

irreversibly rearranged to $\text{CH}_2=\text{CX}-\text{CH}=\text{CH}_2$. The iodide rearranges spontaneously. The direct bearing of these facts on theories concerning the mechanism of 1,4-addition and of α,γ -rearrangement is discussed.

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Acetylene Polymers and their Derivatives. XVI. The Preparation of Orthoprenes by the Action of Grignard Reagents on Chloro-4-butadiene-1,2

BY WALLACE H. CAROTHERS AND GERARD J. BERCHET

The term orthoprene is here presented as a designation for derivatives of butadiene-1,3 having a single substituent and that in the 2-position (III). Isoprene is the historically important member of this class and (except for a single reference¹ to ethylbutadiene) it was the only one known until the discovery of chloroprene² and bromoprene.³ The extraordinarily superior properties of these compounds from the standpoint of rubber synthesis prompted the preparation and examination of other dienes.⁴ The results⁵ suggested that similarly desirable properties are not likely to be found among any other types of dienes than the orthoprenes as such, and it became important to obtain further members of this class. The lack of any satisfactory general method for this purpose led to the development of the method described here, which is based on the observation that chloro-4-butadiene-1,2 (I) like other substituted allyl halides⁶ reacts with Grignard reagents to produce abnormal (III) as well as normal (II) products. The theoretical implications of this fact have been discussed in the preceding paper.⁷



For the purpose in view the new method leaves much to be desired. Yields are rather low, and separation of the desired product from by-products is rather laborious. No doubt further study would lead to considerable improvement. In its present state, however, the method has sufficed for the isolation of two orthoprenes especially wanted: *n*-heptoprene and phenoprene. As precursors of rubber neither of these compounds approaches chloroprene; they are in fact probably inferior to isoprene. Heptoprene polymerizes rather more rapidly than isoprene but the

(1) Ipatiew, *J. prakt. Chem.*, [2] **59**, 534 (1899).

(2) Carothers, Williams, Collins and Kirby, *THIS JOURNAL*, **53**, 4203 (1931).

(3) Carothers, Collins and Kirby, *ibid.*, **55**, 786 (1933).

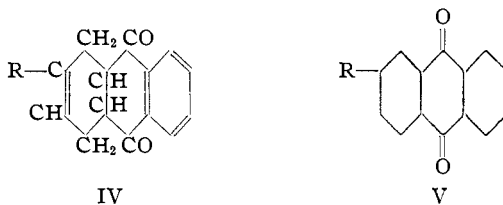
(4) Carothers and Coffman, *ibid.*, **54**, 4071 (1932); Jacobson and Carothers, *ibid.*, **55**, 1624 (1933).

(5) See also Whitby and Galloway, *Can. J. Research*, **6**, 280 (1932).

(6) Prévost and Daujat, *Bull. soc. chim.*, [4] **47**, 588 (1930).

(7) Carothers and Berchet, *THIS JOURNAL*, **55**, 2807 (1933).

product obtained under most conditions appears to be softer and weaker. Phenoprene polymerizes ten to one hundred times as rapidly as isoprene. Under most conditions the predominating product is the dimer, a crystalline solid which has, of course, no rubber-like properties. The high polymer formed, for example, at very high pressure appears to have a relatively low molecular weight and, although slightly rubber-like, it is soft and deficient in strength and elasticity. The experiments here reported dealt with reagents in which R was methyl, *n*-butyl, *n*-heptyl, phenyl and benzyl. From methylmagnesium chloride or iodide or from *n*-heptylmagnesium bromide only the abnormal products (III) were isolated in a state of purity. The product from *n*-butylmagnesium bromide contained a considerable amount of *n*-octane from which the butyl-2-butadiene-1,3 could not be completely separated. The presence of the latter compound was, however, demonstrated by the Diels-Alder reaction. Phenylmagnesium bromide gave both the normal and the abnormal products which were separated and isolated in a state of purity. From benzylmagnesium chloride only the normal product was isolated. The structures of the orthoprenes were established by their reaction with naphthoquinone to form the crystalline addition products (IV), which were readily oxidized to the corresponding anthraquinones (V). The phenyl-4-butadiene-1,2 was identified by hydrogenation to *n*-butylbenzene. Benzyl-4-butadiene-1,2 was identified by its conversion to phenylpropionaldehyde by ozonization.



Experimental Part

Preparation of Isoprene.—A Grignard reagent from 312 g. (2.2 moles) of methyl iodide and 53 g. of magnesium (2.2 moles) in *n*-butyl ether was treated slowly with 177 g. of chloro-4-butadiene-1,2 (2 moles). The mixture was refluxed for one-half hour, acidified, and the material boiling below 120° (74 g.) removed from the butyl ether by distillation. In a similar manner methylmagnesium chloride from 40 g. (1.65 moles) of magnesium in butyl ether with 132 g. of chloro-4-butadiene-1,2 (1.5 moles) yielded 35 g. of liquid boiling below 110°. The products from the two experiments were combined and distilled. Except for a considerable dark residue having the odor of dibutyl ether, only a single fraction was obtained. This was isoprene (47 g.) boiling at 34.5 to 35°.

In alcohol solution it reacted readily with naphthoquinone yielding methyl-2-tetrahydro-1,4,4a,9a-anthraquinone-9,10 (IV, R = CH₃) which crystallized from alcohol in white needles melting at 86° (copper block).⁸ When suspended in alcoholic potash it was readily oxidized by air to β-methylantraquinone, m. p. 177°.⁹

(8) Diels and Alder [*Ber.*, **62**, 2357 (1929)] report 81°.

(9) Diels and Alder report 175°.

***n*-Butyl-2-butadiene-1,3**.—Six moles of butylmagnesium bromide in ethyl ether was treated with 5 moles of chloro-4-butadiene-1,2. After acidification, distillation of the ethereal layer yielded a series of fractions boiling between 33–45° at 49 mm. and a residue composed of a viscous, somewhat elastic mass. The largest fraction (126.5 g.) boiled at 44–45° (29 mm.) (121–123° (760 mm.)). This is very close to the boiling point of *n*-octane (125°) and analysis (C, 84.8; H, 13.5) showed that its composition lay between that of octane and butylbutadiene. Bromine titration indicated the presence of about 57% of the latter compound, and this was demonstrated to be butyl-2-butadiene-1,3 by the fact that the mixture when heated for two hours with an equal weight of naphthoquinone yielded butyl-2-tetrahydro-1,4,4a,9a-anthraquinone-9,10, (IV, R = *n*-C₄H₉), white microscopic crystals from 80% alcohol, m. p. 63–64° (copper block).

Anal. Calcd. for C₁₈H₂₀O₂: C, 80.59; H, 7.46. Found: C, 79.40, 80.31; H, 7.21, 7.53.

Oxidation with air in dilute alcoholic potassium hydroxide gave β-*n*-butylanthraquinone (V, R = *n*-C₄H₉); yellow crystals from alcohol, m. p. 89° (copper block).

Anal. Calcd. for C₁₈H₁₄O₂: C, 81.81; H, 6.06. Found: C, 81.08, 80.83; H, 6.43, 5.69.

***n*-Heptyl-2-butadiene-1,3 (Heptoprene)**.—One mole of *n*-heptylmagnesium bromide in ethyl ether was treated with one mole of chloro-4-butadiene-1,2. After acidification, distillation of the ethereal solution yielded (a) 13 g. boiling at 47–48.5° (5 mm.), (b) 32 g. at 52–54° (5 mm.), and (c) 42 g. boiling chiefly at 99–101° (3 mm.). Fraction (c) crystallized on being cooled, and it was apparently tetradecane (calcd.: C, 84.84; H, 15.15. Found: C, 84.05; H, 15.19); m. p. 5–7°. Analysis of fraction (a) showed that it contained considerable amounts of material other than hydrocarbon. Fraction (b) was *n*-heptyl-2-butadiene-1,3; n_D^{20} 1.4511; d_4^{20} 0.7796; M_R calcd., 52.05; M_R found, 52.52.

Anal. Calcd. for C₁₁H₂₀: C, 86.84; H, 13.15. Found: C, 85.43, 85.44; H, 12.96, 13.40.

When heated with naphthoquinone at 90–100° for two hours it gave *n*-heptyl-2-tetrahydro-1,4,4a,9a-anthraquinone-9,10 (IV, R = *n*-C₇H₁₅); white needles from acetone; m. p. 81°.

Anal. Calcd. for C₂₁H₂₆O₂: C, 81.29; H, 8.38. Found: C, 81.02; H, 8.64.

Oxidation with air in the presence of alcoholic potash gave β-*n*-heptylanthraquinone; pale yellow crystals from alcohol; m. p. 87° (copper block).

Anal. Calcd. for C₂₁H₂₂O₂: C, 82.35; H, 7.18. Found: C, 81.77; H, 6.96.

Action of Phenylmagnesium Bromide on Chloro-4-butadiene-1,2.—This reaction was complicated by the fact that considerable amounts of phenol were always formed even when attempts were made to exclude air by passing a stream of nitrogen into the reaction flask. The following experiment is typical. Seven moles of phenylmagnesium bromide in ethyl ether was treated with 6 moles of chloro-4-butadiene-1,2. The mixture was washed first with dilute acid and then with dilute alkali to remove the phenol, dried and distilled. A certain amount of benzene due to the excess of the Grignard reagent distilled first, and then the following fractions were collected: (a) 52–60° (17 mm.), 23.5 g.; (b) 60–61° (17 mm.), 72 g.; (c) 61–72° (17 mm.), 8.5 g.; (d) 72–73° (17 mm.), 31 g.; (e) residue, 209 g.

The fractions (b), (d) and (e) were further purified as described below and the following compounds obtained: phenyl-4-butadiene-1,2 (4–7.2%), phenyl-2-butadiene-1,3 (8.4–9.2%), dimer of phenyl-2-butadiene-1,3 (25.3–26.7%). The yields are based on the chloro-4-butadiene-1,2 applied, and the two sets of figures result from two separate experiments. By a slight modification of the conditions the yield of phenyl-2-butadiene-

1,3 was greatly increased. The reaction product was decomposed very rapidly with ice and dilute acid, the ethereal solution was kept at low temperature until it could be distilled, the ether was evaporated *in vacuo*, and the distillation was carried out at a lower pressure (2.5 mm.) than was used in previous experiments. The yield of pure phenyl-2-butadiene-1,3 was 24%.

Fraction (b) was redistilled and then showed n_D^{20} 1.5489; d_4^{20} 0.9226; M_R calcd 43.85; M_R found, 44.93. It was identified as phenyl-2-butadiene-1,3 (phenoprene).

Anal. Calcd. for $C_{10}H_{10}$: C, 92.31; H, 7.69. Found: C, 91.60; H, 7.69.

When heated with an equal weight of naphthoquinone at 90–100° it gave phenyl-2-tetrahydro-1,4,4a,9a-anthraquinone-9,10 (IV, R = C_6H_5); crystallized from acetone, m. p. 146–147° (copper block).

Anal. Calcd. for $C_{20}H_{18}O_2$: C, 83.33; H, 5.55. Found: C, 83.00; H, 6.00.

Oxidation with air in the presence of alcoholic potash gave β -phenylanthraquinone, identified by mixed melting point (163–164°).¹⁰

Anal. Calcd. for $C_{20}H_{12}O_2$: C, 84.50; H, 4.22. Found: C, 84.14; H, 4.43.

Fraction (d).—After redistillation this showed n_D^{20} 1.5460; d_4^{20} 0.9220; M_R calcd., 43.85; M_R found, 44.64. It was identified as phenyl-4-butadiene-1,2 by its analysis and by hydrogenation to *n*-butylbenzene. It failed to react with naphthoquinone.

Anal. Calcd. for $C_{10}H_{10}$: C, 92.31; H, 7.69. Found: C, 92.44; H, 7.77.

Hydrogenation in alcohol with PtO_2 catalyst was rapid and complete. The product had b. p. 178–179°; d_{20}^{20} 0.863; n_D^{23} 1.4895. *n*-Butylbenzene has b. p. 180°; d^{15} 0.864; $n_D^{13.5}$ 1.494.¹¹

Fraction (e).—Distillation of fraction (e) gave first some diphenyl, and then the bulk of the material distilled at 220–225° (10 mm.) with only a very small residue. The distillate solidified when cooled, and after crystallization from methanol gave white needles melting sharply at 62°. The same product was slowly formed from phenyl-2-butadiene-1,3 on long standing or more rapidly under the action of heat, but not from phenyl-4-butadiene-1,2. Analysis shows that it is a dimer of phenyl-2-butadiene-1,3.

Anal. Calcd. for $C_{20}H_{20}$: C, 92.31; H, 7.69; mol. wt. 260. Found: C, 92.92; H, 7.71; mol. wt. (in freezing benzene), 232, 232.

Benzyl-4-butadiene-1,2.—One and one-half moles of benzylmagnesium chloride in ethyl ether was treated with 1.13 moles of chloro-4-butadiene-1,2. The reaction had a tendency to proceed by spurts. Distillation of the reaction product through an efficient column gave three fractions: (a) 30.5 g. 72–73° (7 mm.); (b) 73 g. 76–77° (7 mm.); and (c) 30 g. of residue. Fraction (c) was probably mostly dibenzyl. Neither (a) nor (b) reacted with naphthoquinone. Fraction (b) was identified as benzyl-4-butadiene-1,2 and (a) was apparently a less pure specimen of the same material. Fraction (b) showed n_D^{20} 1.5400; d_4^{20} 0.9169; M_R calcd., 48.45, M_R found, 49.28.

Anal. Calcd. for $C_{11}H_{12}$: C, 91.66; H, 8.33. Found: C, 91.12; H, 8.87.

When oxidized with potassium permanganate it yielded benzoic acid. Ozonization in chloroform solution followed by hydrolysis gave an oil having the odor of phenylpropionaldehyde. Its oxime melted at 95–97°.

Anal. Calcd. for $C_9H_{11}ON$: C, 72.48; H, 7.38; N, 9.39. Found: C, 71.68; H, 7.32; N, 8.83.

(10) Scholl and Neovius [*Ber.*, **44**, 1075 (1911)] give 160 to 161°. The melting point recorded above is observed in a capillary tube on slow heating. On a copper block the substance first melts at about 145° with the evolution of some gas; it then solidifies and melts again at 161 to 165°. If the substance is first heated *in vacuo* at 125°, only a single melting point of 163–164° is observed. β -Phenylanthraquinone from another (commercial) source showed a similar behavior.

(11) Beilstein, IV ed., Vol. V, p. 413.

Summary

Diene hydrocarbons of the formulas $\text{CH}_2=\text{CR}-\text{CH}=\text{CH}_2$ and/or $\text{CH}_2=\text{C}=\text{CHCH}_2\text{R}$ are obtained by the action on chloro-4-butadiene-1,2 of RMgX where R is methyl, *n*-butyl, *n*-heptyl, phenyl and benzyl. Some polymers and derivatives are described.

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Chemical Studies of the Mechanism of the Narcosis Induced by Hypnotics. I. The Synthesis of Colored Derivatives of Phenobarbital¹

BY MARY M. RISING, JOHN H. SHROYER AND JULIUS STIEGLITZ

In an effort to throw light upon the fundamental mechanism of the narcosis induced by hypnotics, an extensive program of research² has been undertaken at the instigation and under the direction of two of the authors. The end in view for the work discussed in the present paper has been the modification of the molecular structure of the synthetic hypnotic phenyl-ethylbarbituric acid, or phenobarbital, $(\text{C}_6\text{H}_5)(\text{C}_2\text{H}_5)\text{C}\text{---}\text{CONHCONHC}=\text{O}$, in such a way as to give it color. It is hoped that some dye derivatives of phenobarbital may be found in this way which retain in their molecules the pronounced hypnotic effect of phenobarbital. It has been reasoned that, should such products be obtained, their color may render them useful for a study of the action of hypnotics in the cells of the brain and nerves, where the chief action of such sedatives occurs. The problem is a complex one: to be of any use for the purpose named the dye derivatives of phenobarbital must be, first of all, hypnotics; further, they must possess the property of staining nerve tissues selectively, a behavior by no means universal among dyes.

It is obvious that the pursuance of our program to its logical conclusion will necessitate the coöperation of chemists with pharmacological and histological experts. The present paper discusses the first investigations undertaken, which have been largely chemical. The dyes so far prepared by us have been studied pharmacologically by Dr. A. L. Tatum, Professor of Pharmacology at the University of Wisconsin.

Probably the first use of dye derivatives of drugs as an aid to the study of the mechanism of drug action was made by Ehrlich and Einhorn,³ who

(1) The work here described forms part of the dissertation of John H. Shroyer, presented in partial fulfillment of requirements for the doctorate degree at the University of Chicago.

(2) The Julius Stieglitz Research Fund for Chemistry Applied to Medicine, made available by the Chemical Foundation, is supporting the main part of this work.

(3) Ehrlich and Einhorn, *Ber.*, **27**, 1872 (1894).