

419. *Properties and Reactions of Free Alkyl Radicals in Solution.*
Part III. Some Reactions with Organic Halogen Compounds.*

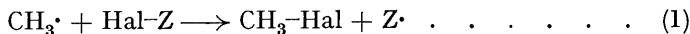
By M. C. FORD and WILLIAM A. WATERS.

Tertiary aliphatic radicals $RR'C(X)\cdot$ (R and R' = Alkyl; X = CN or CO_2Me) abstract halogen atoms from the "positive" halogen compounds ethyl α -bromomalonate and $\omega\omega\omega$ -tribromoquinoline and react with allyl bromide and iodide. No reaction occurs with simple halides such as *n*-butyl bromide, isopropyl iodide, benzyl iodide, or iodobenzene. These radicals readily abstract bromine from *N*-bromosuccinimide and are good catalysts for homolytic brominations effected by this reagent. Even *cyclohexane* can be brominated under these conditions.

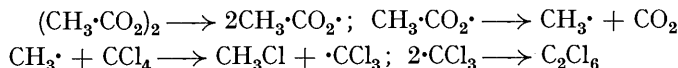
IN continuation of Part II * we have now investigated further reactions of the tertiary aliphatic radicals which can be derived from the tertiary aliphatic azo-compounds

* Part II, *J.*, 1951, 1851.

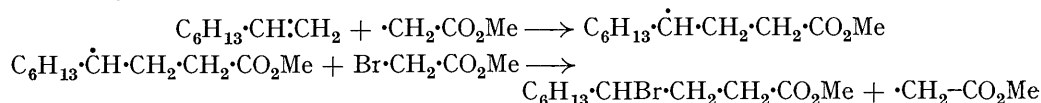
$RR'C(X)\cdot N:N\cdot C(X)RR'$ (R and R' = Alkyl; X = CN or CO₂Me) by thermal decomposition in solution.



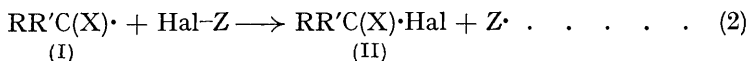
The occurrence of the metathetic reaction (1) has been demonstrated by Kharasch and his colleagues (*Science*, 1945, **102**, 128; *J. Amer. Chem. Soc.*, 1941, **63**, 526; 1946, **68**, 154; 1947, **69**, 1100, 1105; *J. Org. Chem.*, 1948, **13**, 895) who have shown that the thermal decomposition of diacyl peroxides yields alkyl radicals which are capable of reacting with carbon tetrachloride to give alkyl chlorides and hexachloroethane, *e.g.* :



Similar halogen-transfer reactions have been effected between methyl radicals and carbon tetrabromide, bromoform, dibromodichloromethane, bromotrichloromethane, bromodichloromethane, and methyl bromoacetate, though with chloroform and methyl dichloroacetate (Kharasch, Urry, and Jensen, *J. Amer. Chem. Soc.*, 1945, **67**, 1626) hydrogen transfer occurred instead. The formation of free radicals such as $\cdot CCl_3$ and $\cdot CH_2\cdot CO_2Me$ by these reactions has been established by demonstrating that they could be added on to olefins, *e.g.* :



Individual free alkyl radicals however may differ greatly in their chemical reactivity according to the natures of their substituent groups and, as the previous papers in this series have shown, the tertiary aliphatic radicals which we have examined are much less reactive than is free methyl. Although Ziegler (*Brennstoffchemie*, 1949, **30**, 182; *Chem. Abs.*, 1950, **44**, 2914) has reported that the radicals (I; R = R' = Me; X = CN) can initiate addition of carbon tetrachloride to styrene, the extent of chlorine abstraction from this substance is so slight as to be virtually undetectable except in the presence of an olefin; indeed carbon tetrachloride has been used as a convenient solvent in the present study (*cf.* Part II).



With C-halogen compounds the reaction (2) would be expected to occur to a reasonable extent only if it is exothermic, and, since it involves the breaking of one carbon-halogen bond and the formation of another, this halogen exchange would be favoured only if (a) the C-Hal bond in the halogen compound is less stable than that in (II) or (b) the radical Z· is more stable than the radical (I). Now since the radicals (I) which we have examined must be resonance-stabilised to a considerable extent on account of the group X (C≡N or

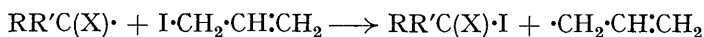
$\left. \begin{array}{l} C=O \\ \diagdown \\ OMe \end{array} \right)$ directly attached to the trivalent carbon centre, no reaction of this type would be expected to occur with simple alkyl or aryl halides since the radicals Z· which might be formed (*e.g.*, methyl, phenyl) are highly reactive. In fact there is no detectable reaction between our tertiary aliphatic radicals and *n*-butyl bromide, isopropyl iodide, benzyl iodide, or iodobenzene.

For reasons which have been previously discussed by one of us (Waters, *J.*, 1933, 1551; 1942, 153) the so-called "positive" halogen compounds ethyl α-bromomalonate and ωωω-tribromoquinaldine, which have been shown to be active catalysts for the autoxidation of tetralin (Robertson and Waters, *J.*, 1947, 492), are much more prone to undergo homolytic fission of their C-Br bonds. Again, Brown and Hammick (*J.*, 1950, 628) and Brown, Grice, Hammick, and Thewlis (*J.*, 1951, 1149) have found that ωωω-tribromoquinaldine

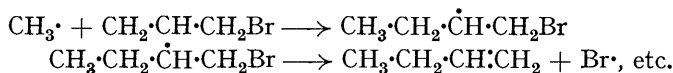
could be used to brominate tetralin, *m*-xylene, mesitylene, and cyclohexene. With these two halogen compounds it has now been possible to establish the direct occurrence of reaction (2). In our experimental work, the particular azo-compound chosen for each reaction was selected with the object of achieving (i) a controllable liquid-phase reaction without the necessity of recourse to an inert solvent and (ii) easy fractionation of the reaction products.

Ethyl α -bromomalonate reacts with 2-carbomethoxy-2-propyl radicals (I; R = R' = Me; X = CO₂Me) to give a 7% yield of methyl α -bromo*isobutyrate* (II; R = R' = Me; X = CO₂Me; Hal = Br), and $\omega\omega\omega$ -tribromoquinaldine reacts violently with 1-cyano-1-methyl-*n*-propyl radicals (I; R = Me; R' = Et; X = CN) to give a 32% yield of (\pm)- α -bromo- α -methylbutyronitrile (II; R = Me; R' = Et; X = CN; Hal = Br). From the latter reaction $\omega\omega$ -dibromoquinaldine was also isolated in 15% yield, so that the (C₉H₆N)·CBr₂· radical must evidently dehydrogenate available substances in the reacting system in preference to dimerising to (C₉H₆N)·CBr₂·CBr₂·(C₉H₆N).

Allyl iodide reacts with 2-cyano-2-propyl radicals (I; R = R' = Me; X = CN) to give an 8% yield of α -iodo*isobutyronitrile* (II; R = R' = Me; X = CN; Hal = I) together with a little iodine, but not diallyl. In this case the simple reaction

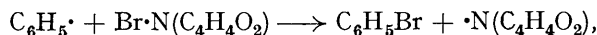


would be favoured on account of the high degree of resonance stabilisation of the symmetrical allyl free radical ($\cdot CH_2\cdot CH\cdot CH_2$). However, Kharasch and Büchi (*J. Org. Chem.*, 1949, 14, 84) have shown that the decomposition of acetyl peroxide in allyl bromide gives a complex mixture containing both but-1-ene and 5-bromo-4-bromomethylpent-1-ene and much polymeric materials, but little methyl bromide and no diallyl. They therefore suggested that the methyl radical preferentially attacks the terminal methylene group of allyl bromide:



The slight liberation of iodine in our reaction accords with this type of mechanism, since, as was shown in Part II, though iodine does combine with the radicals RR'C(X)· its complete removal requires a large excess of radicals. With allyl bromide there was again evidence of attack, but the characterisation of the reaction products was not successfully accomplished.

Some years ago it was tentatively suggested by one of us that the characteristic reactivity of the *N*-halogen compounds might be due to the ease with which they underwent homolysis (see Waters, *J.*, 1937, 2010; 1942, 156; *Nature*, 1944, 154, 772) and this theory is especially relevant to the characteristic reactivity of *N*-bromosuccinimide which, as Bloomfield first postulated (*J.*, 1944, 118), acts as a brominating agent by way of a radical-chain reaction (for confirmation of mechanism, see Bateman and Cunneen, *J.*, 1950, 943) especially when catalysed with benzoyl peroxide (Schmid and Karrer, *Helv. Chim. Acta*, 1946, 29, 573). However, the actual occurrence of the chain-starting reaction



has not yet been substantiated conclusively by the isolation of bromobenzene from the direct reaction between *N*-bromosuccinimide and benzoyl peroxide in an inert solvent.

We have now found that 1-cyano-1-methyl-*n*-propyl radicals react vigorously with *N*-bromosuccinimide in carbon tetrachloride suspension giving (\pm)- α -bromo- α -methylbutyronitrile in 39% yield, together with succinimide in 20% yield. Unless careful precautions are taken to moderate the violence of this reaction it may become dangerously explosive. Disuccinoylhydrazine, (C₄H₄O₂)N·N(C₄H₄O₂), did not appear to be formed, showing that the free succinimidyl radical, (C₄H₄O₂)N·, must be a very strong dehydrogenating agent. This accords with the view that in the allylic bromination reactions of *N*-bromosuccinimide it is this free *nitrogen* radical which is the effective hydrogen abstractor, and not atomic bromine.

As catalysts for homolytic brominations by *N*-bromosuccinimide the tertiary aliphatic azo-compounds appear to be very effective, since with one mole % of catalyst toluene gave benzyl bromide in 66% yield, together with about 10% of benzylidene dibromide. As was expected, this side-chain substitution could be inhibited by small amounts of iodine or chloranil. *cyclo*Hexene gave a 75% yield of 3-bromocyclohexene whilst even *cyclo*hexane gave a 48% yield of *cyclo*hexyl bromide. In the absence of the azo-catalyst both toluene and *cyclo*hexane could be refluxed with *N*-bromosuccinimide without the occurrence of any bromination.

The bromination of *cyclo*hexane with *N*-bromosuccinimide, which has not been hitherto reported, demonstrates the great value of the azo-compounds as halogenation catalysts (compare Part II).

EXPERIMENTAL

Reaction with Allyl Iodide.—The iodide (b. p. 31–32°/53 mm.), purified by distillation under nitrogen, contained less than 4.5×10^{-4} g.-atom of iodine/mole. $\alpha\alpha'$ -Azoisobutyronitrile (20.5 g., 0.125 mole) and allyl iodide (36.4 g., 0.4 mole) were gently warmed together in the dark under nitrogen. Solution of the azo-nitrile was complete before evolution of nitrogen commenced. The gassing lasted for 20 minutes, after which the mixture, which had rapidly darkened during the decomposition, was refluxed for a further 20 minutes. To the cooled mixture, light petroleum (b. p. 40–60°; 40 ml.) was added and the mixture was left overnight at 0°. The liquid portion, after decantation from tetramethylsuccinonitrile and tar, was distilled. The portion boiling above 40°/10 mm. was shaken with 0.1*N*-sodium thiosulphate, then water, dried, and refractionated, giving α -iodoisobutyronitrile (4.0 g., 8% calc. on the azo-nitrile; b. p. 47–57°/10–12 mm.) which was identified by conversion into α -iodoisobutyramide, m. p. and mixed m. p. 181–182°.

Further similar decompositions were tested as follows. (i) Chloroform was added to the initial reaction product to serve as a carrier for diallyl (b. p. 60°); the fraction boiling between 58° and 64° did not decolourise a dilute solution of bromine in chloroform. (ii) The reaction product was diluted to a measured volume with toluene, and aliquots were then titrated with 0.01*N*-sodium thiosulphate. The titres indicated the formation of not less than 2×10^{-2} g.-atom of iodine per mole of allyl iodide, corresponding to a yield of 3% calc. on the azo-nitrile. Allyl iodide heated under the same conditions but without the addition of the azo-nitrile developed less than 4×10^{-4} g.-atom/mole.

Reaction with Allyl Bromide.—A solution of dimethyl $\alpha\alpha'$ -azoisobutyrate (10.0 g., 0.0435 mole) in allyl bromide (b. p. 71°; 15 ml.) was gently refluxed under nitrogen for 45 minutes. The excess of the bromide was then removed at atmospheric pressure and the residual brown oil was distilled through a short column under diminished pressure. Three fractions were collected: (i) b. p. 47–53°/15–20 mm. (2.0 g.; n_D^{20} 1.4417; Br, 30.4%), (ii) b. p. 93–94°/13 mm. (0.9 g.; n_D^{20} 1.4474; Br, 26.0%), and (iii) b. p. 104–124°/13 mm. (1.6 g.). Fractions (i) and (ii) immediately decolourised neutral 0.01% potassium permanganate solution; (i) consisted mainly of methyl α -bromoisobutyrate [b. p. 38°/9 mm.; n_D^{16} 1.4531; Br, 44.2% (cf. Part II)] but attempts to prepare α -bromoisobutyramide from it were unsuccessful; (ii) possibly contained some methyl (\pm)- $\alpha\beta$ -dibromoisobutyrate (b. p. 80°/9 mm.; n_D^{17} 1.5092; Br, 61.5%), whilst (iii) consisted of methyl tetramethylsuccinate which was identified by hydrolysis to the corresponding acid, m. p. and mixed m. p. 192–193°.

Decomposition of $\alpha\alpha'$ -azoisobutyronitrile was similarly carried out in (a) boiling *n*-butyl bromide, (b) boiling isopropyl iodide, (c) iodobenzene at 100°, and (d) a boiling solution of benzyl iodide in toluene, but in no case could any attack upon the halogen compound be detected.

Reaction with Ethyl α -Bromomalonate.—Liquid dimethyl $\alpha\alpha'$ -azoisobutyrate (11.5 g., 0.05 mole) at 30° was added dropwise to ethyl α -bromomalonate (11.9 g., 0.05 mole) kept at 150° in an oil-bath. The product was kept at this temperature for 30 minutes and then, after the addition of carbon tetrachloride (5 ml.), refluxed for a further 30 minutes. The resulting pale brown liquid was directly distilled, two fractions being collected: (i) b. p. 40–100°/7 mm. and (ii) b. p. 100–160°/7 mm. Fractionation of (i) gave methyl α -bromoisobutyrate (0.6 g., 7% calc. on the bromomalonate ester), b. p. 67–73°/37 mm., characterised by conversion into α -bromoisobutyramide, m. p. and mixed m. p. 147°, and a higher-boiling fraction (0.8 g.; b. p. 175–199°) which may have contained ethyl malonate, though its identification by conversion into malonamide was not successful. Fraction (ii) consisted principally of unchanged bromomalonate ester together with dimethyl tetramethylsuccinate.

When the reaction was carried out at the temperature of boiling carbon tetrachloride no abstraction of bromine from the bromomalonic ester occurred. At the higher temperature used above, the gradual addition of the azo-ester was essential since an explosive decomposition occurred when a solution of $\alpha\alpha'$ -azoisobutyronitrile in bromomalonic ester was heated on the steam-bath.

Reaction with $\omega\omega\omega$ -Tribromoquinaldine.—An intimate mixture of $\alpha\alpha'$ -azo-(α -methylbutyronitrile) (9.4 g., 0.049 mole) and $\omega\omega\omega$ -tribromoquinaldine (10.4 g., 0.027 mole) (Hammick, *J.*, 1923, 123, 2883) was gently heated over a gauze. A steady evolution of nitrogen occurred, with the formation of a brown solution, but unless the reaction mixture was cooled at this point a violent and uncontrollable decomposition set in, producing an intractable tar. From a suitably controlled decomposition, however, there was obtained a dark oil. To this was added carbon tetrachloride (10 ml.), and the whole mixture was then refluxed gently for 15 minutes to complete the decomposition of the azo-nitrile. The solvent was then removed from the greenish-brown solution, light petroleum was added to the residue, and the mixture was left overnight at 0°. The petroleum extract was decanted and fractionated, giving (i) b. p. 43—45°/18 mm. (0.3 g.) and (ii) b. p. 57—60°/18 mm. (1.4 g.); (i) consisted principally of (\pm)- α -methylbutyronitrile whilst (ii) was (\pm)- α -bromo- α -methylbutyronitrile (32%, calc. on tribromoquinaldine) which was identified by conversion into (\pm)- α -bromo- α -methylbutyramide, m. p. and mixed m. p. 45.5—48°.

The residue from the distillation was combined with the tarry residue from the initial light petroleum treatment, and the whole was distilled in steam. The first 750 ml. of distillate, after ether-extraction, yielded *s*-diethyldimethylsuccinonitrile (3.2 g., 40% calc. on the azo-nitrile), m. p. and mixed m. p. 97—101°. The steam-distillation was continued until no further solid passed over. From this second distillate there was isolated $\omega\omega$ -dibromoquinaldine (1.2 g., 15% calc. on tribromoquinaldine), which after crystallisation from light petroleum (b. p. 80—100°) had m. p. 119—120°, undepressed in admixture with an authentic specimen (Hammick, *J.*, 1926, 1302).

Reaction with N-Bromosuccinimide.—*N*-Bromosuccinimide (Ziegler, Späth, Schaaf, Schumann, and Winkelmann, *Annalen*, 1942, 551, 109) was rapidly recrystallised from hot water (Djerassi, *Chem. Reviews*, 1948, 43, 293) and dried in a vacuum; its purity (iodometric) was 98.5%.

An intimate mixture of $\alpha\alpha'$ -azo-(α -methylbutyronitrile) (15.4 g., 0.08 mole) and the bromo-imide (14.5 g., 0.08 mole) was covered with dry carbon tetrachloride (5 ml.), and the partial solution was gently heated, with constant swirling, over a gauze. Nitrogen evolution soon commenced, and a clear light-brown solution was slowly formed. The temperature of the liquid was *ca.* 110°. After 20 minutes the gassing began to slacken and the liquid became darker, but if a further quantity of carbon tetrachloride (10 ml.) was added to reduce the temperature of the boiling liquid, and the refluxing was continued for a further 20 minutes to complete the decomposition of the azo-nitrile, then tractable products were obtained. On cooling of the mixture to 0°, first a tar, and then nearly pure succinimide were deposited. Titration showed that 98% of the bromo-imide had reacted. The carbon tetrachloride solution, after filtration at 0°, gave on fractionation (\pm)- α -bromo- α -methylbutyronitrile (4.9 g., 39% calc. on the bromo-imide consumed), b. p. 58—59°/15 mm. (amide, m. p. and mixed m. p. 46.5—48°). The residue from the distillation was combined with the solid from the initial reaction product and steam-distilled to remove *s*-diethyldimethylsuccinonitrile (2.7 g., 41% calc. on the azo-nitrile). The hot aqueous solution remaining in the flask was decanted, the tarry residue was repeatedly extracted with warm water, and the combined extracts were evaporated to dryness under diminished pressure. The resulting gum was crystallised from alcohol and, after removal of a little insoluble ammonium bromide, afforded succinimide (1.7 g., 20% calc. on the bromo-imide consumed; m. p. and mixed m. p. 124—125°).

The decomposition in the presence of *N*-bromosuccinimide of a dilute solution of $\alpha\alpha'$ -azoisobutyronitrile in carbon tetrachloride was also investigated but, owing to the lower temperature of the reaction mixture, no bromo-nitrile was formed.

Catalysed Brominations with N-Bromosuccinimide.—Toluene. The bromo-imide (10.8 g., 0.06 mole) was suspended in a solution of dimethyl $\alpha\alpha'$ -azoisobutyrate (0.135 g., 0.0006 mole) in toluene (8.5 ml., 0.08 mole) and carbon tetrachloride (20 ml.), and the whole was gently warmed on a gauze. After a short while a vigorous reaction set in; this was moderated by immersing the flask in ice-water, and the mixture was then refluxed for 30 minutes. After cooling, the precipitated succinimide (5.5 g., 90% calc. on the bromo-imide), m. p. and mixed m. p. 125°, was filtered off and washed with carbon tetrachloride. The filtrate and washings were combined

and distilled through a short column. Two fractions were obtained: (i) b. p. 89.5—91°/16 mm. (6.8 g.) and (ii) b. p. 100—115°/20 mm. (1.2 g.). The first fraction consisted of benzyl bromide (b. p. 197—198.5°/758 mm., 66% calc. on the bromo-imide); its identity was confirmed by conversion into benzyl β -naphthyl ether, m. p. and mixed m. p. 99—100°. Fraction (ii) consisted chiefly of benzylidene dibromide, for on hydrolysis with boiling dilute hydrochloric acid there was obtained benzaldehyde, identified by its 2:4-dinitrophenylhydrazone, m. p. and mixed m. p. 237—238°. The residue from the distillation was a black tar.

The experiment was repeated in the presence of inhibitors:

Inhibitor	Yield of benzyl bromide, %
Iodine, 0.0006 mole	36
Chloranil, 0.0012 mole	10

cycloHexene. A mixture of *cyclohexene* (30.3 ml., 0.3 mole), *N*-bromosuccinimide (10.8 g., 0.06 mole) and dimethyl $\alpha\alpha'$ -azoisobutyrate (0.12 g., 0.0005 mole) was gently warmed on a gauze. After a short while a violent reaction set in; this was moderated by immediately immersing the flask in ice-water. The mixture, which had remained colourless, was finally refluxed for 10 minutes and then was shown to contain no unchanged bromo-imide. After cooling, the precipitated succinimide (5.7 g., 93% calc. on the bromo-imide) was filtered off and washed with carbon tetrachloride. Distillation of the combined filtrate and washings through a short column afforded 3-bromocyclohexene (7.82 g., 75% calc. on the bromo-imide), b. p. 70—72°/30 mm.; Bedos and Ruyer (*Compt. rend.*, 1937, 204, 1350) give 71.5°/26 mm.; Berlande (*Bull. Soc. chim.*, 1942, 9, [v], 644) gives 80°/35 mm. The bromo-olefin was characterised by hydrolysis with cold aqueous sodium hydrogen carbonate (Berlande, *loc. cit.*) to *cyclohex-2-en-1-ol* which was identified by conversion into *cyclohex-2-enyl phenylcarbamate*, m. p. 107.5—108.5° either alone or in admixture with an authentic specimen (Waters, *J.*, 1939, 1807). The residue (1.1 g.) from the distillation was a dark oil which was not further investigated.

cycloHexene. A mixture of *cyclohexane* (64.7 ml., 0.6 mole), the bromo-imide (10.8 g., 0.06 mole), and dimethyl $\alpha\alpha'$ -azoisobutyrate (0.45 g.) was gently refluxed, and after 5 minutes a further quantity (0.2 g.) of the azo-ester (total, 0.003 mole) was added. Succinimide was gradually deposited and the solution became yellow. After a further 20 minutes the reaction appeared to be complete, and hydrogen bromide began to be evolved slowly; the mixture was then cooled and filtered. The solid, after being washed with carbon tetrachloride, was shown to contain 0.15 g. of unchanged bromo-imide. The combined filtrate was washed with dilute aqueous sodium hydrogen carbonate, dried, and fractionated; it yielded *cyclohexyl bromide* (b. p. 63°/18 mm., n_D^{20} 1.4920; 4.6 g., 48% calc. on the bromo-imide consumed). A redistilled sample was converted by the method of Marvel *et al.* (*J. Amer. Chem. Soc.*, 1925, 47, 3009) into *cyclohexylmercuric bromide*, m. p. 152° either alone or in admixture with a sample prepared from authentic *cyclohexyl bromide* (Grignard, Bellet, and Courtot, *Ann. Chim.*, 1919, 12, [ix], 367).

In another experiment, with *cyclohexane* (0.3 mole), the bromo-imide (0.06 mole), and the azo-ester (0.0015 mole), the yield of *cyclohexyl bromide* was 43%.

M. p.s and b. p.s are uncorrected; analyses are by Drs. Weiler and Strauss.

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