troleum ether and the solution chromatographed[10] on a column (12 mm. × 300 mm.) packed with Fisher Alumina (80–200 mesh) using 30–60° petroleum ether as the eluent. On evaporation of the solvent from the percolate the hydrocarbon was obtained as a slightly yellow strongly fluorescent oil which was crystallized from a mixture of ethanol ether and water.[11] The crystals which formed were colorless prisms, m.p. 116–117°.

The other hydrocarbons except for the 2,6-isomer, were prepared in a similar way.

10-(3′,4′-Dimethylphenyl)-1,2-benzanthracene (IV, 3′,4′-Dimethyl).—A mixture of 2 g. of the ketone, 15 ml. of 48% hydrobromic acid and 30 ml. of glacial acetic acid was sealed in a Carius tube and heated in a Carius furnace for 6 hours at 180°. The whole was extracted with benzene, washed in water and dried over calcium chloride. The benzene then was replaced with a solution of ethanol containing a small amount of acetone. When this was seeded with a few crystals of the hydrocarbon (obtained from cyclizing the ketimine hydrochloride as described above) there was obtained a first crop of crystals weighing 1.3 g. and a second crop of 0.2 g.; total yield 1.5 g. (79%), m.p. 122–126°.

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[10] Since the hydrocarbons are sensitive toward light, the chromatography is best performed in the absence of strong light. The progress of the hydrocarbon down the column is observed easily by illuminating the column with ultraviolet light from time to time.

[11] The oil was dissolved in a minimum volume of boiling ether, twice this volume of ethanol was added and the solution brought to a boil again. Water was then added dropwise until the turbidity which immediately formed just disappeared.

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Reversible Dimerization of 2,6-Dibenzylidenecyclohexanone

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In the course of a study of the aromatization of 2,6-dibenzylidenecyclohexanone (I), to be published later, colorless fiber-like crystals (hereafter called "2,6-dibenzylidenecyclohexanone dimer") were obtained, having a molecular weight twice that of 2,6-dibenzylidenecyclohexanone. This compound reverted to 2,6-dibenzylidenecyclohexanone when its ethanolic solution was refluxed.

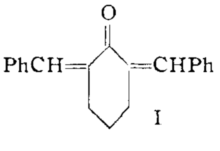
As far as we know, the dimerization of ketones containing a Ph—C═C—CO—C═C—Ph system has been studied only starting from dibenzylideneacetone,[1] and the structure of a dimer has been reported as (II).[1b]

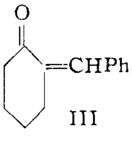
2,6-Dibenzylidenecyclohexanone dimer gave a dioxime and, furthermore, a tetrahydro derivative upon catalytic hydrogenation. When 2,6-dibenzylidenecyclohexanone was oxidized with permanganate, benzoic and glutaric acids (the latter isolated in the form of its diphenacyl ester) were obtained. In contrast, a similar treatment of the dimer did not yield either of the two acids mentioned. This shows the absence of the PhCH═ group in the dimer. The location of the spectral maximum of the dimer (ϵ 42,500 at 293 mμ, in ethanol) is very close to that of 2-benzylidenecyclohexanone (III) (ϵ 11,200 at 290 mμ, in ethanol)[2] and differs from that of 2,6-dibenzylidenecyclohexanone (I) (ϵ 25,100 at 330 mμ, in ethanol),[2] and from that of *cis*- or *trans*-stilbene.[3]

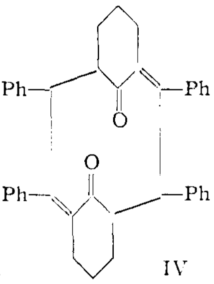
On the basis of the above observations we believe that the dimer (colorless) contains two —CO—C═C groups which are not conjugated with each other, in contrast to the structure of the yellow 2,6-dibenzylidenecyclohexanone (I).

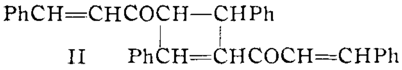
The strong bands (1695, 1608, 754 and 697 cm.$^{-1}$) in the infrared spectrum of the dimer (in carbon disulfide) also show the presence of α,β- (or $\alpha,\beta,\gamma,\delta$)-unsaturated carbonyl group and monosubstituted phenyl group.[4]

A possible structure for the dimer that satisfies all experimental findings is IV, *i.e.*, 2,3,9,10-tetraphenyltricyclo-(9,3,1,1^{4,8})-15,16-diketohexadeca-1,8-diene.


I


III


IV


II

$$\begin{array}{l} \text{PhCH=CHCOCH—CHPh} \\ \qquad\qquad\quad | \qquad\quad | \\ \text{PhCH=CHCOCH=CHPh} \end{array}$$

According to Fawcett,[5] bicyclo(x,y,z)alkene structures containing a double bond at a "bridgehead" are strainless when $x + y + z = 11$ which is the case in IV.

Experimental

2,6-Dibenzylidenecyclohexanone Dimer (IV).—An ethanol (400 ml.) solution of 2,6-dibenzylidenecyclohexanone (10 g.) was refluxed for 120 hours. After cooling the crystals thus obtained were recrystallized from ethanol; colorless fiber-like crystals, m.p. 187–188° (cor.); yield 9 g., 90%.

Anal. Calcd. for $C_{40}H_{36}O_2$: C, 87.56; H, 6.61; mol. wt., 549. Found: C, 87.15; H, 6.52; mol. wt., 545 (cryoscopically in benzene).

Dioxime.—A solution of the dimer (0.55 g.) and hydroxylamine hydrochloride (0.28 g.) in 100 ml. of ethanol was refluxed for 24 hours, then concentrated to half its volume and diluted with 600 ml. of 0.5% sodium carbonate. The precipitate was recrystallized from ethanol; colorless needles, m.p. 197–198°, yield 0.08 g.

Anal. Calcd. for $C_{40}H_{38}N_2O_2$: C, 83.01; H, 6.62. Found: C, 82.65; H, 6.34.

Tetrahydro Derivative of the Dimer.—A solution of 0.55 g. of the dimer in 300 ml. of ethanol absorbed, in the presence of 0.02 g. of Adams platinum oxide, 43.2 ml. of hydrogen (0°, 760 mm., corrected). Calcd. for 2 double bonds 44.8 ml. The filtrate was concentrated to about 50 ml. and the crystals thus obtained recrystallized from ethanol; colorless needles; m.p. 217–218°; yield, 0.44 g.

Anal. Calcd. for $C_{40}H_{40}O_2$: C, 86.93; H, 7.30. Found: C, 86.73; H, 7.21.

Oxidation of 2,6-Dibenzylidenecyclohexanone (I) with Permanganate.—To a solution of 3 g. of I in 60 ml. of chloroform a solution of 9 g. of potassium permanganate in 500 ml. of water was added dropwise at 5° with mechanical stirring. After 4 hours the manganese dioxide was filtered off and extracted with boiling water; this extract was com-

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[1] (a) G. Ciamician and P. Silber, *Ber.*, **42**, 1388 (1909); (b) P. Praetorius and F. Korn, *ibid.*, **43**, 2744 (1910).

[2] H. S. French and L. Wiley, THIS JOURNAL, **71**, 3702 (1949).

[3] R. A. Friedel and M. Orchin, "Ultraviolet Spectra of Aromatic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1951, Figs. 125 and 126; R. N. Beale and E. M. F. Roe, *J. Chem. Soc.*, 2755 (1953).

[4] F. A. Miller, in H. Gilman, "Organic Chemistry," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1953, p. 172.

[5] F. S. Fawcett, *Chem. Revs.*, **47**, 219 (1950).

bined with the filtrate. The solution was made alkaline, evaporated *in vacuo* to about 25 ml., and acidified. The precipitate thus obtained was recrystallized from water; colorless prisms, 0.8 g., m.p. and mixed m.p. with benzoic acid, 121–122°.

Anal. Calcd. for $C_7H_6O_2$: C, 84.07; H, 6.05. Found: C, 83.88; H, 6.25.

The filtrate was made alkaline, evaporated to half its volume, neutralized with 10% sodium hydroxide, then acidified with one drop of dilute hydrochloric acid. To this solution 1 g. of phenacyl bromide and 10 ml. of ethanol were added. After refluxing for two hours, the product was recrystallized from ethanol; colorless needles, 0.4 g., m.p. and mixed m.p. with an authentic sample of diphenacyl glutarate, 103–104°.

Anal. Calcd. for $C_{21}H_{20}O_6$: C, 68.47; H, 5.47. Found: C, 68.95; H, 5.24.

Oxidation of the Dimer with Permanganate.—To a solution of 3 g. of the substance in 40 ml. of chloroform a few drops of a solution of 9 g. of potassium permanganate in 400 ml. of water was added at room temperature under mechanical stirring. The purple color did not fade after 4 hours. Upon the addition of 20 ml. of 10% sulfuric acid, however, the color was bleached out within a few minutes. The permanganate solution (400 ml.) was then added (100 ml. each 30 min.). The manganese dioxide was filtered off. The product when treated as described above did not yield either benzoic acid or a phenacyl ester. The chloroform phase was evaporated to dryness and recrystallized from ethanol. Unoxidized dimer (1 g.) was recovered which was identified by its m.p. and ultraviolet spectrum.

Interconversion of the Dimer and 2,6-Dibenzylidenecyclohexanone.—When an ethanol or benzene solution of either 2,6-dibenzylidenecyclohexanone or its dimer was refluxed for 24 hours, a mixture of the compounds resulted. When a preparation obtained from the dimer was recrystallized from ethanol, first colorless and then yellow crystals separated out. The latter showed m.p. and mixed m.p. (with 2,6-dibenzylidenecyclohexanone), 117–118°; yield 5%.

Anal. Calcd. for $C_{20}H_{18}O$: C, 87.56; H, 6.61. Found: C, 87.35; H, 6.59.

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COMMUNICATIONS TO THE EDITOR

THE SYNTHESIS OF GUANOSINE-5'-PHOSPHATE USING A NEW METHOD OF PHOSPHORYLATION

Sir:

The isolation of guanosine-5'-mono-, di- and triphosphates, from both yeast and animal tissues,[1] recently has been reported from different laboratories and the biochemical importance of these compounds has been established.[2] However, these new nucleotides remain highly inaccessible and efficient chemical syntheses of these important substances are being attempted in this laboratory. Despite the efforts of earlier workers,[3] using several methods of phosphorylation, no satisfactory synthesis of guanosine-5'-monophosphate (GMP), the key substance in the projected synthesis of the higher phosphates, has emerged. Michelson and Todd[3b] have reported a 20% yield of GMP by the phosphorylation of 2',3'-isopropylidene guanosine (IV) with phosphorus oxychloride in a mixture of pyridine and dimethylformamide. In our hands, however, the yield of GMP by this method was even lower and extensive paper and ion exchange chromatography demonstrated the concomitant formation of hitherto unidentified phosphorus-containing products. We now wish to record the preparation of GMP in excellent yield by the use of a new method of phosphorylation.

Invariably side products were formed when pyridine was present in the phosphorylation mixtures. This fact led us to conclude that the solution of the problem lay in the use of a powerful, monofunctional reagent which would not require basic catalysis for the phosphorylation of the 5'-hydroxyl group in IV. Tetra-*p*-nitrophenyl pyrophosphate[4,5] (III), prepared *in situ* by the reaction of di-*p*-tolyl carbodiimide (II) with two equivalents of di-*p*-nitrophenyl phosphate (I) in dioxane, has been found to satisfy these requirements. This reagent[5] was allowed to react with (IV) in the presence of one equivalent of the free acid (I) and after a reaction period of 15 hours at 20°, 2',3'-isopropylidene guanosine-5'-di-*p*-nitrophenyl phosphate (V) was isolated in nearly quantitative yield as an amorphous powder. After crystallization from acetonitrile, the product showed a transition point at 161–163° and dec. 264°. *Anal.* Calcd. for $C_{25}H_{24}N_7O_{12}P \cdot 1H_2O$: C, 45.28; H, 3.95; N, 14.80; P, 4.67. Found: C, 44.95; H, 3.99; N, 15.00; P, 4.80.

The neutral ester (V) was suspended in 50% aqueous acetonitrile and converted to 2',3'-isopropylidene guanosine-5'-*p*-nitrophenyl hydrogen phosphate (VI) under mildly alkaline conditions.[6] A solution of (VI) in *tris*-hydroxymethyl amino-

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(1) Selected references are: H. Schmitz, R. B. Hurlbert and V. R. Potter, *J. Biol. Chem.*, **209**, 11 (1954); H. Schmitz, *Naturwiss*, **5**, 120 (1954); *Biochem. Z.*, **325**, 555 (1954); R. Bergkvist and A. Deutsch, *Acta. Chem. Scand.*, **8**, 1889 (1954).

(2) P. Ayengar, D. M. Gibson and D. R. Sanadi, *Biochem. Biophys. Acta*, **13**, 309 (1954); D. R. Sanadi, D. M. Gibson and P. Ayengar, *ibid.*, **14**, 434 (1954).

(3) (a) J. M. Gulland and G. I. Hobday, *J. Chem. Soc.*, 746 (1940); H. Bredereck and E. Berger, *Ber.*, **73**, 1124 (1940); (b) A. M. Michelson and A. R. Todd, *J. Chem. Soc.*, 2476 (1949).

(4) H. G. Khorana and A. R. Todd, *ibid.*, 2257 (1953).

(5) A detailed study of this and related pyrophosphates as chemical phosphorylating agents will be reported (J. G. Moffatt and H. G. Khorana, forthcoming publication).

(6) The *p*-nitrophenol liberated was estimated spectrophotometrically at 440 mμ.