# New Synthetic Routes to Analogs of DDT

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The  $\alpha$ -,  $\epsilon$ -trichloromethyl migration characteristic of the 4-methyl-4-trichloromethyl-2,5-cyclohexadienylidenes<sup>1,2</sup> has been applied in the synthesis of analogs of DDT. The Wittig reaction<sup>3</sup> and the related reaction of Emmons and Wadsworth<sup>4</sup> were employed in the formation of the intermediate polyenes.

Triphenyl-*p*-xylylphosphonium bromide reacted with phenyllithium, and the resulting aralkylidenetriphenylphosphorane by reaction with 4-methyl-4trichloromethyl-2,5- cyclohexadienone yielded 2,2bis(*p*-tolyl)-1,1,1-trichloroethane (I), the rearranged product of the Wittig reaction. Triphenyl-2,4-dichlorobenzylphosphonium chloride yielded 2-(2,4 - dichlorophenyl) - 2 - (4 - methylphenyl)-1,1,1-trichloroethane (II) by use of the same reaction series.

The reaction of diethyl *p*-xylyl phosphonate with sodium hydride and the dienone did not lead to isolable quantities of I, nor was there infrared evidence for its formation in the crude reaction product; the dienone was largely recovered. Diethyl 2,4-dichlorobenzyl phosphonate, however, did form II with the same reagents. The selfcondensation reaction of the phosphonate seems to have been less competitive with the desired reaction in this second case, possibly for steric reasons.

The use of these syntheses in the preparation of DDT analogs which are not available by the usual acid condensation is being investigated.

## EXPERIMENTAL

p-Xylyl bromide. This was prepared following the instructions of Wenner<sup>5</sup> except that the N-bromosuccinimide and the p-xylene were treated in equimolar quantities. The product, which tended to crystallize in the system, distilled at 65°/lmm. The yield was 51%, m.p. 34° (all melting points uncorrected).

p-Xylyltriphenylphosphonium bromide. This was prepared from p-xylyl bromide and triphenylphosphine (Eastman Kodak Co.) following the procedure of Harrison *et al.*<sup>6</sup> The nearly quantitative yield of white crystals, m.p. 275-277°, was recrystallized from alcohol-benzene.

4-Methyl-4-trichloromethyl-2,5-cyclohexadienone. This was prepared by Newman's modification of the reaction of Zincke and Suhl.<sup>7</sup>

(2) M. S. Newman and R. L. Tse, J. Org. Chem., 21, 638 (1956).

- (3) G. Wittig, Angew. Chem., 68, 505 (1956).
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- (5) W. Wenner, J. Org. Chem., 17, 523 (1952).
- (6) I. T. Harrison, B. Lythgoe, and S. Trippett, J. Chem. Soc., 4016 (1955).
- (7) M. S. Newman and A. G. Pinkus, J. Org. Chem., 19, 978 (1954).

2,2-Bis(p-tolyl)-1,1,1-trichloroethane. To a stirred suspension of 9 g. (0.02 mole) of p-xylyltriphenylphosphonium bromide in 100 ml. of anhydrous ether (under an atmosphere of dry nitrogen) was added a slight excess of phenyllithium<sup>8</sup> in dry ether. During this addition, the mixture became intensely red. A solution of 4.75 g. (0.021 mole) of 4-methyl-4trichloromethyl-2,4-cyclohexadienone in 75 ml. of anhydrous ether was then slowly added; the color gradually faded to a pale orange. The mixture was further stirred for 2 hr., the ether distilled and replaced by dry tetrahydrofuran and the resulting solution heated under reflux for 5 hr. The solvent was removed under reduced pressure, and the residue extracted with 200 ml. of ether; this extract was washed with water and dried over calcium chloride. After evaporation the residue was taken up in n-hexane. This solution was chromatographed on an alumina (Woelm, neutral, activity grade I) column (2.5  $\times$  6 cm.) with hexane, about 200 ml. of colorless solution being collected. The solvent was evaporated to about 15 ml. and the solution refrigerated; three successive crystallizations yielded 3.4 g. of crude product. Recrystallization from 95% ethanol yielded 3.05 g. (48%) of pure 2,2-bis(p-tolyl)-1,1,1-trichloroethane. This sample, as determined by mixture melting-point and infrared, was identical with a sample prepared by the condensation of toluene and chloral.<sup>9</sup>

2,4-Dichlorobenzyltriphenylphosphonium chloride. Triphenylphosphine and 2,4-dichlorobenzyl chloride<sup>10</sup> reacted in a procedure which was essentially that for the preparation of the *p*-xylylphosphonium salt. However, heating to reflux was necessary. After several hours, the formed phosphonium salt was filtered off and the filtrate again refluxed. This process was repeated several times until the production of salt was no longer significant. The total yield of recrystallized material, m.p. 246-249°, amounted to 93%.

2-(2,4-Dichlorophenyl)-2-(4-methylphenyl)-1,1,1-trichloroethane. The same general procedure was followed as with the 2,2-bis(p-tolyl) analog, substituting 9.15 g. of 2,4-dichlorobenzyltriphenylphosphonium chloride (0.02 mole). Here the intense color of the intermediate phosphorane solution did not fade immediately upon contact with the ketone, and overnight stirring was necessary to bring about nearly complete loss of color. Because of this low reactivity of the phosphorane, the tetrahydrofuran solution was heated at reflux overnight. Working up the crude mixture as before, provided 1.1 g. (15%) of white crystals, m.p. 104-105°. This sample showed no melting point depression with, and the same infrared spectrum as, a sample obtained by the aluminum chloride-condensation of  $\alpha$ -trichloromethyl-2,4-dichlorobenzyl alcohol and toluene.

Anal.: Calcd. for  $C_{15}H_{11}Cl_5$ : C, 48.85; H, 2.98; Cl, 48.17. Found: C, 48.27; H, 3.33; Cl, 47.27.

Diethyl p-xylylphosphonate and diethyl 2,4-dichlorobenzyl phosphonate. These were prepared according to the procedure (using triethyl phosphite<sup>11</sup> and the corresponding benzyl halide) of Saunders et al.<sup>12</sup> The p-xylyl phosphonate distilled at 126-128°/1 mm. (88% yield), and the dichlorobenzyl phosphonate at 144-146°/1 mm. (83%).

2-(2,4-Dichlorophenyl)-2-(4-methylphenyl)-1,1,1-trichloroethane. This was prepared in the same general manner in which Emmons and Wadsworth<sup>4</sup> prepared *trans*-stilbene using 0.03 molar quantities. The reaction was held at 60° until hydrogen evolution ceased; the reaction mixture was then heated at reflux for 1 hr. Here, no crystallization oc-

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- (9) D. A. Shirley, Preparations of Organic Intermediates, Wiley, New York, 1951, p. 287.
- (10) Sample provided by Heyden Newport Chemical Corp.
- (11) Sample provided by Virginia Carolina Chemical Corp.
- (12) B. C. Saunders, G. J. Stacey, F. Wild, and I. G. E. Wilding, J. Chem. Soc., 699 (1948).

<sup>(1)</sup> K. v. Auwers and W. Julicher, Ber., 55, 2167 (1922).

curred upon treatment with water, so the organic material was extracted with ether, washed and dried. The ether was evaporated, the residue taken up in *n*-hexane, and the solution chromatographed on alumina. An oil came down in the earlier fractions; the more polar, unchanged ketone was eluted layer. The oil gave crystals from hexane. Upon recrystallization from alcohol the expected product was not immediately obtained. However, the crystals were seen to become pasty upon a week's standing; the infrared spectrum now showed a great similarity to that of II. This material, recrystallized twice from alcohol, gave an 11% yield of pure II.

This same method was used in an attempt to prepare 2,2bis(*p*-tolyl)-1,1,1-trichloroethane. Although several minor variations were made, only the dienone could be recovered; there was no infrared evidence for formation of the desired product.

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# Reaction of D-Glucopyranosylamine with Phosgene

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Zemplén et al.<sup>1</sup> prepared a " $\mu$ -thioglucoxazoline" by a reaction of D-glucose with potassum thiocyanate. Oxidation of the compound with hydrogen peroxide gave the corresponding " $\mu$ -hydroxyglucoxazoline" to which they assigned the structure I.



Bromund and Herbst<sup>2</sup> failed to prove unequivocally the structure of Zemplén's compound by hydrolysis. They also attempted unsuccessfully to cyclize amorphous *N*-carbethoxy and *N*-carbomethoxy derivatives of *D*-glucopyranosylamine to the corresponding oxazolidone.

Edward and Martlew<sup>3</sup> identified D-glucopyranosylamine and di-D-glucosylamine, but no D-glucosamine, among the acid hydrolysis products of Zemplén's "µ-thiolglucoxazoline". Therefore, structure II was proposed for it.



On the basis of periodic acid oxidation Schwarz<sup>4</sup> proposed for Zemplén's compound the furanose rather than the pyranose structure.

No reactions of phosgene with sugar amines seem to have been reported to date. It was expected that a reaction of phosgene with 1-D-glucopyranosylamine might give the known 1,3-bis(1-D-glucopyranosyl)urea.

Contrary to expectations, reactions of phosgene with aqueous solutions of D-glucopyranosylamine in the presence of sodium hydroxide, sodium carbonate, triethylamine, or pyridine gave a product for which formula III is proposed.



Compound III consumed one molar equivalent of periodic acid without formation of either formic acid or formaldehyde. It gave a tetraacetyl derivative IV.

Both III and IV are different from the corresponding compounds made by Zemplén and coworkers,<sup>1</sup> as can be seen from Table I.

TABLE I

COMPARISON OF MELTING POINTS AND OPTICAL ROTATIONS

	M.P.	[α] <sub>D</sub>
Zemplén's µ-hydroxy- glucoxazoline I		$+6.79^{a}$
I tetraacetate	95	$+104.8^{b}$
Oxazolidone III	220 - 222	$+56.0^{a}$
Tetraacetate IV	150 - 151	$+12.14^{b}$

<sup>a</sup> In H<sub>2</sub>O. <sup>b</sup> In CHCl<sub>3</sub>.

As oxazolidone III was made from D-glucopyranosylamine of established structure, it is safe to assume that the nitrogen atom is attached to carbon 1 of D-glucose. The results of periodic acid oxidation indicate that the compound has the pyranose ring. A furanose would yield formaldehyde on periodate oxidation, and an open chain com-

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<sup>(2)</sup> W. H. Bromund and R. M. Herbst, J. Org. Chem., 10, 267 (1945).

<sup>(3)</sup> J. T. Edward and E. F. Martlew, Chem. & Ind. (London), 1034 (1952).