274. *Synthesis of Di*[ar-^{14}C]*benzoyl Peroxide from* [^{14}C]*Benzene.*

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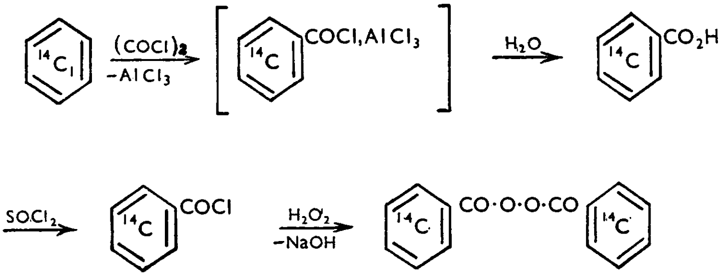
Di[*ar*-^{14}C]benzoyl peroxide has been synthesised on the 1 mmole scale from [^{14}C]benzene *via* [*ar*-^{14}C]benzoic acid and [*ar*-^{14}C]benzoyl chloride.

Trial syntheses with inactive compounds indicated an overall yield of 40—50%, while radiochemical assay of the active peroxide indicated an overall yield of 35%.

Recent studies in these laboratories of the polymerisation of vinylic monomers in the presence of natural rubber have demonstrated the importance of the initiating catalyst on the reaction, *viz.*, benzoyl peroxide leads to extensive rubber-polymer interaction ("grafting"), but azo*iso*butyronitrile, while initiating polymerisation, does not cause significant interaction.[1] A mechanistic study of the "grafting" process is being undertaken using [^{14}C]-labelled initiators, and the present paper describes the synthesis of di[*ar*-^{14}C]benzoyl peroxide from [^{14}C]benzene.

The synthetic route chosen is shown in the following scheme:



Staudinger's method[2] was used to convert benzene into benzoyl chloride, which was hydrolysed, without isolation, to benzoic acid. Trial syntheses on the 1 mmole scale gave yields of 80—95% of substantially pure benzoic acid, and in the final radioactive synthesis a 95% yield of [*ar*-^{14}C]benzoic acid was obtained. This was converted into the peroxide by reaction as shown.[3] Experimental conditions influence the yield of peroxide considerably. An excess of sodium hydroxide considerably reduces the yield, probably by hydrolysis of the peroxide before it could be isolated, while addition of a trace of oleic acid as emulsifying agent increases the yield.[4] Pure inactive benzoyl chloride gave yields of peroxide up to 85%, but when the benzoyl chloride was prepared from benzoic acid the yield of peroxide was lowered to 50—55% based on the acid, probably owing to partial

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[1] Merrett, *Trans. Faraday Soc.*, 1954, **50**, 759.

[2] Staudinger, *Ber.*, 1908, **41**, 3558.

[3] Vanino and Herzer, *Arch. Pharm.*, 1915, **253**, 426; Gambarjan, *Ber.*, 1909, **42**, 4004.

[4] Oosterhuis, Dutch P., 51,098/1941.

loss of benzoyl chloride during the removal of unchanged thionyl chloride and the resultant inability to assess the correct amount of sodium hydroxide to be used. Rigorous removal of thionyl chloride was imperative for the successful synthesis of the peroxide since small amounts remaining are readily converted by the sodium hydroxide into sulphite which then is oxidised by the hydrogen peroxide, thus resulting in loss of both reagents.

The di[*ar*-^{14}C]benzoyl peroxide was diluted with pure inactive peroxide, equilibrated in chloroform, and precipitated with methanol to give di[*ar*-^{14}C]benzoyl peroxide (1). A second sample (2) of the peroxide was obtained from the mother-liquors of the first sample, and its radiochemical purity demonstrated by two dilution experiments involving recrystallisations from different solvents to give samples (3) and (4). Table 1 indicates the radiochemical purities. From the specific activities and the counting efficiency of the Geiger–Müller tube (determined by radioassay of compounds of known specific activity) it was calculated that the radiochemical yield of the peroxide was 35% based on [^{14}C]benzene.

TABLE 1. *Radiochemical assay of di*[ar-^{14}C]*benzoyl peroxide.*

Sample	1	2	3	4
Observed activity (counts/min./mmole)	$2·75 \times 10^7$	$6·45 \times 10^6$	$1·34 \times 10^5$	$5·88 \times 10^4$
Calculated activity * (counts/min./mmole)	$2·82 \times 10^7$	—	$1·38 \times 10^5$	$5·97 \times 10^4$

* Based on the specific activity of sample (2) and the known dilution factors.

EXPERIMENTAL

Inactive Materials.—Commercial benzoyl peroxide was recrystallised twice from ether, then once from acetone, precipitated twice from chloroform with methanol, and dried *in vacuo*, to give pure peroxide (Found : C, 69·4; H, 4·2. Calc. for $C_{14}H_{10}O_4$: C, 69·4; H, 4·2%). Analysis by Nozaki's method[5] indicated a purity of 99·7%. Reagents and solvents were purified by standard procedures or were of " AnalaR " grade.

FIG. 1.

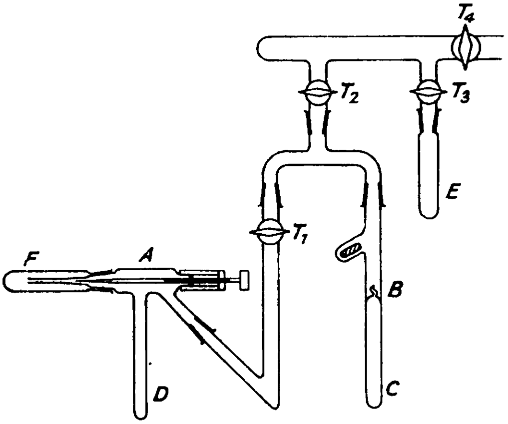
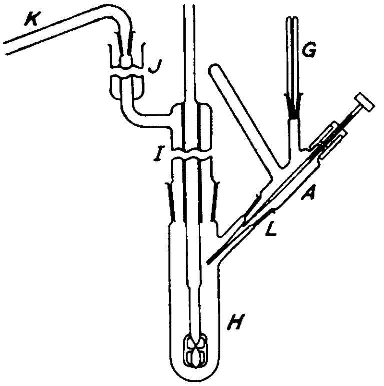


FIG. 2.



[ar-^{14}C]*Benzoic Acid.*—[^{14}C]Benzene in carbon disulphide was introduced into the micro-dropping funnel *A* (see Fig. 1) by the following procedure. With the entire apparatus evacuated, tap T_1 open, and T_2 and T_4 closed, the seal at *B* was broken, and [^{14}C]benzene (0·078 g., 1 mmole; 0·5 mc) was distilled from tube *C* into tube *D* cooled in liquid oxygen. Taps T_2 and T_3 were then opened and carbon disulphide (4·0 ml.) was distilled from *E* into *D*. T_1 was then closed, the dropping funnel was detached from the vacuum manifold, and the contents of *D* were melted and mixed by gentle shaking. Air was introduced through T_1 into the dropping funnel which was attached to the apparatus shown in Fig. 2 at *L*. The long capillary tube *G* prevented loss by evaporation.

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[5] Nozaki, *Ind. Eng. Chem. Anal.*, 1946, **18**, 583.

Simultaneously with the above, aluminium chloride (1·34 g., 10 mmole) and carbon disulphide (2·0 ml.) were placed in the tube *H* (Fig. 2). The apparatus also comprised a precision-ground stirrer *I*, a solid carbon dioxide condenser *J* and an " Anhydrone " drying tube *K*. Oxalyl chloride (1·15 g., 9 mmole) in carbon disulphide (5·0 ml.) was added to vessel *H* with stirring and the whole kept at 25° for 30—40 min., during which gentle effervescence occurred (evolution of carbon monoxide as carbonyl chloride was formed). The contents of *H* were then cooled to 0°, and with vigorous stirring the [^{14}C]benzene solution was introduced from *A* at the rate of one drop per 12—15 sec. (total time of addition, 75 min.). The syringe *A* was washed with further carbon disulphide (2 ml.), and the washings were added to *H*. Tube *K* was then replaced by a stopper, *I* was sealed at the top with thick " Silicone " grease, and the volatile material removed *via L* at 15 mm. into a trap cooled in liquid oxygen. Water (8·0 ml.) was slowly added to the solid complex in *H* at 0°, and the mixture then refluxed for 15—30 min. On cooling, benzoic acid crystallised. Next morning, tube *H* was transferred to an extraction apparatus described elsewhere.[6] The aqueous mixture was extracted with ether (5, 3, and 2 ml.), the combined ether extracts were extracted with 10% aqueous sodium hydroxide (3, 2, and 1 ml.), and the alkaline extracts washed with ether (5 ml.) and then acidified with concentrated hydrochloric acid (1 ml.). The [*ar*-^{14}C]benzoic acid was extracted with ether (3 × 5 ml.), the resulting solution evaporated to dryness, and the acid dried over phosphorus pentoxide at 200 mm. (yield, 0·116 g., 95%). In trial syntheses the benzoic acid, m. p. and mixed m. p. 120—121°, was obtained in yields of 80, 85, and 95% (Found: C, 68·2; H, 5·0; ash 0·8%; equiv., 124. Calc. for $C_7H_6O_2$: C, 68·9; H, 5·0%; equiv., 122).

[ar-^{14}C]*Benzoyl Chloride*.—A mixture of [*ar*-^{14}C]benzoic acid (0·116 g., 0·95 mmole) and thionyl chloride (2 ml., 27·5 mmole) was refluxed for 4 hr. in a 25 ml. pear-shaped flask protected with an " Anhydrone " drying tube. A fine capillary nitrogen-leak was then fitted to the flask and the excess of thionyl chloride distilled off into a trap cooled in liquid oxygen, the final traces being removed at room temp./15 mm. during 5—10 min. Benzene (0·75 ml.) was then added to the [*ar*-^{14}C]benzoyl chloride and distilled off as for the thionyl chloride.

Di[ar-^{14}C]*benzoyl Peroxide*.—The apparatus used is shown in Fig. 2. Sodium hydroxide solution (2·4%) and " AnalaR " hydrogen peroxide solution (1%) were standardised before use. The calculated quantities of sodium hydroxide solution and hydrogen peroxide, based on a quantitative yield of [*ar*-^{14}C]benzoyl chloride from the acid and under the conditions of expt. 3, Table 2, were pipetted into tube *H* together with 6 drops of 0·7% aqueous oleic acid. The [*ar*-^{14}C]benzoyl chloride in acetone (0·5 ml.) was added dropwise from *A* into the vigorously stirred aqueous solution at −2° to 0°; vessel *A* was then washed with further acetone (0·5 ml.) which was added to *H*. The solid product was rapidly dissolved in ether (5 ml.), the aqueous layer was extracted with further ether (2 × 5 ml.) and the combined ether extracts were evaporated to dryness by a stream of nitrogen in a 50 ml. recrystallising flask of the type described elsewhere.[6] Final drying of the solid *in vacuo* gave di[*ar*-^{14}C]benzoyl peroxide (0·068 g.).

Trial syntheses on the 1 mmole scale with pure inactive benzoyl chloride had indicated the optimum conditions for the preparation of the peroxide (Table 2). Under the conditions of expt. 3 (Table 2) trial syntheses from pure benzoic acid gave overall yields of 52% and 54%; similar syntheses from benzene gave the peroxide in overall yields of 43% and 58%.

TABLE 2. *Trial syntheses of benzoyl peroxide from benzoyl chloride* (1 *mmole scale*) *at* 0°.

Expt.	Molar ratio NaOH (aq.) : BzCl	Molar ratio H_2O_2 (aq.) : BzCl	Yield † (%)
1	1·0	0·5	57
2 *	1·0	0·5	83
3 *	1·0	0·75	89
4 *	1·5	0·5	67

* 6 Drops of 0·7% aq. oleic acid present. † Determined iodometrically.[5]

Dilution of Di[ar-^{14}C]*benzoyl Peroxide*.—The above peroxide was transferred with chloroform (5 ml.) *via* the filter disc into a second crystallising flask containing pure inactive peroxide (1·505 g.). After complete dissolution and thorough equilibration the peroxide was precipitated at 0° with methanol (5 ml.), and the solid peroxide separated, redissolved in chloroform (4 ml.),

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[6] Ayrey, Moore, and Watson, *J. Polymer Sci.*, 1956, **19**, 1.

and reprecipitated at 0° with methanol (4 ml.) to give di[*ar*^{14}C]benzoyl peroxide (1) (0·978 g.), which when assayed as described below had an activity of 1·97 × 10^6 counts/min./mmole of CO_2.

The combined mother-liquors were evaporated to dryness at room temp./15 mm. and the peroxide, together with inactive peroxide (2·004 g.), dissolved in chloroform and precipitated three times with methanol as described above to give sample (2) (1·48 g.) having an activity of 4·61 × 10^5 counts/min./mmole of CO_2. The radiochemical purity of sample (2) was demonstrated by two further dilution experiments. First, sample (2) (33·07 mg.) and inactive peroxide (1·511 g.) were equilibrated in warm acetone (4·5 ml.) and crystallised at 0°; the solid peroxide was twice precipitated with methanol from chloroform to give sample (3) (0·694 g.) having an activity of 9·56 × 10^3 counts/min./mmole of CO_2. Secondly, sample (2) (14·19 mg.) and inactive peroxide (1·518 g.) were equilibrated in, and crystallised from, ether, then precipitated as above from chloroform solution, to give sample (4) (0·684 g.) having an activity of 4·20 × 10^3 counts/min./mmole of CO_2. The observed specific activities of samples (1), (3), and (4) (Table 1) are in good agreement with those calculated from the observed specific activity of sample (2) and the known dilution factors.

Assay of Samples for [^{14}C].—The samples were oxidised to water and $^{14}CO_2$ by the standard dry microcombustion technique, the water was removed in an " Anhydrone " drying tube and a trap cooled in ethanol-carbon dioxide, and the $^{14}CO_2$ collected in a trap[7] cooled in liquid oxygen. Sample weights were such as to give a maximum of 1·25 mmole of carbon dioxide. The $^{14}CO_2$ was diluted, if necessary, with inactive carbon dioxide and then transferred, together with carbon disulphide, to the Geiger-Müller counter of the type described by Audric and Long[8] (Bevington, Guzman, and Melville's technique[9]). The counter was placed in a lead shield (1½" thick), and the plateau determined for all samples; the plateaux usually had a slope of $<$0·05% per volt, and their length exceeded 100 volts. Counting was done at 75 v. from the beginning of the plateau and sufficient counts were taken to give a standard error of less than ±1%. Count rates recorded have been corrected for lost counts due to an imposed paralysis time of 1 msec. in the scaler, background (*ca.* 20 counts/min.), and dilution. Memory effects in the combustion apparatus, the vacuum manifold, and the counter were shown to be negligible. In all combustions the yield of $^{14}CO_2$ was 100 ± 1·0%, indicating that the carbon dioxide is truly representative of the carbon content of the compound burnt. The performance of the counter was determined by using samples of $^{14}CO_2$ of different specific activity, and was satisfactory up to 5000 counts/min. (linearity of the plot of count rate against relative activity). The count rates of $^{14}CO_2$ samples derived from [^{14}C]poly(methyl methacrylate) and barium [^{14}C]carbonate of known specific activity showed the efficiency of the counter to be 45%.

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[7] Buchanan and Nakao, *J. Amer. Chem. Soc.*, 1952, **74**, 2389.

[8] Audric and Long, Report No. CRL/AE 51, Chemical Research Laboratory, Teddington.

[9] Bevington, Guzman, and Melville, *Proc. Roy. Soc.*, 1954, *A*, **221**, 437.