Tetrahedron, 1958, Vol. 3, pp. 105-112. Pergamon Press Ltd., London

OXIDATIVE REACTIONS OF NITRILES—II

REACTIONS WITH *TERT.*-BUTYL HYDROPEROXIDE*

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(*Received* 16 *January* 1958)

Abstract—Diphenyl-, *cyclo*hexylphenyl- and methylphenyl-acetonitrile react with *tert.*-butyl hydroperoxide in the presence of cuprous ions at 80°. By this means, α-*tert.*-butylperoxydiphenyl-, α-*tert.*-butylperoxyphenyl*cyclo*hexyl- and α-*tert.*-butylperoxymethylphenyl-acetonitrile, respectively, were obtained in good to excellent yields. Under similar experimental conditions, phenylacetonitrile gave oxygen, benzoic acid, *tert.*-butyl benzoate and *tert.*-butyl perbenzoate. In the absence of copper catalyst little reaction was observed. Dimethylacetonitrile did not react with *tert.*-butyl hydroperoxide in the absence of copper catalyst at 80°; in the presence of cuprous ions, however, it catalyzed the decomposition of the hydroperoxide to give oxygen in quantitative yield.

IN Part I,[1] the autoxidation of some substituted acetonitriles in the presence of a base and a copper catalyst was discussed. The present work is an extension of these studies. It deals with the reactivity of these nitriles towards *tert.*-butyl hydroperoxide in the presence of cuprous salts.‡ The reaction of the nitriles with *tert.*-butyl hydroperoxide was conducted in an unreactive solvent, and the amount of diluent was such that the copper-catalyzed decomposition of *tert.*-butyl hydroperoxide to form oxygen was limited to 5–10 per cent.

It was found that in the absence of cuprous ions diphenylacetonitrile reacts only slightly with *tert.*-butyl hydroperoxide; the nitrile alone does not catalyze the decomposition of *tert.*-butyl hydroperoxide to form oxygen. However, when cuprous bromide was added and the reaction mixture was stirred for 108 hr at room temperature, a high yield of α-*tert.*-butylperoxydiphenylacetonitrile was formed. This reaction, when carried out at 80°, was complete within a few hours. When cobaltous 2-ethylhexoate was used instead of cuprous bromide, the reaction proceeded rapidly at room temperature; however, there was also a rapid decomposition of *tert.*-butyl hydroperoxide to form oxygen.

It has previously been reported[1] that dimethylacetonitrile does not react with certain oxidants under the conditions investigated. A solution of dimethylacetonitrile in benzene, when stirred with *tert.*-butyl hydroperoxide in the presence of cuprous bromide at room temperature, did not give a mixed peroxide; instead, oxygen was liberated in quantitative yield. On the other hand, only traces of oxygen were produced even at 80° in the absence of either the nitrile or cuprous bromide. At present, the most plausible explanation of this observation is that copper salts

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* This investigation is supported by a grant from the Office of Naval Research, Project NR 005–319.

† Deceased.

‡ Replacement of active hydrogen atoms in organic molecules by peroxy groups has been studied by Kharasch and Fono.[2]

[1] M. S. Kharasch and G. Sosnovsky, *Tetrahedron*, 3, 97 (1958).

[2] M. S. Kharasch and A. Fono, *J. Org. Chem.* 23, 324 (1958).

are quite soluble in dimethylacetonitrile and related substances. As a consequence, much larger quantities of catalyst become available for the reaction. At high concentrations of the catalyst the side-reaction, decomposition of the hydroperoxide to form oxygen, is favored (see "Discussion"). This hypothesis is supported by the fact that, under similar reaction conditions, cobaltous 2-ethylhexoate, which is soluble in organic solvents, always causes formation of large amounts of oxygen.

In the presence of cuprous bromide *cyclo*hexylphenylacetonitrile reacts smoothly with *tert.*-butyl hydroperoxide to give the expected mixed peroxide. The purification of this compound presented some difficulties, because of its high boiling point even at pressures below 0·1 mm. Although the compound was repeatedly distilled before it was analyzed, the infrared spectrum showed a very weak absorption in the carbonyl region. It was therefore concluded that small quantities of *cyclo*hexylphenyl ketone may have been formed during the reaction.

Methylphenylacetonitrile gave, in addition to appreciable amounts of oxygen, α-*tert.*-butylperoxymethylphenylacetonitrile. However, the following by-products were also identified: *tert.*-butyl benzoate, *tert.*-butyl perbenzoate, benzoic acid and traces of acetophenone. The occurrence of the first three products may be attributed to the presence of small amounts of phenylacetonitrile in the starting material. The presence of acetophenone was probably due to the oxidation of methylphenylacetonitrile.

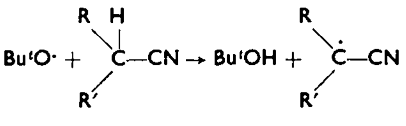
The infrared spectra of these mixed peroxides showed an unusual feature. The parent nitriles have a medium to strong absorption band at 2225 cm^{-1} but the peroxides show little or no absorption in that region. This phenomenon has been previously described by Kitson and Griffith.[3] As a rule, compounds with a nitrile group attached to a carbon atom carrying another electronegative group have only very weak or no absorption in the nitrile region.

Benzaldehyde reacted with *tert.*-butyl hydroperoxide in the presence of cuprous bromide to form *tert.*-butyl perbenzoate, benzoic acid and oxygen.

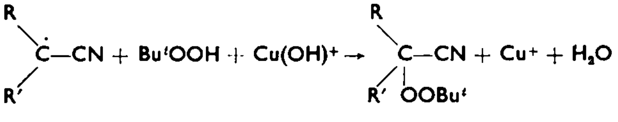
DISCUSSION

The formation of mixed peroxides may be explained by the following mechanism:

$$Cu^+ + Bu^tOOH \rightarrow Bu^tO\cdot + Cu(OH)^+ \qquad (1)$$



$$Bu^tO\cdot + RR'CH{-}CN \rightarrow Bu^tOH + RR'\dot{C}{-}CN \qquad (2)$$



$$RR'\dot{C}{-}CN + Bu^tOOH + Cu(OH)^+ \rightarrow RR'C(OOBu^t){-}CN + Cu^+ + H_2O \qquad (3)$$

This mechanism involves (1) the formation of *tert.*-butoxy radical, (2) the attack of *tert.*-butoxy radical on the nitrile to form the nitrile radical and (3) the reaction of the nitrile radical with another molecule of hydroperoxide and cupric ion to give

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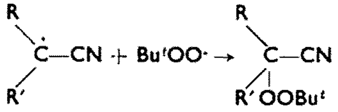
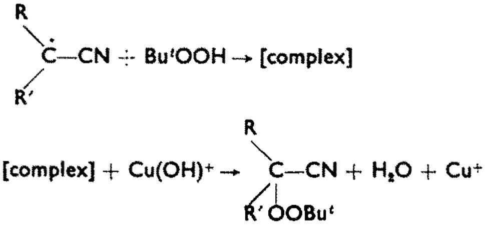
[3] R. E. Kitson and N. E. Griffith, *Analyt. Chem.* **24**, 334 (1952).

the peroxide and to regenerate the cuprous ion. Reaction (3) may be formulated in two different ways: (*a*) oxidation of *tert.*-butyl hydroperoxide by cupric ion to give a *tert.*-butylperoxy radical, followed by the combination of two radicals, or (*b*) formation of a complex between the nitrile radical and *tert.*-butyl hydroperoxide, followed by oxidation of the complex by cupric ion:

$$\mathrm{Bu^tOOH + Cu(OH)^+ \rightarrow Bu^tOO\cdot + Cu^+ + H_2O}$$



$$\mathrm{RR'\dot{C}{-}CN + Bu^tOO\cdot \rightarrow RR'C(OOBu^t){-}CN} \tag{3a}$$



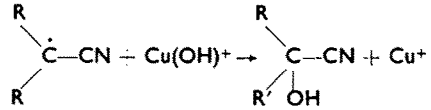
$$\mathrm{RR'\dot{C}{-}CN + Bu^tOOH \rightarrow [complex]}$$

$$\mathrm{[complex] + Cu(OH)^+ \rightarrow RR'C(OOBu^t){-}CN + H_2O + Cu^+} \tag{3b}$$

The competitive side-reactions are: (4) generation of *tert.*-butylperoxy radicals by the reaction of *tert.*-butoxy radical with the hydroperoxide, (5) oxidation of *tert.*-butylperoxy radical by cupric ion to give oxygen and (6) oxidation of the nitrile radical by cupric ion to give cyanohydrin.

$$\mathrm{Bu^tO\cdot + Bu^tOOH \rightleftharpoons Bu^tOO\cdot + Bu^tOH} \tag{4}$$

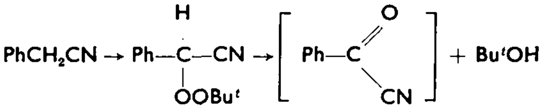
$$\mathrm{Bu^tOO\cdot + Cu(OH)^+ \rightarrow Bu^tOH + Cu^+ + O_2} \tag{5}$$



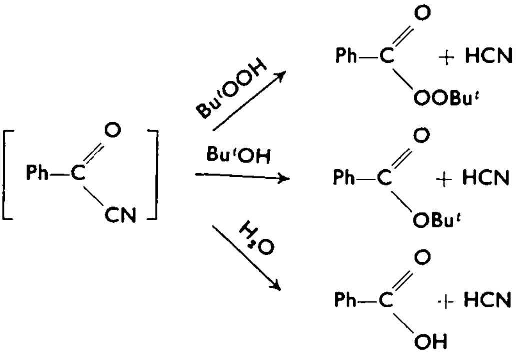
$$\mathrm{RR\dot{C}{-}CN + Cu(OH)^+ \rightarrow RR'C(OH){-}CN + Cu^+} \tag{6}$$

The mechanisms proposed for the side-reactions are supported by the fact that generation of oxygen is the main reaction when a nitrile of low reactivity (e.g., dimethylacetonitrile) is used or when the concentration of catalyst is high. Reactions (4) and (5) then become relatively more important than reaction (3). Ketones have been shown to be minor products when methylphenylacetonitrile and *cyclo*-hexylphenylacetonitrile are used.

When phenylacetonitrile reacts with *tert.*-butyl hydroperoxide in the presence of cuprous bromide, the reaction products are: oxygen, benzoic acid, *tert.*-butyl benzoate, *tert.*-butyl perbenzoate, hydrocyanic acid and *tert.*-butyl alcohol. The ratio of *tert.*-butyl benzoate to *tert.*-butyl perbenzoate varies with the rate of addition of *tert.*-butyl hydroperoxide to phenylacetonitrile. When the two substances are mixed at once, about equal quantities of the two esters are formed; however, when *tert.*-butyl hydroperoxide is added gradually to phenylacetonitrile, formation of the benzoate is favored. In the absence of a copper catalyst only traces of these esters are formed. It has also been established that oxygen inhibits this reaction. Thus, the yield of benzoic acid is reduced from 43 to 5 per cent by the presence of oxygen.



(7)



(8)

The mixed peroxide formed from phenylacetonitrile would be a secondary, and therefore unstable, peroxide,[4] which would be expected to decompose to form the hypothetical intermediate benzoyl cyanide. Benzoyl cyanide would react with *tert.*-butyl hydroperoxide (at high concentration) to give the perbenzoate; at low concentration *tert.*-butyl benzoate or benzoic acid would be formed. Inhibition of the reaction by molecular oxygen may be due to competition between oxygen and *tert.*-butyl hydroperoxide in the oxidation of cuprous to cupric ion. Here the extent of reaction (1) (as well as that of the subsequent reactions (2), (3), (7) and (8)) is diminished.

EXPERIMENTAL

α-tert -*Butylperoxydiphenylacetonitrile*

Method (a). A mixture of diphenylacetonitrile (9·7 g, 0·05 mole), *tert.*-butyl hydroperoxide (96 per cent purity, 10·8 g, 0·115 mole), cuprous bromide (0·25 g, 0·8 millimole) and benzene (200 ml) was heated under reflux for 3½ hr. Oxygen (200 ml, 13 per cent based on the hydroperoxide) was evolved. Cuprous bromide was removed by filtration, and the filtrate was concentrated at reduced pressure. The remaining oil (12 g, 86 per cent) solidified, m.p. 46–50°. A portion of this solid (1·55 g) was chromatographed on an alumina column, light petroleum being used as eluent. The compound recovered was α-*tert.*-butylperoxydiphenylacetonitrile (1·42 g, 79 per cent), m.p. 50–52°. A sample was recrystallized for analysis from light petroleum, m.p. 52·0–52·5°. *Anal.* Calcd. for $C_{18}H_{19}O_2N$: C, 76·84; H, 6·81; N, 4·98; mol. wt., 281. Found: C, 76·80; H, 6·82; N, 4·80 per cent; mol. wt., 268 (cryoscopic method in benzene). Infrared bands: 1385, 1365 cm^{-1} (*tert.*-butyl group); 755, 695 cm^{-1} (monosubstituted benzene); no band at 2250 cm^{-1} region.

Method (b). *tert.*-Butyl hydroperoxide (96 per cent purity, 23 g, 0·245 mole) in benzene (100 ml) was added with stirring over a period of 30 min to a mixture of diphenylacetonitrile (9·7 g, 0·05 mole), cobaltous 2-ethylhexoate (3 ml of a 15 per cent

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[4] M. S. Kharasch, P. L. Pauson and W. Nudenberg, *J. Org. Chem.* **18**, 322 (1953).

solution in benzene, 0·0013 mole) and benzene (100 ml). An exothermic reaction began, and the temperature was kept at 25–30° by external cooling. After addition of the hydroperoxide, stirring was continued for 3 hr. During this period 1800 ml of oxygen was collected. Another portion of the hydroperoxide (23 g, 0·245 mole) in benzene (100 ml) was added during the next 30 min, and stirring was continued for a further 15 hr. A total volume of 4810 ml (0·213 mole, 87 per cent based on hydroperoxide) of oxygen was collected. A sufficient amount of alumina to decolorize the solution was added. The mixture was filtered, and the filtrate was concentrated at reduced pressure. The remaining oil (12·5 g, 90 per cent) upon standing crystallized, m.p. 50–52°.

Method (c). A mixture of diphenylacetonitrile (9·7 g, 0·05 mole), *tert.*-butyl hydroperoxide (98 per cent purity, 10·8 g, 0·115 mole), cuprous bromide (0·25 g, 0·8 millimole) and benzene (200 ml) was stirred at room temperature for 108 hr. By that time, all but a trace of the hydroperoxide had been consumed, and only 100 ml of oxygen had been formed. After removal of the catalyst and solvent, the remaining oil crystallized rapidly to a yellow solid, m.p. 46–48°. Recrystallization from light petroleum gave a white solid identical with α-*tert.*-butylperoxydiphenylacetonitrile isolated from previous experiments.

Method (d). When diphenylacetonitrile (9·7 g, 0·05 mole) and *tert.*-butyl hydroperoxide (96 per cent purity, 10·8 g, 0·115 mole) were heated under reflux for 6 hr, only a small amount of oxygen (140 ml) was evolved. Most of the peroxide (92 per cent) and diphenylacetonitrile (8·2 g, 84 per cent) were recovered. α-*tert.*-Butylperoxydiphenylacetonitrile (1·2 g, 9 per cent) was isolated from the remaining oil.

Reaction of tert.*-butyl hydroperoxide and dimethylacetonitrile in the presence of cuprous bromide*

When a mixture of dimethylacetonitrile (3·5 g, 0·05 mole), *tert.*-butyl hydroperoxide (96 per cent purity, 10·8 g, 0·115 mole) and cuprous bromide (0·1 g, 0·35 millimole) in benzene (100 ml) was stirred at room temperature for 8 hr, oxygen (0·05 mole) was evolved. The reaction mixture was distilled through a twenty-plate column. An azeotrope of benzene and *tert.*-butanol (21 g, containing 38 mole per cent of *tert.*-butanol)[5] b.p. 73–74° was collected. All the *tert.*-butanol formed during the reaction was thus accounted for. Successive fractions were composed of benzene, what appeared to be an azeotrope of benzene and dimethylacetonitrile, and dimethylacetonitrile.

In the absence of dimethylacetonitrile, it was found that at 80° and under comparable conditions only 10 per cent of the hydroperoxide was decomposed.

Reaction of phenylacetonitrile with tert.*-butyl hydroperoxide*

Method (a). A mixture of phenylacetonitrile (11·7 g, 0·1 mole), *tert.*-butyl hydroperoxide (96 per cent purity, 43 g, 0·46 mole) and cuprous bromide (0·1 g, 0·35 millimole) in benzene (340 ml) was heated under reflux for 7 hr. Oxygen (2350 ml, 46 per cent based on the peroxide used) was collected. The reaction mixture was extracted with 2 N sodium hydroxide to remove benzoic acid. The alkaline extract was acidified with hydrochloric acid, and the resulting precipitate of benzoic acid (4·5 g, 37 per cent)

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[5] *International Critical Tables* (Vol. 3) p. 321. McGraw-Hill, New York (1933).

was collected and recrystallized from methanol, m.p. 121°; the m.p. of a mixture with an authentic sample showed no depression. The benzene solution was washed with water, dried over sodium sulphate, and concentrated at reduced pressure. The remaining oil had a boiling range of 50 to 110° at 5 mm of mercury. A portion of this oil (10·5 g) was fractionally distilled through a spinning-band column to give two main fractions:

(1) *tert.*-butyl benzoate (3·5 g, 23 per cent), b.p. 78–82/4 mm, n_D^{20} 1·4942. *Anal.* Calcd. for $C_{11}H_{14}O_2$: C, 74·16; H, 7·86. Found: C, 74·13; H, 7·90. Infrared bands: identical with those of an authentic sample of *tert.*-butyl benzoate.

(2) *tert.*-butyl perbenzoate (2·8 g, 18 per cent), b.p. 87–90/2 mm, n_D^{20} 1·5012. *Anal.* Calcd. for $C_{11}H_{14}O_3$: C, 68·50; H, 7·26; mol. wt., 194. Found: C, 68·40; H, 7·20; mol. wt., 187. Infrared bands: identical with those of an authentic sample of *tert.*-butyl perbenzoate.

Method (b). A mixture of phenylacetonitrile (24 g, 0·2 mole) and cuprous bromide (0·1 g, 0·35 millimole) in benzene (250 ml) was placed in a reaction flask equipped with a pressure-equalized dropping funnel. The flask was also connected through a condenser to a two-necked receiver. The receiver was equipped with a reflux condenser connected to a gas burette. The reaction flask was heated, and, when the distillation began, a solution of *tert.*-butyl hydroperoxide (96 per cent purity, 47 g, 0·5 mole) in benzene (250 ml) was added through the dropping funnel over a period of 2 hr. Benzene, *tert.*-butanol and water distilled into the receiver. Oxygen (1270 ml, 23 per cent based on hydroperoxide) was evolved. The distillate contained hydrogen cyanide (0·6 g). The reaction mixture was filtered and then concentrated at reduced pressure. The remaining oil was diluted with light petroleum and extracted with 2 N sodium hydroxide. The alkaline extract was acidified with hydrochloric acid, and the resulting precipitate of benzoic acid was collected (10·5 g, 43 per cent) and recrystallized from methanol, m.p. 121°; the m.p. of a mixture with an authentic sample showed no depression. The light petroleum solution was washed with water, and the solvent was removed at reduced pressure. The remaining oil (19 g) b.p. 65–95°/3 mm, n_D^{20} 1·5000, was fractionally distilled through a spinning-band column. The fractions were:

(1) *tert.*-butyl benzoate (8·6 g, 24 per cent), b.p. 75–78/3–4 mm, n_D^{20} 1·4940.

(2) *tert.*-butyl perbenzoate (2·7 g, 8 per cent), b.p. 90–92/2 mm, n_D^{20} 1·5010.

Method (c): *reaction in the presence of oxygen.* A mixture of phenylacetonitrile (11·7 g, 0·1 mole), *tert.*-butyl hydroperoxide (96 per cent purity, 24 g, 0·247 mole) and cuprous bromide (0·1 g, 0·35 millimole) was heated under reflux in an atmosphere of oxygen. After the usual treatment of the reaction mixture, *tert.*-butyl benzoate and perbenzoate and unreacted phenylacetonitrile were obtained. However, the amount of benzoic acid was much smaller (0·6 g, 5 per cent) than that obtained in the reaction from which oxygen was excluded.

Method (d): *in the absence of cuprous bromide.* A mixture of phenylacetonitrile (11·7 g, 0·1 mole) and *tert.*-butyl hydroperoxide (96 per cent purity, 24 g, 0·247 mole) in benzene (250 ml) was heated under reflux for 2½ hr. The benzene solution was concentrated at reduced pressure, and the remaining oil was fractionally distilled through a spinning-band column. This procedure gave only traces of *tert.*-butyl benzoate (1·1 g, 4 per cent) and *tert.*-butyl perbenzoate (0·2 g, 1 per cent), in addition to unchanged phenylacetonitrile (8 g, 67 per cent).

Reaction of tert.*-butyl hydroperoxide with benzaldehyde*

Method (a). A mixture of benzaldehyde (21·2 g, 0·2 mole) and cuprous bromide (0·1 g, 0·35 millimole) in benzene (250 ml) was stirred under an atmosphere of nitrogen. To this mixture, a solution of *tert.*-butyl hydroperoxide (96 per cent purity, 47 g, 0·5 mole) in benzene (250 ml) was added over a period of 2 hr. Oxygen (870 ml, 16 per cent based on the hydroperoxide used) was evolved. The benzene solution was extracted with 2 N sodium hydroxide to remove the copper salt and benzoic acid (10 g, 43 per cent), m.p. 121°, after recrystallization from methanol; the m.p. of a mixture with an authentic sample showed no depression. The benzene solution was concentrated at reduced pressure, and the remaining oil was distilled three times. The product recovered was *tert.*-butyl perbenzoate (6·5 g, 17 per cent), b.p. 104°/3–4 mm, n_D^{20} 1·5015. Infrared bands: identical with those of an authentic sample of *tert.*-butyl perbenzoate.

Method (b) When the *tert.*-butyl hydroperoxide was added in one portion, a similar result was obtained: oxygen (1320 ml); benzoic acid (17 g, 50 per cent); *tert.*-butyl perbenzoate (7·5 g, 19 per cent). No reaction was observed at room temperature.

α-tert-*Butylperoxy*cyclo*hexylphenylacetonitrile*

A mixture of *cyclo*hexylphenylacetonitrile (12·5 g, 0·063 mole) and cuprous bromide (0·1 g, 0·35 millimole) in benzene (250 ml) was heated under reflux. A solution of *tert.*-butyl hydroperoxide (96 per cent purity, 15·3 g, 0·16 mole) in benzene (200 ml) was added dropwise over a period of 2 hr. The reaction mixture was heated under reflux for another 5½ hr. Oxygen (580 ml) was collected. The reaction mixture was filtered, and the filtrate was concentrated at reduced pressure. The remaining oil (17 g) was distilled repeatedly for analysis. Efforts to purify the material by other means were unsuccessful. α-*tert.*-Butylperoxy*cyclo*hexylphenylacetonitrile, b.p. 107–108°/0·025 mm, n_D^{20} 1·5100. *Anal.* Calcd. for $C_{18}H_{25}O_2N$: C, 75·50; H, 8·76; N, 4·92. Found: C, 76·43; H, 8·44; N, 5·21. Infrared bands: 2220 cm^{-1} (just detectable, nitrile group); 1675 cm^{-1} (very weak, ketone group, probably *cyclo*hexyl phenyl ketone; 1390, 1365 cm^{-1} (*tert.*-butyl group).

α-tert.-*Butylperoxymethylphenylacetonitrile*

To a mixture of methylphenylacetonitrile[1] (13·1 g, 0·1 mole), cuprous bromide (0·1 g, 0·35 millimole) and benzene heated under reflux was added a solution of *tert.*-butyl hydroperoxide (96 per cent purity, 33 g, 0·34 mole) in benzene (220 ml) over a period of 6 hr. Oxygen (1720 ml, 44 per cent based on hydroperoxide) was collected. The reaction mixture was worked up in the usual manner to give an oil (17·5 g), b.p. 60–100°/3 mm, which was distilled through a spinning-band column. A number of fractions was collected; these fall in two groups:

(1) b.p. 70–74°/3 mm (3·7 g). This group of fractions was a mixture of several products. To judge from infrared analyses, refractive indexes and chemical properties, it appeared to consist of phenylacetonitrile (impurity in the starting material), methylphenylacetonitrile (ca. 14 per cent), *tert.*-butyl benzoate (6 per cent) and acetophenone (0·2 per cent, based on methylphenylacetonitrile; 2,4-dinitrophenylhydrazone, m.p. 237°).

(2) b.p. 97–99°/3 mm (9·3 g). This group of fractions consisted mainly of α-*tert.*-butylperoxymethylphenylacetonitrile (71 per cent). The first cuts (4·9 g)

were contaminated with benzoic acid (0·5 g) and traces of *tert.*-butyl perbenzoate. The last cuts (4·4 g, n_D^{20} 1·4853) were analytically pure. *Anal.* Calcd. for $C_{13}H_{17}NO_2$ C, 71·50; H, 7·78; N, 6·42; mol. wt., 219. Found: C, 71·60; H, 7·78; N, 6·36; mol. wt., 211 (cryoscopic method in benzene). Infrared bands: 1395, 1370 cm^{-1} (*tert.*-butyl group); no band in the 2250 cm^{-1} region.

Acknowledgements—We sincerely thank Dr. T. P. Rudy and Dr. N. C. Yang for helpful discussions during the preparation of manuscript and Mr. W. Saschek for microanalyses.