mended for α-acylation[3]) the resultant keto acid was cyclized to 1,2-benz-9,10-anthraquionone by the procedure of Badger and Cook.[4] The desired hydrocarbon was obtained by the method of Sandin and Fieser,[5] who after condensing the quinone with the Grignard reagent of methyl iodide, conducted a two-step reduction with hydrogen iodide followed by stannous chloride. The over-all yield of 9,10-dimethyl-1,2-benzanthracene-9,10-C^{14} (2.77 millicuries per millimole) from barium carbonate was 18%.[6]

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(6) The experimental details of this synthesis have been deposited as Document number 4392 with the ADI Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington 25, D. C. A copy may be secured by citing the Document number and by remitting in advance $1.25 for photoprints, or $1.25 for 35 mm. microfilm by check or money order payable to Chief, Photoduplication Service, Library of Congress.

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Synthesis of Centrally Labeled (15,15′)-β-Carotene

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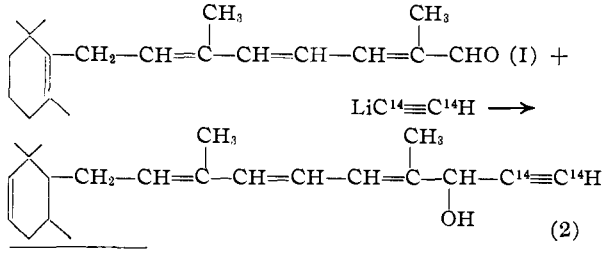
The synthesis of β-carotene with centrally-labeled carbons 15 and 15′ may be accomplished by use of radioactive acetylene in the reaction, expressed schematically[2]

$$C_{19} + C^{14}{}_2 + C_{19} \longrightarrow C_{19}\text{–}C_2{}^{14}\text{–}C_{19} \qquad (1)$$

Grignard acetylene is normally prepared with a large excess of the gas, reacting for a considerable period. It is formed slowly, and the reaction is incomplete when the acetylene is limiting, and since dilution of C^{14}-acetylene with inert gas must be kept at a minimum, it has been necessary to modify the procedure,[3a] and the acetylene is first partially condensed with β-C_{19}-aldehyde[3b] and the β-C_{21}-acetylenecarbinol, (compound II) is obtained, then coupled, in a second reaction with additional C_{19}-compound to form the C_{40}-yn-diol. Lithium acetylide is formed readily, the reaction proceeds quantitatively in liquid ammonia, and no large excess of acetylene is required. The over-all scheme, equation 1, may be represented by steps 2–6



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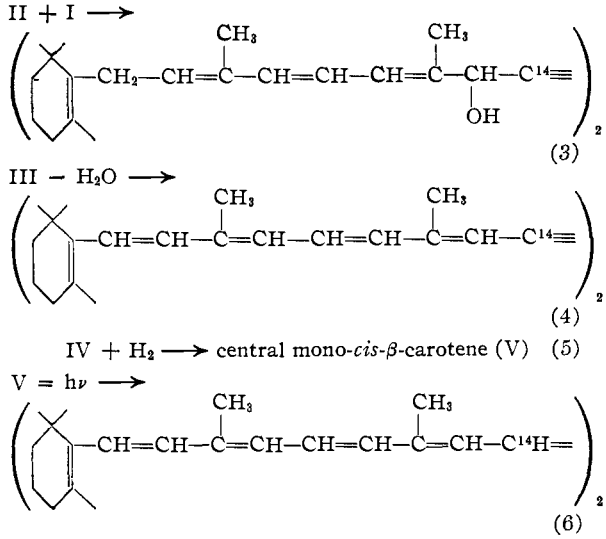
(2) H. H. Inhoffen, F. Bohlmann, G. Rummert and H. Pommer, *Ann.*, **570**, 54 (1950).
(3) (a) H. H. Inhoffen, U. Schwieter and G. Raspé, *ibid.*, **588**, 117 (1954); (b) H. H. Inhoffen and G. Leibner, *ibid.*, **575**, 105 (1951).



IV + H_2 ⟶ central mono-*cis*-β-carotene (V) (5)

The condensation of II with a second mole of I proceeds smoothly to form the 15,15′-yn-diol III. The removal of water to yield IV, a dehydrocarotene $C_{40}H_{54}$ and subsequent selective partial hydrogenation of the central triple bond gives rise experimentally only to central mono-*cis*-β-carotene.[4] This is then irradiated for a suitable length of time. The course of the reaction is followed spectrophotometrically, to determine maximum yield of β-carotene. This is then isolated chromatographically and crystallized.

Experimental[5,6]

Acetylene.—The yield of acetylene from the original $BaC^{14}O_3$ was 94 to 96% of theoretical, achieved by placing 100 mg. of carbonate between layers of finely ground barium metal. The subsequently evolved acetylene was condensed as a solid at the temperature of liquid nitrogen. Inactive acetylene completes the reaction with lithium ammonia.

β-C_{21}-Acetylenecarbinol.—The acetylene is in excess of the theoretical amount to couple with the C_{19}-aldehyde. As the reaction progresses, some acetylene is released from the mixture. It is trapped as silver acetylide and recycled to conserve activity. The removal of the lithium from the lithium acetylide addition compound with the C_{19}-aldehyde, to form the C_{21}-acetylenecarbinol is presumably a hydrolysis. The ammonium chloride used to effect the removal of the lithium was dried under vacuum at 80° as the presence of water is detrimental, and acetylene will be released.

Irradiation.—Formation of the all-*trans*-β-carotene from the central mono-*cis* isomer was followed spectrophotometrically, by noting the ratio of the maximum at 450 mμ to that of the *cis* peak at 338 mμ. The reaction is stopped when the ratio is *ca.* 10:1. The ratio will continue to rise for a while on prolonging the irradiation, but the absolute value at 450 mμ begins to fall. This must be avoided. The solution is then concentrated under vacuum and chromatographed. The all-*trans*-β-carotene is adsorbed above the residual mono-*cis* isomer and also above any dehydrocarotene that may be present. The all-*trans* isomer is crystallized and the other two components recycled.

(4) H. H. Inhoffen, F. Bohlmann and G. Rummert, *ibid.*, **571**, 75 (1950).
(5) We are particularly indebted to Dr. B. M. Tolbert and Dr. Richard M. Lemmon of the Donner Laboratory for advice and use of facilities.
(6) Complete details of the experimental work reported in this paper have been deposited as Document number 4410 with the ADI Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington 25, D. C. A copy may be secured by citing the Document number and by remitting in advance $1.25 for photoprints, or $1.25 for 35 mm. microfilm payable to: Chief, Photoduplication Service, Library of Congress.

Total Yield of all-*trans*-β-Carotene.—One hundred mg., recrystallized; this represents a 10% yield, based on C_{19}-aldehyde; specific activity, 1 μc. per mg., which is a 1.2% yield, based on activity.

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Halomethylquinolines[1]

BY C. E. KASLOW AND JAMES M. SCHLATTER

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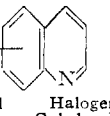
Several of the halomethylquinolines have been reported, particularly those with the $-CH_2X$ group attached to the pyridine portion of quinoline molecule. 2-Bromomethylquinoline[2] has been prepared by the reduction of 2-tribromomethylquinoline with stannous bromide in hydrobromic acid. It has been obtained also by the action of N-bromosuccinimide upon quinaldine.[3] 8-Bromomethylquinoline[4] was produced, with other materials, when 8-methylquinoline hydrobromide perbromide was heated to 150°. The corresponding 8-chloromethyl[4] compound was obtained by the action of hydrochloric acid upon 8-bromomethylquinoline. Campbell[5] has prepared 4-bromomethylquinoline by the bromination of lepidine with N-bromosuccinimide. Both 3- and 4-bromomethylquinoline have been obtained by the action of phosphorus tribromide upon the corresponding quinolinemethanol.[2]

It was of interest to study the remaining chloro- and bromomethylquinolines. These were prepared from the corresponding quinolinemethanols which were obtained, in turn, by a method[6] reported previously. Experimental conditions were worked out using 6-quinolinemethanol. The phosphorus tribromide method was not usable in the preparation of 6-bromomethylquinoline. About a 60% yield could be obtained when 6-quinolinemethanol was warmed with excess 48% hydrobromic acid at 70–80°. However, the best method consisted of treating a glacial acetic acid solution of the quinolinemethanol with gaseous hydrogen bromide then precipitation of the hydrobromide by dilution of the solution with absolute ether. The base is obtained by careful neutralization of an aqueous solution of the hydrobromide with dilute alkali. The best method for obtaining the chloromethylquinoline is the one described recently by Mosher.[7]

The bromomethylquinolines are much more reactive and difficult to handle than the chloromethylquinolines. Although this high reactivity has been reported by previous workers,[2–5] Johnson and Hamilton[8] have found that 4-bromomethylcarbostyril[9] and 4-(α-chloroethyl)-quinoline resisted attempts at hydrolysis. The bromomethylquinolines could not be recrystallized without a great loss except by dissolving them in a hydrocarbon solvent at room temperature and cooling the solution to a sub-zero temperature. The higher melting points of the bromomethylquinolines could be obtained only by insertion of the capillary tube into the bath at a temperature just below that determined by previous trials. In the case of both the chloro and bromo compounds, continued heating would cause solidification in the capillary tube, due, presumably, to the formation of the quaternary compounds of poly-N-methylenequinolinium halides.

The substances summarized in Table I were prepared from the corresponding quinolinemethanols by the same methods as are described in the Experimental part for 6-bromomethyl- and 6-chloromethylquinoline. Since 8-chloromethylquinoline has been prepared previously only by halogen exchange from 8-bromomethylquinoline, its formation from 8-quinolinemethanol was included. Howitz and Nother[4] reported a melting point of 56° for 8-chloromethylquinoline.

TABLE I

HALOMETHYLQUINOLINES XCH_2– 

Substituent	Yield, %	M.p., °C.	Empirical formula	Halogen, % Calcd.	Halogen, % Found
5-CH_2Cl	67	88–89.5	$C_{10}H_8ClN$	19.96	19.99
5-CH_2Br	64	75.5–76.5	$C_{10}H_8BrN$	35.98	35.48
7-CH_2Cl	76	53–54	$C_{10}H_8ClN$	19.96	20.48
8-CH_2Cl	70	53.5–54.5[a]	$C_{10}H_8ClN$	19.96	20.06
7-CH_2Br	36	69.5–70.5	$C_{10}H_8BrN$	35.98	35.35
3-CH_2Cl	63	33–34	$C_{10}H_8ClN$	19.96	19.87
4-Cl-3-CH_2Cl	74	121–122	$C_{10}H_7Cl_2N$	33.34	33.57

[a] Melting point reported by ref. 4 is 56°.

Experimental[10]

6-Quinolinemethanol.—This substance was prepared from methyl 6-quinolinecarboxylate by reduction with lithium aluminum hydride according to published procedure.[6]

The hydrobromide was prepared by the action of hydrogen bromide upon a benzene solution of 6-quinolinemethanol and was recrystallized from absolute ethyl alcohol; m.p. 199° dec.

Anal. Calcd. for $C_{10}H_{10}BrNO$: Br, 33.29. Found: Br, 33.29.

The methiodide was prepared by the action of 0.5 g. of methyl iodide upon 0.5 g. of 6-quinolinemethanol dissolved in 5 ml. of absolute ether. The pale yellow solid was recrystallized from absolute ethyl alcohol; m.p. 168.5° dec.

Anal. Calcd. for $C_{11}H_{12}INO$: I, 42.13. Found: I, 42.59.

6-Chloromethylquinoline.—6-Quinolinemethanol (2.5 g., 0.016 mole) was dissolved in 75 ml. of dry benzene and the solution was saturated with hydrogen chloride. The precipitated hydrochloride was removed by filtration, dried and treated with 7.5 ml. of purified thionyl chloride contained in a 200-ml. round-bottomed flask. After the initial reaction had subsided, the solution was refluxed for one hour, then cooled and 125 ml. of dry benzene was added. After the white solid was collected and dried, it was dissolved in 25 ml. of ice-water and neutralized with 1 *N* sodium hy-

(1) Taken mainly from a thesis submitted by J. M. S. to the Faculty of the Graduate School, Indiana University, in partial fulfillment of the requirements for the M. A. degree, February, 1954.

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(10) Microanalyses were performed by Miss Joanna Dickey of this Laboratory.