Communications TO THE EDITOR

A New Synthesis of 3,6-Dibromopyridazine

Sir:

A new method for the preparation of 3,6-dibromopyridazine makes it possible to employ this substance in the synthesis of 3-sulfanilamido-6-methoxypyridazine which has recently shown great promise as a drug. 3,6-Dibromopyridazine is much more reactive than the corresponding dichloropyridazine and may be used to advantage in the following reactions.

Phosphorus oxybromide (3 parts) reacted vigorously with 3,6-dioxohexahydropyridazine (1 part) at 70–80° for 2 hours; the OH groups were substituted by Br and the partially unsaturated ring became fully aromatized. The excess $POBr_3$ was removed *in vacuo* and the residue treated with water and made basic with ammonia. The product, 3,6-dibromopyridazine, separates on cooling; recrystallization from cyclohexane yields soft white needles, m.p. 118–119,° which is identical with material prepared from maleic hydrazide.[1] Yields higher than 50% may be obtained by operating in the presence of bromine (1.5 parts). In this case the reaction is violent at the beginning and requires cooling; short heating is then sufficient to complete the reaction. Phosphorus trichloride–bromine reacts similarly although with inferior yields.

An intimate mixture of 3,6-dibromopyridazine (1 part), potassium carbonate (1.1 parts) and sulfanilamide (1.4 parts) was heated in an oil bath (bath temp. 150–160°) until it began to melt and evolve carbon dioxide. Upon completion of gas evolution the mixture was extracted with hot water. Insoluble sulfanilamide was removed after cooling by filtration. Acidification of the filtrate with acetic acid yielded 3-sulfanilamido-6-bromopyridazine in yields exceeding 75%. A sample recrystallized from alcohol (yellow needles) became brown at 210° and melted at 243–244° (dec.).

Anal.: Calcd. for: $C_{10}H_9BrN_4O_2S$: Br, 24.31. Found: Br, 24.29; 24.60.

The replacement of bromine by alkoxyl may be accomplished easily by the Williamson reaction. A methanolic solution of 3-sulfanilamido-6-bromopyridazine (1 mole) was heated for 10 hours at 100–110° with 2.5 moles of sodium methoxide. The product, 3-sulfanilamido-6-methoxypyridazine, resulted in yields exceeding 85%.

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(1) E. A. Steck, R. P. Brundage, and L. T. Fletcher, *J. Am. Chem. Soc.*, **76**, 3225 (1954).

Trialkyl Phosphites as Reagents in a Novel Reductive *O*-Alkylation of Quinones[1]

Sir:

We have shown[2] that in the reaction of chloranil with either triphenylphosphine or triethyl phosphite, phosphorus-oxygen bonds are exclusively established, as in I and II. With triethyl phosphite, a subsequent group translocation takes place and yields an ether-phosphate V as the final product. The reaction of *p*-benzoquinone with triphenylphosphine, however, takes an entirely different course and yields a product in which a phosphorus-carbon bond has been established (VIII).[2a]

The purpose of this communication is to describe the interesting behavior of the *p*-benzoquinone-triethyl phosphite system. In this system, over 90% of diethyl(4-ethoxyphenyl)phosphate (VII) was formed, presumably *via* intermediate IV. The ether-phosphates V, VI (obtained from chloranil and trimethyl phosphite), and VII, were readily hydrolyzed to the corresponding quinol-monoalkyl-ethers, namely, tetrachlorohydroquinone-monoethylether (IX), tetrachlorohydroquinone-monomethylether (X)[3] and hydroquinone-monoethyl-ether (XI). Likewise, 2,5-dimethylhydroquinone-monomethylether was obtained from 2,5-dimethyl-*p*-benzoquinone and trimethyl phosphite. These reactions proceed in high yields under mild conditions. Thus, trialkyl phosphites become reagents in a facile method for the reductive *O*-alkylation of quinones and for the synthesis of monoalkylethers of hydroquinones.

The quinone and the trialkyl phosphite were allowed to react for several hours at room temperature in anhydrous benzene (or for shorter periods at reflux temperature). The products were isolated (after alkaline extraction of small amounts of acidic by-products) by distillation or recrystallization. Hydrolysis to the quinol-monoalkylethers (such as IX, X, and XI) was effected with 5% aqueous-alcoholic alkali (15–20 hours reflux).

If the trialkyl phosphite is slowly added to a solution of the quinone in benzene containing aqueous ethanol, the only products isolated are the

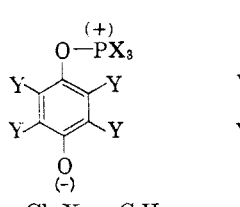
(1) The Structure of Quinone-Donor Adducts. III. Carried out under Public Health Service Grant CY-3250; we are also grateful to the Eli Lilly Research Grants Committee for initial financial support.

(2) (a) F. Ramirez and S. Dershowitz, *J. Am. Chem. Soc.*, **78**, 5614 (1956); (b) *J. Org. Chem.*, **22**, 856 (1957).

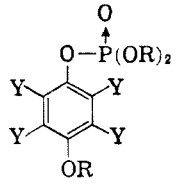
(3) The naturally occurring antibiotic Drosophilin A has been identified as tetrachlorohydroquinone-monomethylether (X) [M. Anchel, *J. Am. Chem. Soc.*, **74**, 2943 (1952)].

trialkyl phosphate and the unalkylated hydroquinone, in high yields. This is essentially the coupling of the two half-equations[4]: $X_3P + H_2O \rightleftarrows X_3PO + 2H^{(+)} + 2e$ and quinone $+ 2H^{(+)} + 2e \rightleftarrows$ hydroquinone, where X_3P is a tricovalent organophosphorous compound with phosphorous in the +3 oxidation state. In other words, trialkyl phosphites can be used, in the presence of water, to reduce quinones. Intermediates such as II, III, and IV (*cf.* isolation[2a] of I) would explain these processes. Evidently, the possibility of an irreversible group translocation (to V, VI, and VII) in the phosphorus compound, as well as the structural features of the quinone itself (oxidation potential, steric effects) can determine the over-all course of the reactions.[2]

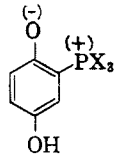
The ether-phosphates, V,[2b] VI, and VII, exhibited the typical nonbonded phosphate P → O band at 7.85 μ and the expected ultraviolet spectra. VI had m.p. 94–95° (cyclohexane); found: C, 29.4; H, 2.7. VII had b.p. 139–140° (0.25 mm.), $n_D^{25°}$ 1.4829; found: C, 52.2; H, 6.0. The quinol-monoalkylethers (IX, m.p. 84–85°; X, m.p. 114–115°; XI, m.p. 66–67°) were characterized as such and as the corresponding well-known dialkyl ethers.[3,5]



I, Y = Cl, X = C_6H_5
II, Y = Cl, X = OC_2H_5
III, Y = Cl, X = OCH_3
IV, Y = H, X = OC_2H_5



V, Y = Cl, R = C_2H_5
VI, Y = Cl, R = CH_3
VII, Y = H, R = C_2H_5



VIII; X = C_6H_5

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(4) Standard potentials are known for half-equations involving certain phosphorus compounds with phosphorus in +1 and +3 oxidation states:

$H_3PO_2 + H_2O \rightleftarrows H_3PO_3 + 2H^{(+)} + 2e$, E° = 0.50 volt
$H_3PO_3 + H_2O \rightleftarrows H_3PO_4 + 2H^{(+)} + 2e$, E° = 0.276 volt

The expressions given for the hypophosphorus and phosphorus acids involve four atoms around the phosphorus. For a recent summary see: H. H. Sisler in M. C. Sneed and R. C. Brasted, *Comprehensive Inorganic Chemistry*, D. van Nostrand Co., Inc., N. Y., 1956; Vol. V, pp. 118, 126.

(5) (a) *Cf.* Beilstein's *Handbuch der organishen Chemie*, 4th Ed., **6**, 843 (I 416), (II 840), J. Springer, Berlin 1918; (b) A. Binz and C. Rath, *Ber.*, **58**, 309 (1925); (c) C. Graebe, *Ann.*, **146**, 20 (1868); (d) E. Banberger and J. Frei, *Ber.*, **40**, 1932 (1907), p. 1944.

Radiolysis of 1-Hexene[1]

Sir:

In order to investigate the mechanism of radiation-induced polymerization of simple olefins, we have irradiated 1-hexene with high energy electrons and gamma rays[2] at room temperature with exclusion of oxygen. Total doses varied from 12 to 40 × 10^{20} ev/g at rates between 6 × 10^{19} (gamma) and 6 × 10^{22} (electron) ev/g per hour. Gaseous products were analyzed mass spectrometrically and found to consist of hydrogen (G_{H_2} 0.8 ± 0.1) plus light hydrocarbons ($G_{L.H.}$ 0.12 ± 0.03). The recovered 1-hexene, analyzed by gas chromatography, was found to contain *n*-hexane ($G_{n\text{-}C_6H_{14}}$ 0.11 ± 0.02) and smaller amounts of other hexenes. The heavier materials consisted entirely of polymeric compounds, with G<0.01 for the total of compounds with carbon numbers not multiples of six. Yields determined by fractional distillation, with molecular weight confirmation by mass spectrometry, were G_{dimer} 0.98 ± 0.05, G_{trimer} 0.76 ± 0.05, $G_{tetramer}$ 0.22 ± 0.1 and $G_{pentamer}$ 0.35 ± 0.1 with overall $-G_{1\text{-hexene}}$ 10.5 ± 0.5. Unsaturation appeared to increase with molecular weight; the pentamer had as much diolefin as monoolefin.

The dimeric fraction by mass spectrometric analysis appeared to be approximately 90% monoolefin, with some saturated hydrocarbon and some diolefin. This is in contrast with the diolefinic dimer obtained from 1-octene by Kharasch, Schwartz, and Nudenberg,[3] who used free radicals from isopropyl bromide photolysis, and demonstrates that, in the present case, dimerization does not occur predominantly by combination of allyl-type radicals. The infrared spectrum of the dimer showed 27% terminal, 57% trans non-terminal and 3% vinylidene-type double bonds. Information on the location of the non-terminal double bonds was obtained by gas chromatographic analysis of methyl esters of the carboxylic acids obtained by oxidation of ozonolysis products. Methyl acetate, propionate, *n*-butyrate, *n*-valerate, hexanoate, 2-methylhexanoate, heptanoate, octanoate, nonanoate, and decanoate, plus the methyl esters of a branched C_{10} acid and a branched C_8 acid (not 2-methylheptanoate) were the only monocarboxylic esters found. Traces of dicarboxylic acids (from diolefins) and ketones (from vinylidene double bonds) were also products of ozonolysis. Identification of these compounds is in progress.

(1) This research was supported in part by the United States Air Force under Contract No. AF 33(616)-3875 monitored by Aeronautical Research Laboratory (WCRRC).

(2) The source of electrons was the 3 Mev. Van de Graaff accelerator at the Shell Development Company, Emeryville, Calif. The source of gamma rays was the High Level Gamma Irradiation Facility of the Argonne National Laboratory, Lemont, Ill.

(3) M. S. Kharasch, D. Schwartz, and W. Nudenberg, *J. Org. Chem.*, **18**, 337 (1953).