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WITTIG REACTIONS. I. PREPARATION OF 2,3-DIHYDRO-1-BENZOXEPIN AND NOVEL REARRANGEMENT TO 2-METHYL-3-CHROMENE

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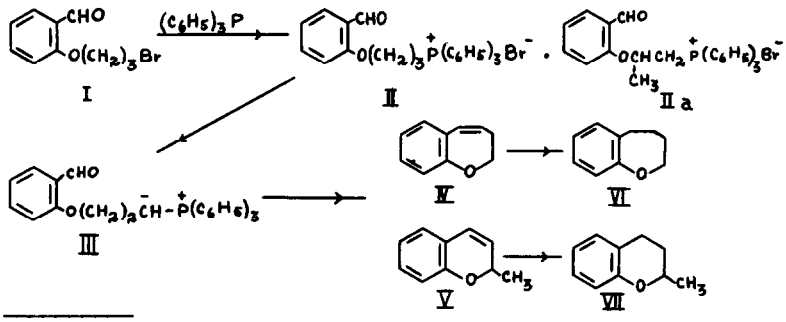
In view of the current interest in intramolecular Wittig reactions[1,2,3,4] for the preparation of carbocyclic ring systems, we wish to report an intramolecular Wittig reaction to produce a heterocyclic ring system. We also wish to report an unusual rearrangement of a type heretofore unreported.



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Salicylaldehyde (1 mole) was allowed to react with pure 1,3-dibromopropane (1.22 mole) in the presence of sodium hydroxide (1 mole) and gave a 64% yield of γ-salicyloxypropylbromide (I). An analytically pure sample had b.p. 131-132° (0.4 mm Hg), $N_D^{24.5}$ 1.5735; $C_{10}H_{11}BrO_2$ (Found: C, 49.25%; H, 4.53%; Br, 32.75%). The N.M.R. and I.R. spectra were consistent with the structure assigned. The N.M.R. showed the following: three methylene triplets, each with weight 2, centered at 8.8 τ, 6.5 τ, and 6.0 τ; one aromatic triplet weight 2, centered at 3.1 τ; two aromatic doublets each with weight 1, centered at 2.7 τ and 2.4 τ respectively.

Equimolar quantities of the γ-salicyloxypropylbromide (I) and triphenylphosphine were dissolved in anhydrous ethyl acetate and refluxed for 72 hours. Filtering and washing the white precipitate with hot solvent gave a 62% yield of analytically pure salt II, m.p. 162°; $C_{28}H_{26}BrO_2P$ (Found: C, 66.53%; H, 5.23%). The N.M.R. and I.R. spectra were consistent with the n-propyl structure assigned. The N.M.R. spectrum gave the following: three peaks with weight 2 each centered at 7.8 τ, 6.5 τ, and 5.8 τ respectively; one peak with weight 4, centered at 2.9 τ; one peak with weight approximately 15 centered at 2.2 τ.

The salt II (0.26 mole) was added in small portions over a period of 16 hours to a solution of sodium ethoxide (0.3 mole) in ethanol and the solution was refluxed overnight. Concentration and short path distillation gave an 83% yield of crude mixture. This crude material was shown to contain 87% of 2-methyl-3,4-chromene (V) and 8% 2,3-dihydro-1-benz-

oxepin (IV) by gas chromatographic analysis. Redistillation gave an analytically pure sample of the chromene, V, (50% yield) b.p. 34° (0.2 mm Hg), N_D^{25} 1.5658, molecular weight 155, $C_{10}H_{10}O$ (Found: C, 82.04%; H, 6.86%). The I.R. and N.M.R. spectra were consistent with the structure assigned. The N.M.R. spectrum had: centered at 9.1τ, doublet, weight 3, assigned to the C-methyl hydrogens; centered at 5.6τ, multiplet, weight 1, assigned to the hydrogen at the 2-position; centered at 5.05τ, pair of doublets weight 1, assigned to the hydrogen at the 3-position; centered at 4.2τ, pair of split peaks, weight 1, assigned to hydrogen at the 4-position; centered at 3.62τ, multiplet, weight 4, assigned to the four aromatic hydrogens.

An essentially quantitative uptake of 1 mole of hydrogen was observed on hydrogenation of the 2-methyl-3,4-chromene (V) over 10% palladium on charcoal catalyst. An analytically pure sample of the recovered 2-methyl-1-benzopyran (VII) had b.p. 72° (3 mm Hg), N_D^{25} 1.5316 [Lit.[5] b.p. 223-226° (762 mm Hg)].

The N.M.R. spectrum had: centered at 9.1τ, doublet, weight 3, assigned to the C-methyl hydrogens; centered at 8.7 τ and 7.8τ, two multiplets weight 2 each, assigned to the hydrogens at the 3- and 4-positions; centered at 6.45τ, multiplet, weight 1, assigned to the hydrogen at the two-position; centered at 3.5τ, multiplet, weight 4, assigned to the four aromatic hydrogens.

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The 2,3-dihydro-1-benzoxepin (IV) was isolated by gas chromatographic separation of the final fractions from a spinning band distillation of the combined mixture of a number of crude samples. An analytically pure sample[6] of the oxepin, IV, had b.p. 35° (0.07 mm Hg), $N_D^{23.5}$ 1.5926, $C_{10}H_{10}O$ (Found: C, 82.15%; H, 6.88%). The I.R. and N.M.R. spectra were consistent with the structure assigned, and were identical with that of an authentic sample[7]. The N.M.R. spectrum had: centered at 7.4τ, split quadruplet, weight 2, assigned to the C-3 hydrogens; centered at 5.82τ, triplet, weight 2, assigned to the C-2 hydrogens; centered at 4.15τ, sextuplet weight 1, assigned to the C-4 hydrogen; centered at 3.71τ, split doublet, weight 1, assigned to the C-5 hydrogen; centered at 3.03τ, multiplet, weight 4, assigned to the aromatic hydrogens.

A quantitative uptake of 1 mole of hydrogen was observed on hydrogenation of a sample of 2,3-dihydro-1-benzoxepin (IV). The product was shown to be identical by I.R. and N.M.R. spectra with an authentic sample of 2,3,4,5-tetrahydro-1-benzoxepin (VI) prepared[8] according to Cagniant[9].

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6 This sample was shown to be more than 99.5% pure by V.P.C.

7 We gratefully acknowledge the gift of an authentic sample from Professor V. J. Traynelis of the University of Notre Dame.

8 The authors wish to thank Mr. B. L. Horowitz for the preparation of this sample.

9 P. Cagniant, Compt. rend. 229, 889 (1949).

The results suggest a rearrangement of the dihydro-oxepin, IV, to the chromene, V, under the conditions of the reaction; however, the following data indicate that all the 2-methyl-3-chromene (V) was not produced exclusively via the intermediacy of the 2,3-dihydro-1-benzoxepin (IV):

a) The oxepin, IV, was found to be unchanged by refluxing in absolute ethanol, or in absolute ethanol in the presence of triphenylphosphine oxide, for a one week period.

b) Refluxing the oxepin, IV, in an alcoholic sodium ethoxide solution for 20 hours gave only a 9% conversion to the methylchromene, V. Refluxing for 14 days gave a 97% conversion of the oxepin, IV. The 2-methyl-3-chromene (V) obtained from the rearrangement of 2,3-dihydro-1-benzoxepin (IV) was isolated and shown to be identical by I.R. and V.P.C. to the analytical sample. This is the first example of the rearrangement of a seven-membered, oxygen containing heterocyclic system where the oxygen remains as a part of a new heterocyclic system[10,11,12,13]. The rearranged product also contained a small amount of an, as yet, unidentified product.

c) The salt, II, was added to all at once in a 10% molar excess to a cold solution of sodium ethoxide in ethanol, heated to reflux over a 20 minute period (at which time the characteristic deep red ylid color had developed) and allowed to reflux for 15 minutes (at which time the deep red ylid color had disappeared) and then quenched immediately in ice-water and extracted with ether. The crude concentrated ether extracts showed only 9% of the 2,3-dihydro-1-

benzoxepin (IV) and 90% of the 2-methyl-3,4-chromene (V) by V.P.C.

It has thus been shown that the oxepin, IV, may be rearranged to give the chromene, V, under the influence of base. However, the reaction is very slow employing sodium ethoxide in ethanol (the reaction rate may be measurably increased by employing sodamide in liquid ammonia[10]). Initial results indicate a possible unusual rearrangement of the salt, II, or of the corresponding ylid, III, under the influence of alcoholic sodium ethoxide to give the unexpected high yield of 2-methyl-3,4-chromene (V).

Work is in progress to elucidate the mechanism of this reaction and to prepare the oxepin, IV, in high yield, and will be published in detail at a later date.

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