350. *Synthetic Aspects of Free-radical Addition. Part III.*[1] *Intramolecular Radical-addition Reactions*

By J. I. G. Cadogan, D. H. Hey, and S. H. Ong

From a study of the variations in type and concentration of solvent and of radical initiator, conditions have been established for radical-induced cyclisation in ethyl 2-acetylhept-6-enoate, ethyl 2-cyanohept-6-enoate, and diethyl pent-4-enylmalonate, to give derivatives of cyclohexane.

Recently, it was shown [2] that direct *C*-alkylation of malonic, acetoacetic, and cyanoacetic esters, acetylacetone, and related compounds can be readily achieved by a free-radical-induced addition reaction with a suitable olefin, thus:

$$RCH{:}CH_2 + \cdot CH(CO\cdot CH_3)\cdot CO_2Et \longrightarrow R\dot{C}H\cdot CH_2\cdot CH(CO\cdot CH_3)\cdot CO_2Et \quad (I)$$

$$R\dot{C}H\cdot CH_2\cdot CH(CO\cdot CH_3)\cdot CO_2Et + CH_3\cdot CO\cdot CH_2\cdot CO_2Et \longrightarrow RCH_2\cdot CH_2\cdot CH(CO\cdot CH_3)\cdot CO_2Et + \cdot CH(CO\cdot CH_3)\cdot CO_2Et \quad (i)$$

The reaction was extended in Part II [1] to embrace direct alkylation of acetic acid and its derivatives:

$$RCH{:}CH_2 + CH_3\cdot CO_2H \xrightarrow{(But O)_2} RCH_2\cdot CH_2\cdot CH_2\cdot CO_2H$$

Each of the above reactions involves homolytic scission of the α-C–H bond to give resonance-stabilised radicals, *e.g.*,

$$CH_3\cdot CO\cdot \dot{C}H\cdot CO_2Et \longleftrightarrow CH_3\cdot C(\dot{O})=CH\cdot CO_2Et \longleftrightarrow CH_2\cdot CO\cdot CH=C(\dot{O})\cdot OEt$$

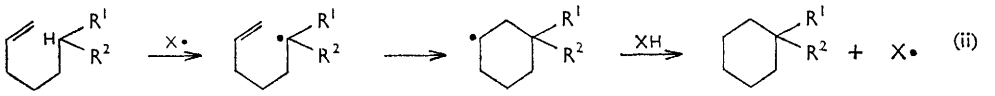
$$\cdot CH_2\cdot CO_2H \longleftrightarrow CH_2=C(\dot{O})\cdot OH$$

and it is relevant that good yields of the required 1 : 1 adducts were formed only when the ratio of addendum to olefin was high, *i.e.*, under conditions of low probability of removal of the intermediate chain-carrying free radical, *e.g.*, (I), by side-reactions such as dimerisation and disproportionation.

In this Paper, we describe results obtained in a logical extension of these investigations, namely, the radical-induced intramolecular cyclisation of compounds containing both an olefinic double bond and a suitably activated α-C–H bond, *e.g.*, pent-4-enyl-substituted acetoacetic (II: $R^1 = CO_2Et$; $R^2 = CO\cdot CH_3$), malonic (II: $R^1 = R^2 = CO_2Et$), and cyanoacetic (II: $R^1 = CN$; $R^2 = CO_2Et$) esters.

[1] Part II, Allen, Cadogan, and Hey, preceding Paper.
[2] Allen, Cadogan, Harris, and Hey, *J.*, 1962, 4468.

In theory, reaction of a free radical X· with the olefin (II) may proceed either (*a*) by addition to the double bond, followed by dimerisation, displacement, or disproportionation reactions, or (*b*) by abstraction of the α-hydrogen atom from the activated group $-CHR^1R^2$ to give an intermediate radical (III), which, in turn, can add to a new molecule of olefin,



(II) (III) (IV) (V)

a reaction which, if repeated, can give rise to a high-molecular-weight telomer. Alternatively, the radical (III) may undergo cyclisation to give radical (IV). The latter can then abstract hydrogen from a suitable source, XH, which may be a solvent molecule or another molecule of the starting compound (II).

From the foregoing discussion, it would be expected that reaction of radicals with the olefin (II), in the absence of a diluting solvent, would tend *not* to give high yields of ring-closed products, but rather to give telomeric products. The experiments described below were therefore designed to determine the optimum conditions for successful cyclisation of the pent-4-enyl derivatives (II).

While these investigations were in progress, Julia and his co-workers [3] disclosed, in a preliminary communication, that they had effected radical cyclisation of ethyl 2-cyano-hept-6-enoate by means of dibenzoyl peroxide in cyclohexane. They did not state, however, whether or not a catalytic quantity of peroxide was used, nor did they provide details of the dilution.

Reaction of diethyl pent-4-enylmalonate (II: $R^1 = R^2 = CO_2Et$) with benzoyl peroxide (5%) at 80° gave a high yield of telomeric products. The product of ring-closure, diethyl cyclohexane-1,1-dicarboxylate (V: $R^1 = R^2 = CO_2Et$), was not detected. Similar results were obtained when the reaction was carried out in benzene (2·0 mol) or chlorobenzene (10·0 mol). Ethyl 2-acetylhept-6-enoate (II: $R^1 = CO_2Et$; $R^2 = CO{\cdot}CH_3$) also gave telomeric products under similar conditions. A series of exploratory experiments was then carried out, in which the dilution of ethyl 2-acetylhept-6-enoate in chlorobenzene and the concentration of peroxide initiator were altered and the resulting ratio (*R*) of cyclic product to unreacted starting material was measured by means of gas–liquid chromatography (g.l.c.). Such a method of analysis did not reveal the extent of the formation of telomeric products; the ratio *R* referred only to the volatile fraction of the reaction mixture. The true yield of cyclic product could only be determined by isolation of the volatile fraction, followed by g.l.c. analysis. In this way, it was shown that (*a*) there was no appreciable cyclisation of ethyl 2-acetylhept-6-enoate (II; $R^1 = CO{\cdot}CH_3$; $R^2 = CO_2Et$) to ethyl 1-acetylcyclohexane-1-carboxylate (V: $R^1 = CO{\cdot}CH_3$; $R^2 = CO_2Et$) with a catalytic quantity (0·05—0·1 mol.) of initiator, and that (*b*) an increase in the proportion of initiator resulted in an increase in the proportion of the cyclised product in the volatile fraction, but even with 0·5 mol. of benzoyl perxide per mol. of ethyl 2-acetylhept-6-enoate in cyclohexane (20 mol.), *i.e.*, with one initiating radical per molecule of olefin, the olefin had not been consumed completely ($R = 0{\cdot}12$).

It was clear, therefore, that under these conditions the process was not a chain reaction, and that the intermediate radicals were being consumed in other ways. In normal free-radical addition reactions of olefins, such a situation is usually overcome by increasing the dilution, so that the probability of the chain-carrying free radical, $R\dot{C}H{\cdot}CH_2Y$, meeting the addendum, XY, is increased:

$$RCH{:}CH_2 + Y\cdot \longrightarrow R\dot{C}H{\cdot}CH_2Y \xrightarrow{XY} RCHX{\cdot}CH_2Y + Y\cdot$$

[3] (*a*) Julia, Surzur, and Katz, *Compt. rend.*, 1960, **251**, 1030; (*b*) Julia and Goffic, *ibid.*, 1962, **255**, 539, 714.

In intramolecular free-radical addition, however, the addendum and double bond are in the same molecule, and dilution in a solvent such as chlorobenzene leads to a decrease in the probability of successful chain-transfer to give ring-closure, which can only be achieved by the sequence (III) $\longrightarrow$ (IV) $\xrightarrow{(II)}$ (V) + (III). On the other hand, dilution in a solvent which is itself a good hydrogen-donor would be expected to lead to a higher yield of ring-closed product. In accord with this (Table 1), the use of increasing proportions of

TABLE 1

Radical cyclisation of ethyl 2-cyanohept-6-enoate (1 mol.) in cyclohexane, induced by benzoyl peroxide (0·5 mol.) at 80°

Cyclohexane (mol.)	75	150	225	300	600
Ethyl 1-cyanocyclohexanecarboxylate (% yield)	35	35	38	62	70

cyclohexane as solvent led to increasing conversions of ethyl 2-cyanohept-6-enoate (II: $R^1 = CN$; $R^2 = CO_2Et$) into ethyl 1-cyanocyclohexanecarboxylate (V: $R^1 = CN$; $R^2 = CO_2Et$). The latter was identified by comparison of its infrared (i.r.) spectrum and g.l.c. retention times, using two different columns, with those of an authentic sample, and by hydrolysis to cyclohexane-1,1-dicarboxylic acid. It is probable that cyclohexane enters into the reaction by providing, at least in part, an alternative source of the hydrogen atom needed for ring-closure to be effected [eqn. (ii): XH = cyclohexane].

Thus, a high degree of dilution with a participating solvent is necessary in order to reduce telomerisation and to increase the yield of the cyclic product. Under these conditions, the reactivity of the methine group in the olefin (II) must be critical in determining the tendency of the molecule to undergo cyclisation, because there is a possibility of competing addition of radicals derived from the solvent.* Thus, ethyl 2-acetylhept-6-enoate gave rise to only 8·5% of ethyl 1-acetylcyclohexanecarboxylate under the conditions found to be optimum for ring-closure of the α-cyano-analogue. Moreover, diethyl pent-4-enylmalonate, although it was consumed, gave no cyclic isomer under these conditions, whereas at a much higher concentration in cyclohexane there was g.l.c. evidence for the formation of diethyl cyclohexane-1,1-dicarboxylate (<20%). The order of reactivity of the compounds (II) in undergoing radical-induced cyclisations in high dilution in cyclohexane is therefore:

$$(\text{II: } R^1 = R^2 = CO_2Et) < (\text{II: } R^1 = CO{\cdot}CH_3;\ R^2 = CO_2Et) < (\text{II: } R^1 = CN;\ R^2 = CO_2Et).$$

This order corresponds to that obtained by Cadogan, Hey, and Sharp [4] from the results of competitive radical-addition reactions of diethyl malonate, ethyl acetoacetate, and ethyl cyanoacetate with oct-1-ene. The relative reactivities so obtained can be expressed as follows: diethyl malonate (1), ethyl acetoacetate (2·4), ethyl cyanoacetate (14), indicating that the presence of a cyano-group attached to the active methylene group leads to a relatively good yield of addition product. This may be due to the ease of removal of a methylenic (or methine) hydrogen atom and/or to a high reactivity towards an acyclic double bond of an α-cyano-substituted radical. The relative importance of these factors has yet to be determined.

Experiments in cyclohexane, with di-isopropyl peroxydicarbonate as initiator, which decomposes at a relatively low temperature (20—50°), gave cyclohexyl isopropyl carbonate

* This possibility has been exploited in certain circumstances (Cadogan, Hey, and Ong, following Paper).

[4] Cadogan, Hey, and Sharp, unpublished observation.

in good yield, indicating that induced decomposition of the peroxide by radicals derived from the solvent had probably occurred:

$$(Pr^iO{\cdot}CO_2)_2 \longrightarrow 2Pr^iO{\cdot}CO_2{\cdot} \longrightarrow 2Pr^iO{\cdot} + 2CO_2$$

$$Pr^iO{\cdot} + RH \longrightarrow Pr^iOH + R{\cdot}$$

$$R{\cdot} + (Pr^iO{\cdot}CO_2)_2 \longrightarrow R{\cdot}O{\cdot}CO{\cdot}OPr^i + Pr^iO{\cdot}CO_2{\cdot}$$

This observation parallels the results of McBay and Tucker,[5] who noted the formation of arylalkyl isopropyl carbonates during the decomposition of di-isopropyl peroxydicarbonate in cumene or *p*-cymene; *e.g.*, for cumene:

$$(Pr^iO{\cdot}CO_2)_2 + PhCMe_2{\cdot} \longrightarrow Pr^iO{\cdot}CO_2{\cdot} + Pr^iO{\cdot}CO{\cdot}O{\cdot}CMe_2Ph$$

It is noteworthy that unsymmetrical dialkyl carbonates have also been isolated [2] from the di-isopropyl peroxydicarbonate-induced reaction of oct-1-ene with addenda such as acetone, but, in this case, the route is different:

$$Pr^iO{\cdot}CO_2{\cdot} + R'CH{:}CH_2 \longrightarrow Pr^iO{\cdot}CO{\cdot}O{\cdot}CH_2{\cdot}\dot{C}HR'$$

$$Pr^iO{\cdot}CO{\cdot}O{\cdot}CH_2{\cdot}\dot{C}HR' + RH \longrightarrow Pr^iO{\cdot}CO{\cdot}O{\cdot}CH_2{\cdot}CH_2R' + R{\cdot}$$

Experimental

All melting points are corrected.

Gas–Liquid Chromatography (*g.l.c.*).—Measurements were carried out with a Pye Argon Chromatograph, fitted with a β-ray ionisation detector, using argon carrier-gas, and the following 4 ft. columns were used, the choice of column depending on the type of compound to be analysed: (i) APL column, packed with 10% Apiezon L on Celite 545; (ii) APM column, packed with 10% Apiezon M on Celite 545; and (iii) PEGA column, packed with 10% poly(ethyleneglycol adipate) on Celite 545. The relative retention times of separated components are given in parentheses, where relevant.

Preparation of Compounds.—Tetrahydrofurfuryl chloride, b. p. 68—72°/40 mm., n_D^{22} 1·4542, and hence pent-1-en-5-ol, b. p. 130—139°, were prepared by the methods of Brooks and Snyder,[6] who reported b. p.s 47—48°/15 mm. and 134—137°, respectively.

5-Bromopent-1-ene.—Phosphorus tribromide (53·4 g., 0·20 mole) was added dropwise to a rapidly stirred mixture of pent-1-en-5-ol (38·9 g., 0·45 mole) and pyridine (11 g., 0·14 mole), during 70 min., at −25 to −30°. The suspension was poured on to ice and extracted with chloroform (3 × 100 ml.). The extract was washed with 10% aqueous sodium hydroxide solution (100 ml.), water (3 × 50 ml.), and dried ($CaCl_2$). After evaporation of the solvent, the residue was distilled to give: (*a*) 5-bromopent-1-ene (13·6 g., 20%), b. p. 128—131°, n_D^{25} 1·4620 (lit.,[7] b. p. 125—126°, n_D^{20} 1·4632); and (*b*) *di(pent-4-enyl) phosphonate*, b. p. 156—158°/15 mm., n_D^{21} 1·4514, $\nu_{max.}$ 3472 (P–OH), 2427 (P–H), 1639 (C=C), and 1250 (P=O) cm.$^{-1}$ (Found: C, 55·0; H, 9·2. $C_{10}H_{19}O_3P$ requires C, 55·0; H, 8·7%).

Diethyl Pent-4-enylmalonate. Diethyl malonate (27·09 g., 0·17 mole) was added to a solution of sodium (4·07 g., 0·18 g.-atom) in dry ethanol (60 ml.), followed by the dropwise addition of 5-bromopent-1-ene (22·8 g., 0·15 mole). When the addition of the halide was complete, the reaction mixture was boiled under reflux overnight, then cooled, and poured into aqueous calcium chloride solution (200 ml.). The product was extracted with ether (3 × 200 ml.), and the extract washed with water (2 × 50 ml.) and dried ($CaCl_2$). After removal of the ether, the residue yielded, on distillation, diethyl pent-4-enylmalonate (21·1 g., 62%), b. p. 126—127°/10 mm., (lit.,[8] b. p. 130—136°/14 mm.) n_D^{20} 1·4330, $\nu_{max.}$ 1733 (ester C=O) and 1642 (C=C) cm.$^{-1}$ (Found: C, 63·3; H, 9·2. Calc. for $C_{12}H_{20}O_4$: C, 63·1; H, 8·8%).

Ethyl 2-Acetylhept-6-enoate.—This was prepared similarly, from ethyl acetoacetate (13·0 g., 0·1 mole) and 5-bromopent-1-ene (16·4 g., 0·11 mole). When the halide has been added, the reaction mixture was heated under reflux overnight with stirring. The mixture was cooled and the sodium bromide which separated was filtered off and washed with ethanol. The filtrate

[5] McBay and Tucker, *J. Org. Chem.*, 1954, **19**, 869.
[6] Brooks and Snyder, *Org. Synth.*, 1955, Coll. Vol. III, p. 698.
[7] Kharasch and Fuchs, *J. Org. Chem.*, 1944, **9**, 370.
[8] Gaubert, Linstead, and Rydon, *J.*, 1937, 1971.

and washings were concentrated, and further distillation of the residue gave *ethyl 2-acetylhept-6-enoate* (8·19 g., 41%) b. p. 113—114°/10 mm., n_D^{19} 1·4458, $\nu_{max.}$ 1647 (C=C), 1721 (ketone C=O), and 1742 (ester C=O) cm.$^{-1}$ (Found: C, 66·9; H, 8·8. $C_{11}H_{18}O_3$ requires C, 66·6; H, 9·1%).

Ethyl 2-Cyanohept-6-enoate.—Similarly, this compound was prepared from sodium (2·61 g., 0·11 g.-atom) dissolved in ethanol (60 ml.), ethyl cyanoacetate (11·30 g., 0·1 mole), and 5-bromopent-1-ene (16·4 g., 0·11 mole). The reaction mixture was boiled under reflux for 23 hr., the sodium bromide was filtered off, and the filtrate, on distillation, gave ethyl 2-cyanohept-6-enoate (6·43 g., 36%) b. p. 152—153°/30 mm., $n_D^{24.5}$ 1·4418 (lit.,[3a] b. p. 131—132°/14 mm., n_D^{20} 1·4430), $\nu_{max.}$ 1642 (C=C), 1739 (ester C=O), and 2272 (C≡N) cm.$^{-1}$ (Found: C, 65·9; H, 8·4. Calc. for $C_{10}H_{15}NO_2$: C, 66·3; H, 8·3%).

Diethyl (5-Bromopentyl)malonate. Diethyl malonate (192 g., 1·2 moles) was added to sodium (7·74 g., 0·34 g.-atom) dissolved in sodium ethoxide-dried ethanol (100 ml.). To this rapidly stirred mixture, 1,5-dibromopentane (138 g., 0·6 mole) was added. After the solution had been heated under reflux with stirring for 4 hr., it was cooled. The sodium bromide was filtered off, washed with ether (100 ml.), and the washings were added to the main solution. Fractional distillation gave diethyl (5-bromopentyl)malonate (38·27 g., 37%), b. p. 127—129°/0·3 mm., n_D^{20} 1·4598 (lit.,[9] b. p. 144—145°/1·5 mm., n_D^{20} 1·4603.), $\nu_{max.}$ 1742 cm.$^{-1}$ (ester C=O).

Ethyl 2-Acetyl-7-bromoheptanoate.—This was prepared similarly, from ethyl acetoacetate (156 g., 1·2 moles) and 1,5-dibromopentane (138 g., 0·6 mole). Reaction occurred on warming, and the mixture was boiled under reflux for 5 hr. The usual treatment gave *ethyl 2-acetyl-7-bromoheptanoate* (57·46 g., 61%), b. p. 112—114°/0·1 mm., $n_D^{19.5}$ 1·4700, $\nu_{max.}$ 1645 (C=C in the enolic form), 1715 (ketone C=O), and 1739 (ester C=O) cm.$^{-1}$ (Found: C, 47·8; H, 7·2. $C_{11}H_{19}BrO_3$ requires C, 47·3; H, 6·9%).

Ethyl 7-Bromo-2-cyanoheptanoate.—Reaction occurred on shaking a mixture of ethyl 2-cyanoacetate (67·8 g., 0·6 mole) and 1,5-dibromopentane (68·9 g., 0·3 mole) in ethanolic sodium methoxide, the mixture then being heated under reflux for 4 hr. with stirring. The usual treatment gave *ethyl 7-bromo-2-cyanoheptanoate* (11·33 g., 27%), b. p. 126—134°/0·2 mm., n_D^{21} 1·4703, $\nu_{max.}$ 2283 (C≡N) and 1742 (ester C=O) cm.$^{-1}$ (Found: C, 46·3; H, 5·7. $C_{10}H_{16}BrNO_2$ requires C, 45·8; H, 6·1%).

Diethyl Cyclohexane-1,1-dicarboxylate.—Diethyl (5-bromopentyl)malonate (38·27 g., 0·12 mole) was added to a solution of sodium (3·0 g., 0·13 g.-atom) in ethanol (75 ml.). After the reaction mixture had been boiled under reflux for 2 hr., it was cooled. The sodium bromide was filtered off and washed with ether (50 ml.), the washings being added to the main solution. After the solution had been concentrated, water (100 ml.) was added and the mixture extracted with ether (3 × 150 ml.) and dried ($MgSO_4$). After the removal of the ether, distillation of the residue gave diethyl cyclohexane-1,1-dicarboxylate (19·45 g., 69·4%), b. p. 136—137°/16 mm., $n_D^{24.5}$ 1·4468 (lit.,[9] b. p. 100°/2 mm., n_D^{20} 1·4482), $\nu_{max.}$ 1718 cm.$^{-1}$ (ester C=O) (Found: C, 63·3; H, 8·9. Calc. for $C_{12}H_{20}O_4$: C, 63·1; H, 8·8%). Hydrolysis with aqueous alcoholic potassium hydroxide gave cyclohexane-1,1-dicarboxylic acid, m. p. 175—176° (decomp.) [lit.,[10] m. p. 176° (decomp.)]. Decarboxylation gave cyclohexanecarboxylic acid (*S*-benzylisothiouronium salt, m. p. 155·5—156°; lit.,[11] m. p. 155—156°).

Ethyl 1-Acetylcyclohexanecarboxylate.—Similarly, this compound was obtained from ethyl (5-bromopentyl)acetoacetate (52·7 g., 0·19 mole). The reaction mixture was heated under reflux for 2½ hr. The usual treatment gave *ethyl 1-acetylcyclohexanecarboxylate* (9·73 g., 26%), b. p. 123°/12 mm., $n_D^{24.5}$ 1·4505, $\nu_{max.}$ 1727 (ketone C=O) and 1745 (ester C=O) cm.$^{-1}$ (Found: C, 66·3; H, 9·6. $C_{11}H_{18}O_3$ requires C, 66·6; H, 9·1%).

Ethyl 1-Cyanocyclohexanecarboxylate.—Similarly, this compound was prepared from ethyl (5-bromopentyl)-2-cyanoacetate (10 g., 0·038 mole). The reaction mixture was boiled under reflux for 2½ hr. and then worked-up in the usual manner, to give ethyl 1-cyanocyclohexanecarboxylate (3·78 g., 55%), b. p. 126°/12 mm., $n_D^{23.5}$ 1·4518 (lit.,[3] b. p. 121°/18 mm., n_D^{21} 1·4488), $\nu_{max.}$ 2262 (C≡N) and 1742 (C=O) cm.$^{-1}$ (Found: C, 66·0; H, 8·8. Calc. for $C_{10}H_{15}NO_2$: C, 66·3; H, 8·3%).

Reactions of Ethyl 2-acetylhept-6-enoate (Carried Out in the Presence of Dry Air).—(i) *Reaction in chlorobenzene (5 mol.), in the presence of di-t-butyl peroxide (0·1 mol.).* A mixture of ethyl

[9] Gol'mov, *Zhur. obshchei Khim.*, 1952, **22**, 1944.
[10] Wightman, *J.*, 1926, 2541.
[11] Tinker, *J. Amer. Chem. Soc.*, 1951, **73**, 4050.

2-acetylhept-6-enoate (0·50 g., 2·5 mmoles), chlorobenzene (1·4 g., 12·5 mmoles), and di-t-butyl peroxide (0·042 g., 0·29 mmole) was boiled under reflux for 93 hr. The solution turned yellow. Examination of the reaction mixture by g.l.c. (APL at 150°; flow, 60 ml./min.) showed that the main component was ethyl 2-acetylhept-6-enoate and that the other component was ethyl 1-acetylcyclohexanecarboxylate (*ca.* 3%). Reactions carried out with 20 or 75 mol. of chlorobenzene gave similar results.

(ii) *Reactions in cyclohexane, in the presence of dibenzoyl peroxide.* A series of experiments was carried out to determine the conditions under which ethyl 2-acetylhept-6-enoate would undergo intramolecular addition to form ethyl 1-acetylcyclohexanecarboxylate. A typical experiment was as follows. A mixture of ethyl 2-acetylhept-6-enoate (0·50 g., 2·5 mmoles), cyclohexane (1·09 g., 13 mmoles), and benzoyl peroxide (0·06 g., 0·25 mmole) was kept at 80° for 93 hr. On cooling, two layers were formed, which became homogeneous when chloroform (1 ml.) was added. The solution was analysed by g.l.c. (APL at 150°; flow, 60 ml./min.), and the ratio, *R*, of the peak height due to ethyl 1-acetylcyclohexanecarboxylate to that due to ethyl 2-acetylhept-6-enoate, was determined. In this case, *R* was 0·04.

The results of this and related reactions are given in Table 2.

TABLE 2

Intramolecular addition of ethyl 2-acetylhept-6-enoate (1 mol.) in cyclohexane, induced by benzoyl peroxide at 80°

Cyclohexane (mol.)	5 *	20 *	20 †	10 †
Benzoyl peroxide (mol.)	0·1	0·1	0·5	1·0
R ‡	0·04	0·04	0·12	0·19

* For 93 hr. † For 66 hr. ‡ *R* does not give the true yield of the cyclised product, as the quantity of polymeric material is not taken into consideration.

(iii) *Intramolecular addition of ethyl 2-acetylhept-6-enoate (1·0 mol.) in cyclohexane (600 mol.), induced by benzoyl peroxide (0·5 mol.).* A mixture of ethyl 2-acetylhept-6-enoate (1·0 g., 5 mmoles), cyclohexane (252 g., 3000 mmoles), and benzoyl peroxide (0·605 g., 2·5 mmoles) was boiled under reflux for 24 hr. The reaction mixture was shaken with saturated aqueous sodium hydrogen carbonate solution (2 × 20 ml.) and with water (20 ml.) and dried ($MgSO_4$). After removal of the solvent, the residue was distilled to give a mixture (0·389 g.), b. p. 116—118°/11 mm. Examination by g.l.c. (PEGA at 150°; flow, 25 ml./min.) gave ethyl 2-acetylhept-6-enoate (75% of the mixture, *i.e.*, 0·29 g.) and ethyl 1-acetylcyclohexanecarboxylate (15·5% of the mixture, *i.e.*, 0·06 g.). Analysis under different conditions (APM at 150°; flow, 60 ml./min.) also gave these two compounds. The yield was *ca.* 8·5%, based on the quantity of ethyl 2-acetylhept-6-enoate consumed.

Reactions of Diethyl Pent-4-enylmalonate (Carried Out in the Presence of Dry Air).—(i) *Without solvent.* A mixture of diethyl pent-4-enylmalonate (5·0 g., 22 mmoles) and benzoyl peroxide (0·27 g., 1·1 mmoles) was kept at 80° for 24 hr. When cold, the reaction mixture set to a glass, which was dissolved in chloroform, washed with saturated aqueous sodium hydrogen carbonate solution (3 × 25 ml.) and with water (2 × 20 ml.), and dried ($MgSO_4$). After removal of the chloroform, distillation of the residue yielded: (*a*) (0·88 g.), b. p. 40—98°/15 mm., n_D^{20} 1·4120; (*b*) (0·25 g.), b. p. 72—78°/0·02 mm., n_D^{21} 1·4440; and (*c*) a residue (4·39 g.). Fraction (*a*) consisted mainly of diethyl malonate, probably present as an impurity in the starting material. I.r. examination of fraction (*b*) indicated that it probably had the structure $PhCO_2{\cdot}[CH_2]_5{\cdot}CH(CO_2Et)_2$ [$\nu_{max.}$ 1733 (ester C=O), 1637 and 1600 (aromatic C=C) cm.$^{-1}$]. Analysis by g.l.c. (APL at 175°; flow, 60 ml./min.) showed that diethyl cyclohexane-1,1-dicarboxylate was absent. A similar result was obtained by using benzene as solvent.

(ii) *With cyclohexane as the solvent.* A series of experiments, on a small scale, was carried out to determine the conditions under which diethyl pent-4-enylmalonate would undergo intramolecular addition to form diethyl cyclohexane-1,1-dicarboxylate. A typical experiment was as follows. A mixture of diethyl pent-4-enylmalonate (0·575 g., 2·5 mmoles), cyclohexane (4·28 g., 51 mmoles), and benzoyl peroxide (0·30 g., 1·25 mmoles) was kept at 80° for 66 hr. Without isolation of the products by distillation, the reaction mixture was analysed by g.l.c. (APL at 169°; flow, 50 ml./min.) and the ratio, *R*, of the peak height due to diethyl cyclohexane-1,1-dicarboxylate to that due to unreacted diethyl pent-4-enylmalonate, was determined. In this case, *R* was 1·08.

The results of this and related reactions are given in Table 3.

TABLE 3

Intramolecular addition of diethyl pent-4-enylmalonate (1 mol.) in cyclohexane, induced by benzoyl peroxide at 80°

Cyclohexane (mol.)	20 *	20 *	10 *	7 †
Benzoyl peroxide (mol.)	0·5	1·0	1·0	1·0
R ‡	1·08	3·5	5·4	9·4

* For 66 hr. † For 49 hr. ‡ *R* does not give the true yield of the cyclised product, as the quantity of polymeric material is not taken into consideration.

Using the apparent optimum conditions, the same reaction was repeated on a much larger scale, as is now described. A mixture of diethyl pent-4-enylmalonate (5·7 g., 25 mmoles), cyclohexane (14·8 g., 175 mmoles), and benzoyl peroxide (6·1 g., 25 mmoles) was heated under reflux for 66 hr. Most of the cyclohexane (11·06 g.) was distilled off, and ether (25 ml.) was added. The ethereal solution was washed with saturated aqueous sodium hydrogen carbonate solution (2 × 20 ml.) and dried ($MgSO_4$). The solution was filtered, the drying agent was washed with chloroform, and the washings were added to the main fraction. After removal of the solvents, distillation of the residue yielded: (*a*) (1·62 g.), b. p. 108—130°/12 mm.; (*b*) (0·73 g.), b. p. 86—134°/0·1 mm.; and (*c*) a residue (6·56 g.). Analysis by g.l.c. (APM at 150°; flow, 100 ml./min.) indicated that fraction (*a*) consisted mainly of diethyl cyclohexane-1,1-dicarboxylate (82·4%, *i.e.*, 1·3 g.), and that fraction (*b*) contained six components, of which diethyl cyclohexane-1,1-dicarboxylate formed 16% (*i.e.*, 0·12 g.). The total yield of this compound was 25%, based on ethyl pent-4-enylmalonate added. With cyclohexane in large excess (600 mol.), none of this compound was obtained.

Reaction of Diethyl Pent-4-enylmalonate in Cyclohexane, Induced by Di-isopropyl Peroxydicarbonate (Carried Out in the Presence of Dry Air).—A mixture of diethyl pent-4-enylmalonate (0·57 g., 2·5 mmoles), cyclohexane (4·28 g., 51 mmoles), and di-isopropyl peroxydicarbonate (1·13 g., 5·5 mmoles) was kept at 50° for 15 hr. and then the bath temperature was raised to 80° for ½ hr. Examination of the reaction mixture by g.l.c. (PEGA at 138°) indicated that both the starting material and the expected product, diethyl cyclohexane-1,1-dicarboxylate, were absent. Fractional distillation of the mixture gave: (*a*) cyclohexane (3·04 g.), b. p. 70—82°/760 mm.; (*b*) (0·42 g.), b. p. 98°/15 mm., n_D^{19} 1·4408; (*c*) (0·068 g.), b. p. 98—122°/15 mm.; and (*d*) a residue (0·67 g.). Fraction (*b*), $\nu_{max.}$ 1739 $cm.^{-1}$ (carbonate C=O) (Found: C, 65·1; H, 9·5. Calc. for $C_{10}H_{18}O_3$: C, 64·5; H, 9·7%), is considered to be cyclohexyl isopropyl carbonate. Hydrolysis of a portion with methanolic potassium hydroxide solution, followed by acidification, gave a vigorous evolution of carbon dioxide. Work-up of the solution gave cyclohexanol, b. p. 160—164° (correct i.r. spectrum; 3,5-dinitrobenzoate, m. p. and mixed m. p. 112°).

Reactions of Ethyl 2-Cyanohept-6-enoate (Carried Out in the Presence of Dry Air).—(i) A mixture of ethyl 2-cyanohept-6-enoate (0·45 g., 2·5 mmoles), cyclohexane (4·28 g., 51 mmoles), and benzoyl peroxide (0·30 g., 1·25 mmoles) was kept at 80° for 67 hr. A resinous deposit resulted, some of which dissolved when chloroform (1 ml.) was added. Examination of the reaction mixture by g.l.c. (APL at 150°; flow, 60 ml./min., and PEGA at 150°; flow, 30 ml./min.) showed that the starting material had reacted completely and that ethyl 1-cyanocyclohexanecarboxylate was formed.

(ii) A series of experiments was carried out to determine the optimum conditions under which ethyl 2-cyanohept-6-enoate would undergo intramolecular addition to form ethyl 1-cyanocyclohexanecarboxylate. A typical experiment was as follows. A mixture of ethyl 2-cyanohept-6-enoate (0·90 g., 5 mmoles), cyclohexane (126 g., 1500 mmoles), and benzoyl peroxide (0·60 g., 2·5 mmoles) was boiled under reflux for 24 hr. The solution was then shaken with saturated aqueous sodium hydrogen carbonate solution (2 × 10 ml.) and with water (10 ml.) and dried ($MgSO_4$). The residue, left after removal of the cyclohexane, was distilled to give ethyl 1-cyanocyclohexanecarboxylate (0·56 g., 62%), b. p. 115—117°/10 mm., $n_D^{17·5}$ 1·4568. The i.r. spectrum was identical with that of an authentic specimen [$\nu_{max.}$ 2262 (C≡N), 1742 (ester C=O) $cm.^{-1}$]. A portion of the product (0·4 g.) was hydrolysed with aqueous sodium hydroxide solution to give cyclohexane-1,1-dicarboxylic acid, m. p. *ca.* 150—170°; this was decarboxylated at 190—200° to give cyclohexanecarboxylic acid (*S*-benzylisothiouronium salt. m. p. 154°, mixed m. p. 155°).[11]

The results of this and related reactions are given in Table 1.

[*Note added in proof.*—Full details have now been published by Julia and his co-workers of their work on radical cyclisation reactions with α-cyano-esters (*Bull. Soc. chim. France*, **1965**, 1106, 1109, 1116, 1122, 1129). In the reaction with ethyl 2-cyanohept-6-enoate they also used cyclohexane in large excess and an appreciable quantity of benzoyl peroxide. Their yield of ethyl 1-cyanocyclohexanecarboxylate was 51%.]

Thanks are accorded to the Government of the United Kingdom for the award of a Commonwealth Scholarship to S. H. O.

KING'S COLLEGE, UNIVERSITY OF LONDON, STRAND, LONDON W.C.2.

[Present address (J. I. G. C.): ST. SALVATOR'S COLLEGE, UNIVERSITY OF ST. ANDREWS, ST. ANDREWS, FIFE, SCOTLAND.]

[*Received, July 1st*, 1964.]