Preliminary communication

Observations on the use of the Wittig reaction and a related reaction of epoxides in the synthesis of sugar olefins*

N. BAGGETT, J. M. WEBBER, and N. R. WHITEHOUSE

Chemistry Department, University of Birmingham, P.O. Box 363, Birmingham, B15 2TT (Great Britain) (Received February 1st, 1972; accepted for publication, February 7th, 1972)

Early applications¹ of the Wittig method of olefin synthesis in the carbohydrate field involved resonance-stabilised ylids that can be isolated and purified prior to reaction with the carbonyl compound. More recently, satisfactory results^{2,3} have also been obtained with simple alkylidene ylids, although some difficulties have been encountered^{2,4}, particularly when the carbohydrate contains an unprotected hydroxyl group or a baselabile protecting group. Thus, Lance and Szarek² did not obtain any olefin when 1,2-Oisopropylidene- α -D-xylo-pentodialdo-1,4-furanose (2) dimer was treated with methylenetriphenylphosphorane (1), and the 3-acetate 3 gave only 7% of the olefin 6 and 5.5% of the deacetylated olefin 5. We have found that olefin 5 and its 3-benzyl ether 7 can be prepared by the Wittig route, but that the yields of olefin are critically dependent on the conditions used. These olefins may also be obtained from the appropriate epoxides, by a related reaction, and we now report on our studies of both routes.



Triphenylphosphine is known⁵ to convert epoxides into olefins, probably *via* a betaine intermediate that collapses to olefin and triphenylphosphine oxide as in the Wittig reaction. Treatment of 5,6-anhydro-1,2-O-isopropylidene- α -D-glucofuranose⁶ (8) with triphenylphosphine for 2 h in refluxing *N*,*N*-dimethylformamide (containing hydroquinone⁵ to minimise polymerisation) gave 5,6-dideoxy-1,2-O-isopropylidene- α -D-xylo-hex-5-eno-

*Dedicated to Professor M. Stacey, C.B.E., F.R.S., in honour of his 65th birthday.

Carbohyd. Res., 22 (1972) 227-229

furanose (5) in 32% yield*. After sublimation, 5 had m.p. $62-65^{\circ}$, $[\alpha]_{\rm D} -59.3^{\circ}$ (chloroform); lit. m.p. $61-65^{\circ}$, $[\alpha]_{\rm D} -51.5^{\circ}$ (ref. 7); m.p. $70-71^{\circ}$, $[\alpha]_{\rm D} -57.3^{\circ}$ (ref. 8). The yield of olefin was not increased by prolonging the reaction time. Similar treatment (HCONMe₂, reflux, 20 h) of the 3-benzyl ether⁹ 9 gave a 60% yield of syrupy 3-O-benzyl-5.6-dideoxy-1.2-O-isopropylidene- α -D-xylo-hex-5-enofuranose (7), $[\alpha]_{\rm D} -58.9^{\circ}$ (chloroform); lit.¹⁰ $[\alpha]_{\rm D} -56.4^{\circ}$. In refluxing tetrahydrofuran, the reaction of 9 was incomplete (35% recovery of 9) after 70 h but yielded 50% of olefin 7.

For the Wittig reactions, methylenetriphenylphosphorane (1) was prepared by adding a solution of butyl-lithium in hexane to a suspension of methyltriphenylphosphonium iodide in dry tetrahydrofuran [cf. ref. 3(b)]. This procedure, which results in almost complete dissolution of the salt, apparently leads to essentially complete formation of the ylid 1. Optimal yields of olefin were then obtained by the following procedure: addition of the aldehyde to 2 mol. of the ylid solution, storage of this mixture at room temperature for 15 min, addition of a 1:1 complex (A, 1.1 mol.) of potassium *tert*butoxide and *tert*-butyl alcohol, and boiling of the resulting mixture under reflux for 110 h. The use of complex A to increase the yield of olefin in Wittig reactions was reported by Schlosser and Christmann¹¹. Its role is believed¹¹ to involve an exchange of lithium and potassium cations, resulting in an increase in the proportion of the free zwitterion form of the betaine intermediate which is required for olefin formation.

Application of the foregoing conditions to 3-O-benzyl-1,2-O-isopropylidene- α -Dxylo-pentodialdo-1,4-furanose¹² (4) gave a 63% yield of the syrupy olefin 7. When complex A was omitted from the reaction mixture, or only 1 mol. of ylid was employed, the yield of 7 was ca. 26%. Less-satisfactory results were obtained in the reaction of ylid 1 with the dimer¹³ of 1,2-O-isopropylidene- α -D-xylo-pentodialdo-1,4-furanose (2), which gave only a 16% yield of olefin 5 under the optimal conditions described above. Amongst the other products of this reaction of 2 were triphenylphosphine oxide, methyldiphenylphosphine oxide, and unidentified carbohydrates that contained phosphorus.

It is important to note that our use of various literature^{5,14} methods of ylid formation led to zero or very low yields of olefins 5 and 7 (*cf.* the results of Lance and Szarek²). The Wittig reaction conditions described above do give olefin 5 from the hydroxyl-containing aldehyde 2, but the yield is much less than for the 3-benzyl ether 4, and the epoxide method gives a better route to olefin 5. The low yield of olefin obtained with aldehyde 2 in the Wittig reaction is presumably associated with the formation of phosphorus-containing, carbohydrate by-products, and these aspects are being further investigated.

ACKNOWLEDGMENT

Ranks Hovis McDougall (Research) Ltd. are thanked for financial support (N. R. W.).

*All olefinic products were isolated by column chromatography on silica gel, and were identified by comparison (t.l.c. and n.m.r. spectroscopy) with authentic samples.

Carbohyd. Res., 22 (1972) 227-229

PRELIMINARY COMMUNICATION

REFERENCES

- N. K. Kochetkov and B. A. Dmitriev, Chem. Ind. (London), (1963) 864; Yu. A. Zhdanov,
 G. N. Dorofeenko, and L. A. Uzlova, Zh. Obshch. Khim., 33 (1963) 3444; R. E. Harmon,
 G. Wellman, and S. K. Gupta, Carbohyd. Res., 11 (1969) 574; 14 (1970) 123; and references cited therein.
- 2 D. G. Lance and W. A. Szarek, Carbohyd. Res., 10 (1969) 306.
- 3 (1) A. Rosenthal and M. Sprinzl, Can. J. Chem., 47 (1969) 3941; (b) 48 (1970) 3253.
- 4 J. H. Jordaan and S. Smedley, Carbohyd. Res., 16 (1971) 177.
- 5 G. Wittig and W. Haag, Chem. Ber., 88 (1955) 1654.
- 6 H. Ohle and L. Vargha, Ber., 62 (1929) 2435.
- 7 L. D. Hall, L. Hough, and R. A. Pritchard, J. Chem. Soc., (1961) 1537.
- 8 D. Horton and W. N. Turner, Carbohyd. Res., 1 (1966) 444.
- 9 A. S. Meyer and T. Reichstein, Helv. Chim. Acta, 29 (1946) 152.
- 10 J. English and M. F. Levy, J. Amer. Chem. Soc., 78 (1956) 2846.
- 11 M. Schlosser and K. F. Christmann, Angew. Chem. Int. Ed. Engl., 3 (1964) 636.
- 12 M. L. Wolfrom and S. Hanessian, J. Org. Chem., 27 (1962) 1800.
- 13 T. D. Inch, Carbohyd. Res., 5 (1967) 53.
- 14 e.g. U. Schöllkopf, in W. Foerst (Ed.), Newer Methods of Preparative Organic Chemistry, Vol. 3, Academic Press, New York, 1964, p. 111.

Carbohyd. Res., 22 (1972) 227-229

.