acetylenic carbinol had been added and 36 g. (0.5 mole) of ethyl methyl ketone was dropped in. The mixture was stirred for two hours longer and poured into a mixture of 90 ml. (1.1 moles) of concentrated hydrochloric acid and 200 g. of ice. After the magnesium hydroxide had dissolved, the layers were separated, the water layer extracted with ether. After drying the ether solution over anhydrous sodium sulfate, the solvent was removed by distillation. The residue was heated in an an oil-bath to 110° under 18 mm. of pressure to remove volatile material. The residue was recrystallized from petroleum ether (b. p. 30–60°). The product was deposited from the petroleum ether in white needles melting at 69–70° and weighed 57 g. (53% of the theoretical).

Anal. Calcd. for $C_{13}H_{22}O_2$: C, 74.29; H, 10.48. Found: C, 73.85, 73.71; H, 10.17, 10.24.

1-(3-Methyl-3-penten-1-ynyl)-2-methylcyclohexene.—Twenty-two and five-tenths grams of the glycol was dehydrated by heating with 6 g. of potassium bisulfate to 180° in an oil-bath for ten minutes. Water was removed by distillation at 18 mm. pressure. The 1-(3-methyl-3-penten-1-ynyl)-2-methylcyclohexene was distilled at 2 mm. pressure. The yield was 17 g. (90%) of a product boiling at 82–84° (2 mm.). Due to rapid absorption of oxygen by the dienyne, the analysis was low in both carbon and hydrogen, as is usually the case with closely related compounds.[2]

Anal. Calcd. for $C_{13}H_{18}$: C, 89.66; H, 10.34. Found: C, 87.45; H. 10.05.

2-Methyl-1,1′-dicyclohexanolacetylene.—To the Grignard solution prepared from 106 g. (4.4 moles) of magnesium and 490 g. (4.5 moles) of ethyl bromide in 1.5 liters of anhydrous ether was added 250 g. (2 moles) of 1-ethynylcyclohexanol.[2] The solution was stirred for one hour and 280 g. of 2-methylcyclohexanone added as rapidly as possible without loss of ether. The reaction mixture was allowed to stand overnight and poured over ice containing 400 ml. (4.9 moles) of concentrated hydrochloric acid. The product was extracted with ether and the ether solution dried over sodium sulfate. After the low-boiling material had been removed by heating the residue to 100° in an oil-bath and under a pressure of 18 mm., the residue was cooled. Part of the material crystallized on standing. This solid was recrystallized from petroleum ether (b. p. 30–60°) and melted at 94–95°.

Anal. Calcd. for $C_{15}H_{24}O_2$: C, 76.27; H, 10.17. Found: C, 76.13, 76.55; H, 10.26, 10.13.

The yield of the solid material was low (41% or less) and it apparently was one of the two possible stereoisomers. The glycol mixture underwent dehydration on heating and could not be distilled.

2-Methyl-1,1′-dicyclohexenylacetylene.—The crude 2-methyl-1,1′-dicyclohexanolacetylene from the previous preparation, including the crystals which had been removed, was refluxed for three hours with 500 g. of 40% sulfuric acid. The product was extracted with ether and the ether solution was washed free from acid with dilute sodium carbonate solution. The crude material was fractionated and the portion boiling at 115–117° (2 mm.) collected. The yield was 206 g. (51% of the theoretical based on the 1-ethynylcyclohexanol used); $n^{20}D$ 1.5452.

Anal. Calcd. for $C_{15}H_{20}$: C, 89.93; H, 10.07. Found: C, 89.61; H, 10.24.

(2) See Marvel, Mozingo and Kirkpatrick, THIS JOURNAL, **61**, 2003 (1939).

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RECEIVED MAY 1, 1940

COMMUNICATION TO THE EDITOR

VITAMIN K ACTIVITY OF CERTAIN NAPHTHOLS AND TETRALONES

Sir:

The observed high antihemorrhagic activity of the 5,8-dihydro and 2,3-oxido derivatives of vitamin K_1 and 2-methyl-1,4-naphthoquinone,[1] coupled with the opportunity for the reversion of these substances to the quinones by simple oxidation or reduction, suggests that the activity is not due to the functioning of the derivatives as such but is a manifestation of their biological transformation into the quinones, with somewhat varying efficiency. As a further test of this hypothesis we investigated 3-methyl-1-naphthol and 2-methyl-1-naphthol, for these naphthols are quite remote from the quinone–hydroquinone type but could yield methylnaphthohydroquinone by hydroxylation. When assayed in chicks by the eighteen-hour method, both substances showed remarkably high antihemorrhagic activity (response at a dosage of 1 γ). In striking contrast is the observation that 1-methyl-2-naphthol, 3-methyl-2-naphthol, and 4-methyl-1-naphthol are all inactive at 1000 γ; these isomers are not convertible into the potent 2-methyl-1,4-naphthoquinone. 2-Methyl-1-naphthylamine is active at

(1) Fieser, Tishler and Sampson, THIS JOURNAL, **62**, 996, 1628 (1940).

5 γ and may also function merely as a precursor of this quinone, and possibly further of a compound of the actual vitamin K type. Even β-methylnaphthalene gives some response at 1000 γ. To see if indications could be obtained of still more extensive biological transformations, we investigated 3-methyl-1-tetralone and 2-methyl-1-tetralone as possible precursors of the active methylnaphthols. Since the completion of our work, the synthesis of the former compound has been reported by Bachmann and Struve.[2] Both tetralones are highly active and comparable in potency with the corresponding dehydrogenation products. In view of our previous observation that hexahydro-vitamin K_1 shows evidence of only slight activity at 1000 γ, it would appear that dehydrogenation occurs less readily when four hydrogens must be removed than when the ring contains a double bond (5,8-dihydride, enolized tetralones).

The antihemorrhagic ethers and esters of methylnaphthohydroquinone may also function not as such but by virtue of a biological conversion to the quinone. While Ansbacher, Fernholz and Dolliver[3] consider this interpretation unlikely as applied to the dimethyl ether because of its probable resistance to hydrolysis, we may note that a second possible route is by direct oxidation. Thus the dimethyl ether can be oxidized smoothly to the quinone with chromic acid at 60°. With esters the oxidative route is clearly open[4] in addition to hydrolysis, and slight differences in activity may be occasioned by the absorbability factor. That hydrolysis probably plays an important part seems indicated by the observation that the highly hindered dimesitoyl derivative of methylnaphthohydroquinone (m. p. 204–205°, found: C, 80.11; H, 6.70) is only about $^1/_{200}$ as active as the corresponding dibenzoate.

Fernholz, MacPhillamy and Ansbacher[5] have recently cited certain apparent discrepancies between their assay results and ours. In our opinion these comments lack validity because they take no account of the possible variations arising from the use of different time periods in the assay procedures.[6] We must emphasize the opening statement in the first of our Communications and point out that, in making preliminary and partial reports of some of our data, we wish to reserve for mature consideration at the completion of our studies all decisions as to exact relative potencies as well as final correlation and comparison of assay data.

(2) Bachmann and Struve, THIS JOURNAL, **62**, 1618 (1940).
(3) Ansbacher, Fernholz and Dolliver, *ibid.*, **62**, 155 (1940).
(4) Doisy, *et al.*, *J. Biol. Chem.*, **131**, 363 (1939).
(5) Fernholz, MacPhillamy and Ansbacher, THIS JOURNAL, **62**, 1619 (1940).
(6) Ansbacher, Fernholz and MacPhillamy, *Proc. Soc. Exptl. Biol. Med.*, **42**, 655 (1939).

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RECEIVED JUNE 20, 1940

NEW BOOKS

Physical Organic Chemistry. By LOUIS P. HAMMETT, Columbia University. McGraw-Hill Book Co., Inc., 330 West 42d St., New York, N. Y., 1940. x + 404 pp. 14.5 × 21 cm. Price, $4.00.

Courses in physical organic chemistry are now offered in an increasing number of chemistry departments. Of the very few books in the field, this one is the first which can be unqualifiedly recommended as a text for a course dealing with the mechanisms of organic reactions. As a physical chemist whose researches on rates, equilibria, and mechanisms of reactions in solution have been of basic importance to theoretical organic chemistry, Professor Hammett is uniquely qualified to write this book. In the preface he credits his original interest in organic chemistry to "three great teachers, E. P. Kohler, H. Staudinger, and J. M. Nelson." How actively that interest has been maintained is shown by the fact that most of the material of this compact book has come into existence since the author last sat under his organic teachers.

Two chapters on structural theory serve as an introduction to the concepts which are important in the later treatment. There is a brief non-technical review of the experimental basis of the wave-mechanical treatment of valence and of the idea of resonance. This will be welcome to those organic chemists who, through no fault of their own, have come to regard this line of thought as a revealed