Improvements in the Preparation of [9-^{14}C]*Fluorene and* [9-^{14}C]*Phenanthrene.*

By A. S. Harris, E. N. White, and D. McNeil.

[Reprint Order No. 6304.]

Improved syntheses of fluorene and phenanthrene labelled with ^{14}C give overall yields of 86% and 82% respectively. Clemmensen reduction of fluorenone yields fluoren-9-ol, fluorene, di-9-fluorenyl, bisdiphenylene-ethylene (di-9-fluorenylidene), and 9-diphenylene-9 : 10-dihydro-10-oxophenanthrene under various conditions.

Isotopic dilution offers the most attractive and in some cases the only possible method for the determination of individual components in a complex mixture such as coal tar. Before this technique can be used methods for the synthesis of the labelled component, preferably in high yield, must be established. Such syntheses for labelled fluorene and Phenanthrene are described.

[9-^{14}C]Fluorene has been prepared by Ray and Geiser (*Cancer Res.*, 1950, **10**, 616) who treated 2-diphenylylmagnesium iodide with [^{14}C]carbon dioxide and cyclised the product to [9-^{14}C]fluorenone. The ketone was reduced by Clemmensen's method, labelled fluorene being obtained in an overall yield of 37%. This synthesis has now been improved to give 86% yield.

Carboxylation of the Grignard reagent in a vacuum manifold gave consistently over 90% yields when the reaction was carried out in ether but not in ether–benzene. Fluorenone was best reduced by the Wolff–Kishner method without an alkaline catalyst which promotes the formation of di-9-fluorenyl. Although experiments in sealed tubes gave almost quantitative yields of the pure hydrocarbon, reduction in a high-boiling solvent was preferred where radioactive materials were involved. Mono-, di-, and tri-ethylene glycols were used, the first giving the best yields.

In the Clemmensen reduction of fluorenone with 7% hydrochloric acid and a short reaction time the main product was fluoren-9-ol, which on further reduction gave fluorene. This is interesting because reduction of ketones by this method does not normally proceed by way of the corresponding alcohols (Martin, " Organic Reactions," Chapman and Hall, London, 1942, Vol. I, p. 156). Longer reduction of fluorenone yielded fluorene (approx. 80%) and di-9-fluorenyl (approx. 20%), in agreement with Ritchie's result (*J. Proc. Roy. Soc. N.S.W.*, 1946, **80**, 33). Bradlow and VanderWerf (*J. Amer. Chem. Soc.*, 1947, **69**, 1254), however, who used 25% acid and a smaller proportion of zinc, obtained mixtures of fluorene and low-melting 9-diphenylene-9 : 10-dihydro-10-oxophenanthrene. Repetition of their work showed that, in addition to these compounds, smaller quantities of di-9-fluorenyl and bisdiphenylene-ethylene were also formed. In view of these results it appears that fluorenone is initially converted into the 9-hydroxyfluorenyl radical which either is reduced directly or by way of fluoren-9-ol to fluorene or dimerises to form 9 : 9′-dihydroxydi-9-fluorenyl (fluorenopinacol). According to the acid concentration this is then reduced to di-9-fluorenyl or rearranges to the pinacolin, 9-diphenylene-9 : 10-dihydro-10-oxophenanthrene, reactions which were shown to occur on Clemmensen reduction of the pinacol.

[9-^{14}C]Phenanthrene has been prepared in 58% yield starting from [^{14}C]carbon dioxide and 9-fluorenyl sodium (Collins, *J. Amer. Chem. Soc.*, 1948, **70**, 2418; Calvin, " Isotopic Carbon," Chapman and Hall, London, 1949, p. 234). This yield has been increased to 82%, mainly by improvements in the preparation of fluorene-9-[^{14}C]carboxylic acid. Consistently, about 95% yields of the acid were obtained by using 9-fluorenyl-lithium instead of the sodium derivative. In addition the fluorenyl-lithium was more conveniently prepared, being obtained by treatment of fluorene with phenyl-lithium in ether. This rapid and quantitative reaction was preferred to Tucker and Whalley's use (*J.*, 1949, 50) of *n*-butyl-lithium in light petroleum. The acid was then converted into labelled phenanthrene in a similar way to that described by Calvin (*op. cit.*).

EXPERIMENTAL

Diphenyl-2-[^{14}C]carboxylic Acid.—The carboxylation was carried out in a manifold similar to that described by Cox, Turner, and Warne (*J.*, 1950, 3167), which was initially evacuated to a pressure of a few microns. 2-Diphenylylmagnesium iodide (from 7 g. of 2-iododiphenyl) in ether (30 c.c.) at $-60°$ was vigorously stirred and treated with carbon dioxide from concentrated sulphuric acid and barium [^{14}C]carbonate (0·245 g.; 0·987 mc). When absorption was complete, the Grignard reagent was allowed to react with carbon dioxide from inactive barium carbonate (3·70 g.). After the initial rapid absorption, the residual gas was transferred to the reaction vessel by liquid nitrogen and stirring was continued for several hours. The acid was isolated in the usual way as a white solid (3·72 g., 94% yield from total barium carbonate), m. p. 103—105°.

[9-^{14}C]Fluorenone.—The above acid (3·72 g.) and concentrated sulphuric acid (10 c.c.) were heated at 80° (20 min.) and the product was poured on ice. The mixture was made slightly alkaline with sodium hydroxide solution and extracted with ether, and the extract was washed with water, dried, and evaporated, to give the yellow ketone (3·21 g., 95% yield), m. p. 79—80°.

[9-^{14}C]Fluorene.—[9-^{14}C]Fluorenone (3·21 g.), 90% hydrazine hydrate (8 c.c.), and ethylene glycol (80 c.c.) were refluxed for 5 hr. The fluorene, most of which had sublimed into the condenser, was extracted with ether, and the solution was washed with dilute hydrochloric acid and water, dried, and evaporated, to give the labelled hydrocarbon (2·87 g., 97%), m. p. 112—114°; activity 50·5 mc/mole. This represents an overall radioactive " yield " of 88·5% on the active $BaCO_3$ used.

Clemmensen Reduction of Fluorenone.—(*a*) Fluorenone (2·56 g.) in ethanol (40 c.c.) was added in portions during ½ hr. to amalgamated zinc (45 g.) in boiling concentrated hydrochloric acid (13 c.c.) and water (5 c.c.). The yellow colour of the ketone rapidly disappeared and the mixture was refluxed for a further hour and then poured into water (200 c.c.). Ether-extraction gave a white solid (2·45 g.) which was chromatographed on alumina. Elution with light petroleum (b. p. 60—80°) yielded fluorene (0·7 g.), and benzene eluted crude fluoren-9-ol (1·7 g.) which from benzene–light petroleum formed prisms, m. p. and mixed m. p. 144—145°.

(*b*) Fluorenone (3 g.) in ethanol (75 c.c.) was added during 1 hr. to amalgamated zinc (75 g.) in boiling concentrated hydrochloric acid (21 c.c.) and water (9 c.c.), additional portions of acid (2·5 c.c.) being added after 2 hr. and 5 hr. Extraction with benzene gave a mixture (2·8 g.) which when chromatographed on alumina yielded fluorene (2·05 g.), m. p. 114—115°, followed by di-9-fluorenyl (0·5 g.), needles (from propan-1-ol), m. p. 245—246°.

(*c*) Fluorenone (4·5 g.), amalgamated zinc (10 g.), ethanol (10 c.c.), and concentrated hydrochloric acid (25 c.c.) were refluxed for 24 hr., additional acid (5 c.c.) being added after 16 hr. Benzene extracted an orange solid (3·9 g.) which when separated on alumina gave successively, fluorene (0·4 g.), m. p. and mixed m. p. 113—114°, bisdiphenylene-ethylene (0·3 g.), m. p. and mixed m. p. 191—192°, di-9-fluorenyl (0·9 g.), m. p. and mixed m. p. 245—246°, and 9-diphenylene-9 : 10-dihydro-10-oxophenanthrene (1·6 g.), m. p. 259—260°.

Clemmensen Reduction of Fluoren-9-ol.—Fluorenol (1 g.), amalgamated zinc (18 g.), concentrated hydrochloric acid (7 c.c.), ethanol (15 c.c.), and water (3 c.c.) were refluxed for 7 hr. Ether extraction afforded a white solid (0·82 g.) from which fluorene (0·55 g.), m. p. and mixed m. p. 113—114°, was obtained by chromatography, the remaining fractions being sticky solids.

Clemmensen Reduction of 9 : 9′-Dihydroxydi-9-fluorenyl.—(*a*) The dihydroxy-compound (3 g.), amalgamated zinc (13 g.), concentrated hydrochloric acid (33 g.), and ethanol (13 c.c.) were refluxed for 24 hr. Evaporation of the benzene extract of the product yielded *9-diphenylene-9 : 10-dihydro-10-oxophenanthrene* (2·6 g.), m. p. 255—257°, which recrystallised from chloroform–light petroleum as prisms, m. p. 261—262° (Found : C, 90·5; H, 4·7. $C_{26}H_{16}O$ requires C, 90·7; H, 4·7%). The infrared spectrum and m. p. and mixed m. p. were identical with those of a specimen prepared by Gomberg and Bachmann's method (*J. Amer. Chem. Soc.*, 1927, **49**, 253). Chromatography of the crystallisation residues yielded di-9-fluorenyl (0·1 g.).

(*b*) The dihydroxy-compound (3 g.), amalgamated zinc (35 g.), concentrated hydrochloric acid (10 c.c.), ethanol (40 c.c.), and water (4·5 c.c.) were refluxed for 8 hr., additional acid being added after 3 hr. and 6 hr. Extraction of the product with benzene gave a sticky solid (2·75 g.) which was chromatographed on alumina. Crystallisation of the fractions yielded di-9-fluorenyl

(1·3 g.), m. p. and mixed m. p. 245—246°, and 9-diphenylene-9 : 10-dihydro-10-oxophenanthrene (0·2 g.), m. p. 256—257°, mixed m. p. 258—259°.

Fluorene-9-[^{14}C]*carboxylic Acid.*—Phenyl-lithium, prepared from bromobenzene (8 g.) and lithium (0·8 g.) (Wittig, " Newer Methods of Preparative Organic Chemistry," Interscience, London, 1948, p. 576), in dry ether (50 c.c.), was added under nitrogen to fluorene (8·4 g.) in a flask attached to a vacuum manifold which was subsequently evacuated to a pressure of a few microns. The reaction was carried out at −60° in two stages, carbon dioxide being generated first from barium [^{14}C]carbonate (0·244 g., 0·984 mc) and then from inactive barium carbonate (3·71 g.). The gas was readily absorbed by the well-stirred orange mixture which became gradually paler. After the mixture had been stirred for several hours to ensure complete reaction, it was acidified with 2N-sulphuric acid. The ether-soluble material was washed with sodium carbonate solution, acidification of which gave the acid (4·01 g., 95% yield from total barium carbonate), m. p. 228—229°.

[9-^{14}C]*Phenanthrene.*—The above acid (4·01 g.) was converted into [9-^{14}C]phenanthrene as described by Calvin (*op. cit.*, p. 234), except that the intermediate 9-hydroxy[^{14}C]methylfluorene (prepared in 99% yield from the acid) was not chromatographed on alumina as there was evidence of slight dehydration to 9-methylenefluorene on the adsorbent. The product formed by Wagner rearrangement of the alcohol was purified by chromatography on alumina (1 in. × 18 in.). Development and elution with light petroleum (b. p. 60—80°) gave the labelled hydrocarbon (2·91 g., 89% yield from the alcohol, 82% from carbon dioxide), m. p. 93—95°; activity 50·2 mc/mole representing a radioactive " yield " of 83·5% on the active $BaCO_3$ used.

The authors thank Dr. J. R. Catch of the Radiochemical Centre, Amersham, for the activity measurements and are grateful to Mr. A. Midgley for experimental assistance and to the Council of The Coal Tar Research Association and the Department of Scientific and Industrial Research for permission to publish this work.

THE COAL TAR RESEARCH ASSOCIATION,
OXFORD ROAD, GOMERSAL, NR. LEEDS.

[*Received, April 6th,* 1955.]