon it was diluted with 1-2 l ether. The solid precipitate was collected and washed with acetone.

The reaction yielded 65 g (85%) of VII, mp 222-240° d, (lit.[14] mp 220°).

Preparation of N-phenyl-triphenylsuccinimidenephosphorane (VIII)

Triphenylphosphine (75 g, 0.30 m) was added in portions with stirring to a hot solution of N-phenylmaleimide (45 g, 0.26 m) in 500 ml of glacial acetic acid. The solution was cooled to 5-10° and diluted with 1-2 l ether until an oil resulted. The oil was washed several times by trituration and decantation with ether until it solidified. The solid product was refluxed in 50% ether-acetone and collected by vacuum filtration. The reaction yielded 65 g (59%) of VIII, mp 184-5°, (lit.[14] mp 176.5-178.5°).

Preparation of Triphenylmethylenecarbethoxyphosphorane (I)

Triphenylphosphine (15 g, 0.1 m) was added to a solution of ethyl bromoacetate (15 g, 0.1 m) in 500 ml benzene. The solution was refluxed for 12 hr and the resulting precipitate collected and dissolved in a small amount of hot 30% ethanol-water. The solution was cooled to 5-10°, made alkaline by the addition with vigorous stirring of 6 N NaOH, and the mixture was set aside in a refrigerator to allow the oil to crystallize. The solid product was collected, washed

with water, and twice recrystallized from ethyl acetate and petroleum ether (60-110°) to yield 16 g (73%) of I, mp 123-124°, (lit.[21] mp 124°).

Preparation of D-ribose di-n-propyl dithioacetal (IX)

D-Ribose (30 g, 0.20 m) was dissolved in 30 ml of conc HCl and the solution cooled to 0°. To this cold solution, n-propyl mercaptan (25.4 g, 0.33 m) was added slowly with stirring. During this addition the temperature was maintained at 0°. The mixture was stirred for 1 hr, poured into 300 ml of cold water, and allowed to stand overnight in a refrigerator. The solid product was then collected and recrystallized from an aqueous $NaHCO_3$ solution to yield 28 g (50%) of IX, mp 78-81°, (lit.[22] mp 85°).

Preparation of 2,3,4,5-tetra-O-acetyl-aldehydo-D-ribose (XI)

D-Ribose di-n-propyl dithioacetal (5 g, 0.02 m) was dissolved in 15 ml pyridine. Acetic anhydride, 20 ml, was added to this solution and the mixture was stirred for 20 hr at room temperature, whereupon it was poured over 100 ml of crushed ice. The gummy oil which formed was washed with water and purified by treatment with Norit followed by reprecipitation from 50% methanol-water. The clear oil (4 g) which

was obtained was dissolved in 20 ml acetone followed by the addition of 2 ml of water. To this stirred mixture was added $CdCO_3$ (9 g) followed by the dropwise addition of $HgCl_2$ (10 g) in 15 ml acetone. The mixture was stirred for 10 hr at 20°, one additional hr at 50°, and finally refluxed for 0.5 hr. The mixture was filtered and concentrated in the presence of added $CdCO_3$ (2 g) under reduced pressure. From the concentrate was evaporated two 100 ml portions of dry acetone to remove traces of water and the concentrate was finally extracted with 100 ml warm chloroform. The chloroform solution was extracted with two 50 ml portions of a 10% NaI solution and two 50 ml portions distilled water, then dried over Na_2SO_4. The chloroform was evaporated under reduced pressure to yield 1 g (18%) of XI, mp 95-96°, (lit.[15] mp 100°).

Preparation of D-glucose diethyl dithioacetal (XII)

Anhydrous D-glucose (100 g, 0.67 m) was dissolved in 85 ml of conc hydrochloric acid and the temperature of the solution lowered and maintained at 0-5°. Ethyl mercaptan (100 ml) was then added to this solution with vigorous stirring and the stirring continued for 1 hr. The precipitate was collected and recrystallized from an aqueous $NaHCO_3$ solution. The product

was collected from cold water and finally washed with cold ethanol and dried to yield 95 g (61%) of XII, mp 125-127°, (lit.[23] mp 127°).

Preparation of 2,3,4,5,6-penta-O-acetyl-D-glucose diethyl dithioacetal (XX)

D-Glucose diethyl dithioacetal (50 g, 0.17 m) was dissolved in 180 ml dry pyridine and the solution cooled to 0°. The solution was stirred maintaining a temperature of 0-5° while 360 ml acetic anhydride was added dropwise. The solution was allowed to stand overnight at room temperature, whereupon it was poured into 3 l of cold water. The water was decanted and the sirup triturated with several portions of cold water. The sirup was then covered with water and placed in a refrigerator where it crystallized completely after 50 hr. The crystals were collected and recrystallized from methanol-water to yield 70 g (81%) of XX, mp 44-46°, (lit.[23] mp 45-47°).

Preparation of 2,3,4,5,6-penta-O-acetyl-aldehydo-D-glucose (IV)

Mercuric chloride (137 g, 0.5 m) was dissolved in 500 ml of acetone and the solution stirred vigorously while 200 g dried cadmium carbonate was added. 2,3,4,5,6-Penta-O-acetyl-D-glucose diethyl dithioacetal (50 g, 0.1 m) dissolved in 500 ml of acetone

was added dropwise. The mixture was stirred for 24 hr at room temperature and finally filtered into a flask containing 150 g of $CdCO_3$. The residue was washed with 500 ml of acetone and the wash combined with the filtrate. The combined acetone solution was evaporated under reduced pressure yielding a residue which was extracted with 700 ml warm chloroform. The chloroform solution was extracted with two 200 ml portions of distilled water, dried using Na_2SO_4, filtered and evaporated under reduced pressure. The product was taken up in 90 ml of warm acetone, 40 ml of ether was added and then sufficient petroleum ether added to cause opalescence. The dispersion was placed in a refrigerator and after 20 hr, 25 g (62%) of IV collected, mp 115-117°, (lit.[23] mp 119.5-120.5°).

Preparation of 2,4-O-benzylidene-D-ribose di-n-propyl dithioacetal (XXI)

Benzaldehyde (3.6 ml, 0.036 m) was dissolved in a solution of 21 ml dioxane containing D-ribose di-n-propyl dithioacetal (85 g, 0.30 m). The solution was cooled and maintained at 0-5° while a solution of 18 ml water and 32 ml concentrated hydrochloric acid was added with vigorous shaking. After 5-10 min, the precipitate was collected and washed with cold water. The product was dissolved in chloroform, extracted

with an aqueous $NaHCO_3$ solution, and finally dried over Na_2SO_4. The chloroform was evaporated under reduced pressure, the residue recrystallized from benzene-petroleum ether (60-110°) and finally from petroleum ether (60-110°) alone to yield 8.5 g (75%) of XXI, mp 96-97°, (lit.[19] mp 101.5-102.5°).

Preparation of 2,4-O-benzylidene-aldehydo-D-ribose (XIX)

Acetone, 30 ml, was used to dissolve 2,4-O-benzylidene-D-ribose di-n-propyl dithioacetal (5.6 g, 0.015 m). To this solution was added 2 ml water and yellow mercuric oxide (9.7 g, 0.045 m) and the solution was vigorously stirred while mercuric chloride (12.3 g, 0.045 m) in 30 ml acetone was added dropwise. The mixture was stirred for 2 hr and refluxed for an additional hour. The precipitate was removed by vacuum filtration and washed with acetone. The wash and filtrate were combined and concentrated in the presence of mercuric oxide (3 g) under reduced pressure to yield a gum. The gum was extracted with three 15 ml portions of dioxane. The extract was filtered and evaporated under reduced pressure to yield a sirup. The sirup was extracted with three 15 ml portions of chloroform and again filtered and concentrated. The resulting sirup was dissolved in 100 ml methanol and decolorized with Norit. This

methanol solution was made weakly alkaline by dropwise addition of 1% aqueous ammonia solution. The resulting white ppt was separated by filtration and the filtrate evaporated under reduced pressure to a sirup. Three 100 ml portions of ethanol followed by three 100 ml portions of benzene were evaporated from the sirup under reduced pressure to remove traces of water. The reaction yielded 2 g (54%) of XIX: mp 80-100° d, (lit.[19] mp-clear glass); ir γ_{max}^{Nujol} (cm^{-1}), 1710 (C=O); nmr (DMSO-d_6) δ 9.78 (s, 1, CHO), 7.47 (s, 5, aromatic).

Preparation of 2,4-3,5-di-O-benzylidene-D-ribose di-n-propyl dithioacetal (XIII)

One stick of fused $ZnCl_2$ (50 g) was stirred in a solution of 100 ml benzaldehyde for 1-2 hr. D-Ribose di-n-propyl dithioacetal (8 g, 0.03 m) was added and the stirring continued for 1 hr. The solution was then poured, with vigorous stirring, into 1 l of hot petroleum ether (60-110°). The petroleum ether solution was decanted and filtered from the red oil phase and the petroleum ether and benzaldehyde evaporated under reduced pressure. The crude product was recrystallized from 95% ethanol to yield 6.6 g (46%) of XIII, mp 108-109°, (lit.[19] mp 110°).

Preparation of 2,4-3,5-di-O-benzylidene-aldehydo-D-ribose (XIV)

2,4-3,5-Di-O-benzylidene-D-ribose di-n-propyl dithioacetal (6 g, 0.013 m) was dissolved in a solution of 86 ml of acetone and 13 ml water. Yellow mercuric oxide (8.2 g, 0.04 m) was added and the mixture refluxed for 1 hr. Mercuric chloride (8.6 g, 0.04 m) in 43 ml acetone was added dropwise in 10 min with vigorous stirring and refluxing continued for 2 hr. The mixture was filtered using a Celite pad and the filtrate evaporated under reduced pressure. The residue was extracted with warm chloroform. The chloroform solution was extracted twice with a 10% aqueous solution of NaI followed by two portions of water. The chloroform solution was dried and evaporated under reduced pressure to yield 40 g, (94%) of XIV, mp 97-99°, (lit.[19] mp 99-101°).

Preparation of ethyl-2,3-dehydro-2,3-dideoxy-4,5,6,7,8-penta-O-acetyl-D-gluco-octanoate (V)

Triphenylmethylenecarbethoxyphosphorane (3.5 g, 0.01 m) was dissolved in 200 ml of absolute ethanol. 2,3,4,5,6-Penta-O-acetyl-aldehydo-D-glucose (3.8 g, 0.01 m) was added to this solution and the solution concentrated to 75 ml by evaporation on a steam bath. The reaction yielded 3.7 g, (80%) of V, mp 133-135°,

(lit.[4,6] mp 127-129°, 133-134.5°).

Anal. Calc. for $C_{20}H_{28}O_{12}$: C, 52.17; H, 6.12.
Found: C, 52.27; H, 5.92.

Preparation of 2,4-3,5-di-O-benzylidene-1-deoxy-1-(2,5-dioxo-3-pyrrolidinylidene)-D-ribitol (XVII)

Triphenylsuccinimidenephosphorane (1.7 g, 0.005 m) was added to a solution of 2,4-3,5-di-O-benzylidene-aldehydo-D-ribose (1.7 g, 0.005 m) in 200 ml ethanol. The solution was concentrated slowly by distillation to a volume of 75 ml and allowed to cool. A white precipitate formed and was collected by vacuum filtration and recrystallized from ethanol to yield 1.7 g (86%) of XVII: mp 194-195°; ir ν_{max}^{Nujol} (cm^{-1}), 3180 (N-H), 1770, 1730, 1680 (C=O); $[\alpha]_D^{25}$ -94.1° (c, 0.12, ethanol); nmr (DMSO-d_6) δ 11.50 (s, 1, NH), 7.50 (s, 10, aromatic), 6.63 (s, 1, olefinic), 6.00 (s, 1, benzyl), 5.83 (s, 1, benzyl).

Anal. Calc. for $C_{23}H_{21}NO_6$: C, 67.80; H, 5.16; N, 3.44.
Found: C, 67.81; H, 5.31; N, 3.40.

Preparation of 2,4-3,5-di-O-benzylidene-1-deoxy-1-(2,5-dioxo-1-phenyl-3-pyrrolidinylidene)-D-ribitol (XVI)

The reaction of N-phenyl-triphenylsuccinimidene-phosphorane with 2,4-3,5-di-O-benzylidene-aldehydo-D-ribose by the above procedure afforded XVI in 85%

yield, mp 212-213°; ir ν_{max}^{Nujol} (cm^{-1}), 1770, 1710, 1680 (C=O); $[\alpha]_D^{25}$ -143.2 (c, 0.38, ethanol); nmr (DMSO-d_6) δ 7.50 (s, 15, aromatic), 6.80 (m, 1, olefinic), 6.07 (s, 1, benzyl), 5.71 (s, 1, benzyl).

Anal. Calc. for $C_{29}H_{26}NO_6$: C, 72.04; H, 5.17; N, 2.90. Found; C, 72.25; H, 5.32; N, 2.91.

Preparation of 2,4-O-benzylidene-1-deoxy-1-(2,5-dioxo-3-pyrrolidinylidene)-D-ribitol (XV)

2,4-3,5-Di-O-benzylidene-1-deoxy-1-(2,5-dioxo-3-pyrrolidinylidene)-D-ribitol (3 g, 0.0074 m) was stirred in 300 ml methanol containing 3 ml concentrated hydrochloric acid for 5 hr. The solvent was evaporated under reduced pressure to give an oil that was triturated with cold water. The resulting precipitate was crystallized from water to yield hydrated colorless needles which after drying at 110° (0.1 torr) for 2 hr afforded 1.6 g (63%) of XV: mp 189-190°, $[\alpha]_D^{25}$ -45.1°, (c, 1, methanol); ir ν_{max}^{Nujol} (cm^{-1}), 3500 (O-H), 3380 (N-H), 1760, 1720, 1680 (C=O); nmr (DMSO-d_6) δ 11.37 (s, 1, NH), 7.47 (m, 5, aromatic), 6.66 (m, 1, olefinic), 5.70 (s, 1, benzyl).

Anal. Calc. for $C_{16}H_{17}NO_6$: C, 60.18; H, 5.36; N, 4.38. Found: C, 59.93; H, 5.31; N, 4.22.

Attempted Reactions of Ylids VII and VIII with D-Ribose and D-Glucose

D-Ribose, 1 g, was dissolved in 100 ml of DMF. An equimolar quantity of ylid VII (or VIII) was then added and the solution heated for 20 hr on a steam bath. Thin-layer chromatography of the solution revealed an undiminished carbohydrate spot and a number of new spots, two of which were identified as triphenylphosphine and triphenylphosphine oxide. The pattern of new spots was reproduced by treating the ylids alone under the above conditions. The results were the same when D-glucose was used in place of D-ribose and were also the same when ethanol replaced DMF. An oil was obtained when the solvent was removed by evaporation under reduced pressure. Extraction of this oil with small amounts of ethanol yielded 30-40% yields of both triphenylphosphine and triphenylphosphine oxide.

Attempted Reactions of Ylids VII and VIII with the Aldehydo Carbohydrates IV or XI

A solution containing 1 g of the aldehydo carbohydrate IV (or XI) in 100 ml ethanol was prepared. An equimolar quantity of ylid VII (or VIII) in 100 ml DMF was then added dropwise over a period of 20 min to the refluxing ethanol solution. The

solution turned black after 5-10 min and was cooled to room temperature 5 min after the last drop of the ylid-DMF solution was added. Thin-layer chromatography of the solution revealed a spot attributed to triphenylphosphine oxide and a broad streak of lower mobility. The solvent was removed by evaporation under reduced pressure to yield a tar from which nothing except small amounts of triphenylphosphine oxide could be obtained.

Attempted Complete Removal of Benzylidene Groups from XV

In an attempt to remove both benzylidene groups from XV, 1 g of XV was dissolved in 100 ml ethanol. Concentrated hydrochloric acid, 3 ml, was then added to this solution and the solution stirred for 15 min. Thin-layer chromatography of the solution revealed two spots of about equal size. One was identified as XVII and the other was thought to be the compound resulting from removal of both benzylidene groups from XV. Thin-layer chromatography showed spots of about the same size when the above solution was heated at 50° for an additional 5 hr. When XV (1 g) was treated with 100 ml concentrated hydrochloric acid at 90° for 2 hr, the tlc showed the same spots although the spot corresponding to XVII was reduced

in size. The above solution was steam distilled to completely remove the benzaldehyde from the reaction mixture. The reaction mixture no longer showed a tlc spot corresponding to XVII and the one remaining spot corresponded to what was thought to be XV after removal of both benzylidene groups. A satisfactory elemental analysis was not obtained on this latter compound although nmr and ir evidence supported a structure where both benzylidene groups were removed from XV.

Determination of Relative Basicities of Three Ylids

The relative pKa_{obs} values of three ylids were determined using the potentiometric titration procedure described by Speziale and Ratts.[18] Methanolic solutions of the ylids (0.003 molar) were titrated using 0.06 N hydrochloric acid. The pH of the solution (Beckman pH meter, mini electrode) at the half-equivalence point was considered the observed pKa value. While pKa_{obs} values determined in such a manner are not readily comparable to values determined in other solvent systems, the only significance given here to these values was relative order of basicities of the two maleimide ylids compared to triphenylmethylenecarbethoxyphosphorane in methanol. The value reported is the mean of four determinations

in which the spread of values was within 0.2 pKa units from the mean. The following were the observed pKa values: triphenylsuccinimidenephosphorane (VII), 7.0; N-phenyl-triphenylsuccinimidenephosphorane (VIII), 6.3; triphenylmethylenecarbethoxyphosphorane (I), 8.9, (lit.[18] 9.2).

SUMMARY

The Wittig reaction of certain stabilized ylids with some monosaccharides and their open chain aldehydo derivatives has been studied. It was shown that two of these ylids derived from maleimide would not react smoothly with the monosaccharides themselves nor with the corresponding open chain acetylated aldehydo derivatives, but did yield the normal Wittig reaction product with the benzylidene protected aldehydo-D-riboses.

The structures of the Wittig products, as well as products resulting from hydrolysis of these products, were determined by elemental analysis, spectral data, and in one case, by an alternative synthetic route.

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VITA

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