

g. of oil which, on trituration in petroleum ether, gave 0.12 g. of white crystals which melted at 135–135.5°. This product had the same elemental analysis and ultraviolet absorption as a sample of 4-hydroxy-2,4,6-tri-*t*-butyl-2,5-cyclohexadien-1-one (XII) prepared by the decomposition of 2,4,6-tri-*t*-butyl-4-nitro-2,5-cyclohexadien-1-one.<sup>11</sup> The mixture melting point was not depressed. Evaporation of the petroleum ether and recrystallization of the residual crystals from petroleum ether and from alcohol ultimately yielded 0.5 g. of an additional white crystalline product, m.p. 234–235°;  $\lambda_{\text{max}}^{\text{CHCl}_3}$  246 m $\mu$  ( $\epsilon$  11,000) and 319 m $\mu$  ( $\epsilon$  420); infrared bands at 5.98 and 6.05  $\mu$  (quinone carbonyl); 5.56 and 5.70  $\mu$  (other carbonyl bands).

*Anal.* Calcd. for  $\text{C}_{16}\text{H}_{22}\text{O}_6$ : C, 75.19; H, 9.78. Found: C, 75.04; H, 9.60.

In a similar experiment using double the amount of maleic anhydride and the same quantities of other reactants, an additional compound was isolated from the neutral fraction

by crystallization from methanol, 0.2 g., m.p. 173–174°;  $\lambda_{\text{max}}^{\text{isooctane}}$  243 m $\mu$  ( $\epsilon$  22,000) and 375 m $\mu$  ( $\epsilon$  64).

*Anal.* Calcd. for  $\text{C}_{16}\text{H}_{22}\text{O}_6$ : C, 75.19; H, 9.78; mol. wt., 639. Found: C, 75.18; H, 9.50; mol. wt., 600, 605.

Acidification of the alkaline extracts did not produce a water-insoluble solid. Maleic acid was recovered by ether extraction of the acidified extracts.

**Dimer of 2,4,6-Tri-*t*-butylphenoxy Radical (XIV).**—In the preparation of VII, 0.55 g. of a yellow crystalline solid, m.p. 145–146°, was isolated by crystallization from the mother liquors;  $\lambda_{\text{max}}^{\text{isooctane}}$  277 m $\mu$  ( $\epsilon$  370), 286 m $\mu$  ( $\epsilon$  420) and 308 m $\mu$  ( $\epsilon$  350);  $\lambda_{\text{max}}^{\text{in}}$  293 m $\mu$  ( $\epsilon$  280). The same product was prepared in 50% yield by heating solid 2,4,6-tri-*t*-butylphenoxy radical at 80° for a week in the absence of air. Isobutylene was identified in the evolved gas.

*Anal.* Calcd. for  $\text{C}_{32}\text{H}_{50}\text{O}_2$ : C, 82.34; H, 10.80; mol. wt., 466. Found: C, 81.93; H, 10.69; mol. wt., 466, 455. WILMINGTON 98, DEL.

[CONTRIBUTION NO. 449 FROM THE CENTRAL RESEARCH DEPARTMENT, EXPERIMENTAL STATION, E. I. DU PONT DE NEMOURS AND CO.]

## Syntheses by Free-radical Reactions. VII. The Reaction of 2,6-Di-*t*-butyl-4-methylphenol and 2,6-Di-*t*-butyl-4-isopropylphenol with Chloroprene

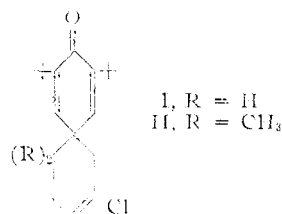
BY W. R. HATCHARD

RECEIVED JANUARY 20, 1958

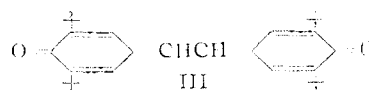
The oxidation of 2,6-di-*t*-butyl-4-methylphenol and of 2,6-di-*t*-butyl-4-isopropylphenol in the presence of chloroprene yielded crystalline 1:1 adducts which are postulated to be spiro[5.5]undeca-1,4,8-trien-3-one derivatives. A mechanism for their formation is proposed.

In an earlier paper<sup>1</sup> it was shown that stable aryloxy radicals add to unsaturates to form 4,4'-alkene- and 4,4'-alkenylene-bis-(2,4,6-trisubstituted-2,5-cyclohexadienone) derivatives. Stable radicals investigated were those formed by the oxidation of hindered 2,4,6-trisubstituted phenols which did not contain hydrogen on the  $\alpha$ -carbon atoms. Chloroprene was found to be the most active unsaturate examined. The present paper describes the reaction of chloroprene under oxidizing conditions with 2,6-di-*t*-butyl-4-methylphenol and 2,6-di-*t*-butyl-4-isopropylphenol, neither of which forms an aryloxy radical of high stability. Oxidations of these phenols have been studied by a number of investigators<sup>2–8</sup> and shown to proceed through free radical intermediates.

In the present work, these phenols were found to react with chloroprene to form crystalline, 1:1 adducts which have the probable structures I and II. Reactions were carried out most conveniently by mixing a benzene solution of the phenol with an excess of lead dioxide and chloroprene in a pressure vessel and shaking at 50° for 16 hours. Under these conditions 2,6-di-*t*-butyl-4-methylphenol gave a 75% yield of the adduct. At 25°, the adduct was



obtained in 34% yield along with a 32% yield of the stilbenequinone, 4,4'-acetylene-bis-[2,6-di-*t*-butyl-2,5-cyclohexadienone] (III).<sup>2</sup>



When the phenol and a stoichiometric amount of aqueous alkaline potassium ferricyanide were added simultaneously to a solution of chloroprene in benzene at 55°, the adduct was formed in 46% yield. About 3% of 4,4'-ethylene-bis-[2,6-di-*t*-butylphenol]<sup>3</sup> also was obtained. There was no evidence for the formation of 2:1 phenol-chloroprene adducts of the type described previously<sup>1</sup> or 2:2 adducts of the additive dimer type described by Coffman and Jenner.<sup>9</sup>

The structure proposed for the 2,6-di-*t*-butyl-4-methylphenol adduct (I) is based upon elemental composition, molecular weight and absorption spectra data and upon the properties of its hydrogenation products. Elemental analysis and molecular weight agree for the composition  $\text{C}_{19}\text{H}_{27}\text{OCl}$ . The infrared absorption spectrum shows bands in

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(2) C. D. Cook, *J. Org. Chem.*, **18**, 261 (1953).

(3) C. D. Cook, N. C. Nash and H. R. Planagan, *THIS JOURNAL*, **77**, 1783 (1955).

(4) R. R. Moore and W. A. Waters, *J. Chem. Soc.*, 243 (1954).

(5) S. L. Cosgrove and W. A. Waters, *ibid.*, 388 (1951).

(6) T. W. Campbell and G. M. Coppinger, *THIS JOURNAL*, **74**, 1469 (1952).

(7) C. D. Cook and B. E. Norcross, *ibid.*, **78**, 3797 (1956).

(8) G. R. Yelke, J. E. Dunbar, R. L. Padrotti, F. M. Scheidt, F. G. H. Lee and E. C. Smith, *J. Org. Chem.*, **21**, 1289 (1956).

(9) D. D. Coffman and E. I. Jenner, *THIS JOURNAL*, **80**, 2872 (1958).



at room temperature to 40 lb./sq. in. of hydrogen pressure in the presence of 0.1 g. of platinum oxide. After being shaken for 18 hours, the reaction mixture was filtered, diluted with water and extracted with ether. The ether extract was washed with sodium carbonate solution, dried and evaporated to give an oil which deposited crystals after standing in an ice-box. Recrystallization from methanol yielded 0.06

g. of white crystals, m.p. 44–44.5°. *Anal.* Calcd. for  $C_{19}H_{22}O$ : C, 82.54; H, 11.66. Found: C, 82.22, 82.19; H, 11.69, 11.69. An infrared spectrum showed the presence of carbonyl and unsaturation bands at 5.95–6.0 and the absence of hydroxyl. Ultraviolet absorption maxima were found at 234  $m\mu$  ( $\epsilon$  8000) and 343  $m\mu$  ( $\epsilon$  410).

WILMINGTON 98, DEL.

[CONTRIBUTION FROM THE PHARMACEUTICAL INSTITUTE OF THE MEDICAL SCHOOL, UNIVERSITY OF KYUSHU, JAPAN]

## Synthesis of Furan Derivatives. XV. 5-Nitrofuryl Polyene Aldehydes

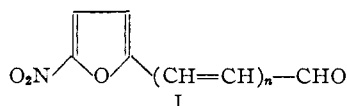
BY HARUO SAIKACHI AND HARU OGAWA

RECEIVED OCTOBER 14, 1957

Four 5-nitrofuryl polyene aldehydes (I,  $n = 1$  to 4) were prepared stepwise from 5-nitrofurfural by repeated condensation with methyl vinyl ether in the presence of boron trifluoride etherate. This method gives considerably better yields than aldol condensation with acetaldehyde. Evidence is presented that the intermediates in this reaction are 1,3-dioxanes (II). The absorption maxima of the polyene aldehydes agree well with the Lewis and Calvin equation. Oximes, semicarbazones, thiosemicarbazones and aminoguanidine derivatives of the aldehydes were prepared, and some were tested for bacteriostatic activity. The oxime of the  $n = 2$  aldehyde is highly active *in vitro* against *M. tuberculosis*, and is of low toxicity in the mouse.

Several years ago it was discovered by American researchers that 5-nitrofurfural semicarbazone and some related compounds possessed notable bacteriostatic and bactericidal activity.<sup>1</sup> The nitro group is essential: in its absence there is little or no activity. Although the exact mechanism of action is not known, it is thought that the compounds inhibit some enzyme system involved in the carbohydrate metabolism of the microorganisms.<sup>2</sup>

We have been investigating this class of compounds for several years.<sup>3</sup> From consideration of reported activities, it appeared to us that the interpolation of a chain of conjugated double bonds between the nitrofuran ring and the aldehyde group might be expected to enhance the antibacterial activity, and this prediction appeared to be borne out by results with three derivatives of 5-nitrofurylacrolein (I,  $n = 1$ ) previously reported.<sup>3</sup> We have therefore tried the effect of further extension of the polyene chain.



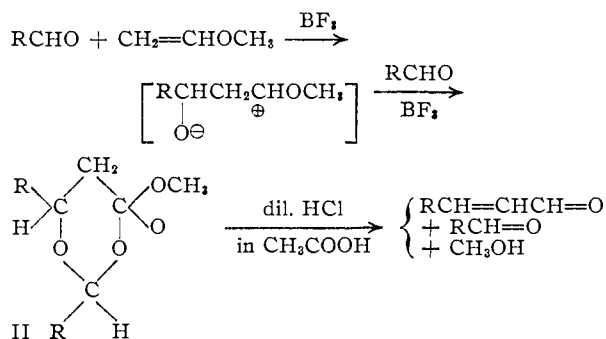
Our first approach to the synthesis of I ( $n = 2$  and 3) was by the aldol condensation of 5-nitrofurylacrolein with acetaldehyde in the presence of piperidinium acetate, in the same way that we had previously prepared 5-nitrofurylacrolein itself. It was necessary to chromatograph the dark, resinous reaction product on alumina. The desired aldehydes were indeed obtained in this way, but in very poor yields.

In the meantime we had found that the condensation of 5-nitrofurfural with methyl vinyl ether in

the presence of boron trifluoride etherate<sup>4</sup> is preferable to the aldol condensation for the preparation of 5-nitrofurylacrolein. In this reaction, unlike the aldol condensation, hardly any resinous by-product is formed, and the one-molar excess of 5-nitrofurfural which must be used is easily recoverable from the reaction mixture.

We therefore applied this same procedure successively to 5-nitrofurylacrolein and to its higher vinyls. In this way we succeeded in building up stepwise, in good yields, not only the  $n = 1$  but also the  $n = 2, 3$  and 4 members of the series. The diene and triene members were shown by mixed melting point to be identical with the specimens previously obtained by aldol condensation. The properties of these aldehydes are given in Table I.

The intermediate product in this reaction is presumed to be a *m*-dioxane (II).



Since the intermediate in the conversion of 5-nitrofurfural to 5-nitrofurylacrolein could not be isolated in a pure state from the brown, viscous reaction mixture, we examined instead the analogous condensation of *p*-nitrobenzaldehyde with methyl vinyl ether. From this reaction mixture, colorless needles melting at 209–211° were obtained readily. The analysis and molecular weight of this compound were in good agreement with the expected

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(4) J. W. Copenhaver, U. S. Patent 2,543,312 (1951); R. I. Hoaglin, *et al.*, U. S. Patent 2,628,257 (1953); O. Isler, *et al.*, *Helv. Chim. Acta*, **39**, 249 (1956).