FREE RADICAL CYCLIZATIONS, XVII. MECHANISTIC STUDIES

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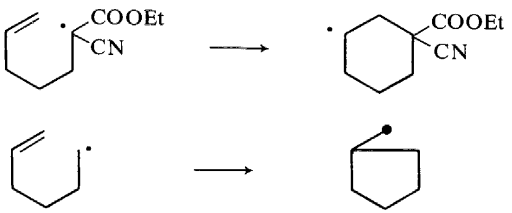
ABSTRACT

Free radical cyclizations of the 4-phenylbutyl radical and analogues carrying naphthyl and vinyl groups instead of phenyl have been studied. A typical reaction scheme is given below involving closures to five- and six-membered rings. Competition rate studies for the various types of ring closure were performed with deuterated analogues. The results can be used as an efficient mechanistic tool for other radical processes, as exemplified for the Kornblum reaction between α-substituted *p*-nitrobenzyl chlorides with the anion of benzylcyanide in a two-phase system. The nature of (cyclic) byproducts supports and confirms the radical chain mechanism for such substitutions.

(1) MECHANISM OF FREE RADICAL CYCLIZATION THROUGH AROMATIC SUBSTITUTION

The large amount of information produced by several groups of investigators has led to some understanding of the mechanism of free radical cyclizations through addition[1]. The problem of the size of the ring which is formed arose early: we began these investigations with heavily substituted resonance-stabilized radicals (cyanoesters) which gave



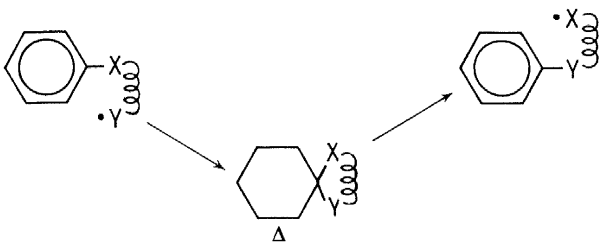
in what seemed a reasonable (Kharasch-like) addition the cyclohexane derivative. But when the unsubstituted hexenyl radical was investigated by R. C. Lamb[15] (and a number of other groups), it cyclized to methyl cyclopentane. It turned out that this is a case of kinetic versus thermodynamic control of a chemical reaction. The cyclization of the hexenyl radical is irreversible. Therefore the formation of a cyclopentane ring must be kinetically favoured. On the other hand, the isomeric cyanoester radicals can be equilibrated in cyclization conditions. The major (sometimes exclusive) product of the

equilibration (or the cyclization) is the more stable cyclohexane derivative (less steric strain in the ring; secondary radical more stable than primary).

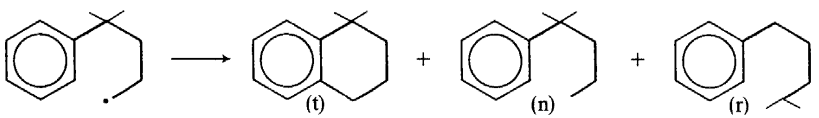
Inhibition of the reverse (reopening) reaction by lowering the temperature or adding efficient hydrogen donors increases the proportion of cyclopentane products formed. This confirms that even in the case of stabilized radicals the cyclopentane derivatives are formed more rapidly than the cyclohexanes, and this of course requires explanation. We shall come back to this point presently.

The cyclizations by homolytic aromatic substitution had not, so far, been investigated in this respect. Since it is now firmly established that the first step in homolytic aromatic substitutions is an addition step, there is an obvious similarity between the two processes (a) and (b). The question then arose of a competition between Ar_15 and Ar_26 cyclizations analogous to the formations of cyclopentane and cyclohexane rings above. In this case, unlike the preceding one, obviously the Ar_15 cyclization, if it occurs at all, must be reversible, since the final products are tetralin derivatives; but can something be said about the relative rates of the two processes?

The literature contains a few examples of rearrangements which have been rationalized by postulating the spiro intermediates shown; most of the systems investigated were heteroatomic, but two cases of carbon compounds deserve special mention.



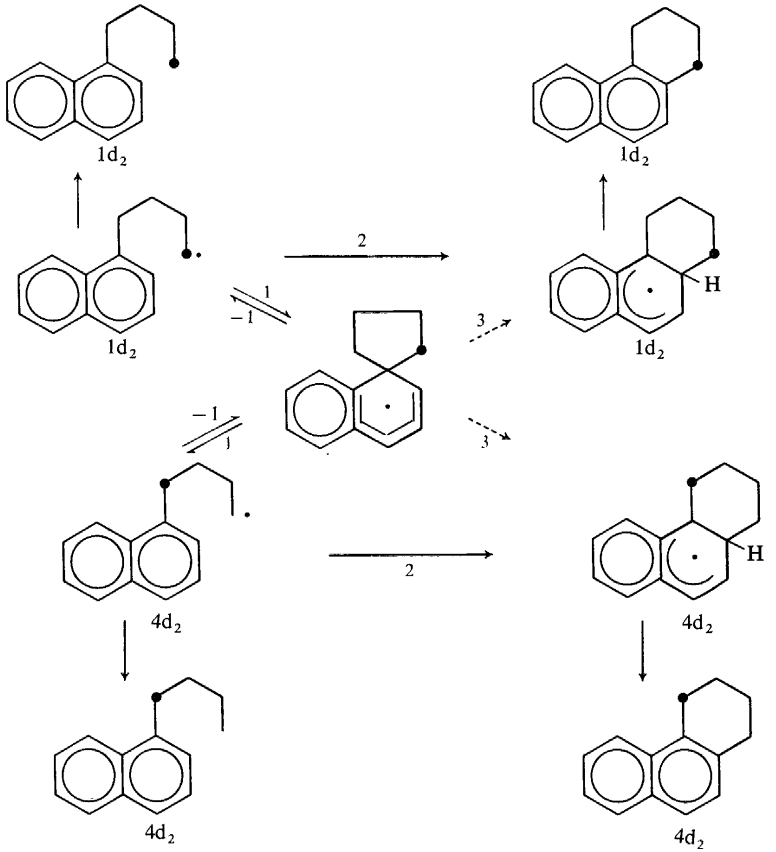
As early as 1956 Winstein and his group[2] discussed the Ar_15/Ar_26 competition in the case of the 4-phenyl-4-methyl-pent-1-yl radical which led to the 'normal' dimethyl tetralin (t) and both the normal (n) and the rearranged



(r) open chain hydrocarbons. More recently Hey and his colleagues[3], investigating diazotized *o*-aminobenzanilides, found (1) both normal and rearranged phenanthridones and (2) a spiro dimer.

There is therefore little doubt that Ar_15 cyclization indeed competes with Ar_26.

In order to get information on this competition we had to have a symmetrical chain—that is a n-butyl chain—and in order to see what had happened it had to be labelled. We chose deuterium labelling for practical reasons, both in the synthesis of starting materials and in the investigation of reaction products[4].



In order to 'label' the ring carbon atoms we chose to work with a naphthalene ring with which the methylenes α to the ring in the 1 and 2 positions are readily distinguished by n.m.r.

We first generated the isometrically labelled naphthylbutyl radicals $1d_2$ and $4d_2$ by pyrolysis of the corresponding labelled homologous acyl peroxides in boiling benzene. Both radicals gave the two isomeric tetrahydrophenanthrenes (THP). A symmetrical (most likely the spiro radical) intermediate is therefore involved. However, the proportions of the two isomeric compounds are not identical but symmetrical: 80/20, 20/80. A secondary isotope effect in the spiro radical is unlikely. The most reasonable explanation is that the cyclized tetrahydrophenanthrene is formed by two competing routes: a scrambling one passing through the spiro intermediate accounting

for 40 per cent of the product and a direct non-rearranging one accounting for the remaining 60 per cent.

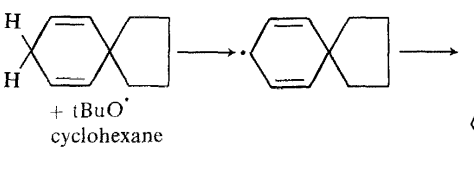
Now the question arises: does the spiro intermediate lead to THP directly through a free radical rearrangement or does it open up back to the starting radical (half normal and half rearranged)? It must be noted that free radical 1,2-rearrangements have not been observed so far (except recently in the case of the 1-phenyl-5-hexenyl radical[37c]). This is in agreement with the high energy to be expected of a bridging carbon radical where the extra electron would have to be accommodated in an antibonding orbital.

If the Ar_15 radical gets opened back to the naphthylbutyl radical, we should expect some scrambling in the open chain compounds; these include naphthylbutane and naphtylbutene together with 1,8-dinaphthyloctane and 1-naphthylbutyl-1-naphthyl valerate. In benzene, however, none of these compounds was rearranged to an appreciable extent.

Since the bridged radical was not appealing, we reasoned that the open chain products could have been formed in cage reactions and that the radicals escaping the cage cyclized faster than they abstracted hydrogen from the solvent. In cyclohexane, a better hydrogen donor, very much the same results were obtained with the open chain compound still not rearranged.

In benzene containing tributyltin hydride, however, very little tetrahydrophenanthrene (0.2 per cent) was formed, but the yield of naphthylbutane was now 19 per cent and this contained 9 per cent of the rearranged isomer. Therefore 18 per cent of the naphthylbutane has been formed via the symmetrical intermediate, which establishes the feasibility of route (1, − 1, 2).

Confirmatory evidence for the reopening of the spirocyclohexadienyl radicals was obtained by heating the spirocyclohexadiene hydrocarbon shown, with di-t-butyl peroxide. Both n-butylbenzene and tetralin were formed[5].



Yields, per cent	
140°	200°
22	35
19	26

Hoping to observe in the same experiment rearrangement of both the cyclized and open chain products, we reduced the naphthylbutyl chlorides by tributyltin hydride (equimolecular). Two experiments were carried out: one at 0.1 M, the other at 0.01 M in boiling benzene: The results are as shown in *Table 1*.

The main results are: (1) both the naphthylbutane and the tetrahydrophenanthrene are rearranged; (2) the yield of naphthylbutane drops sharply

Table 1. Reduction of naphthylbutyl chlorides by Bu_3SnH

	Naphthylbutane		Tetrahydrophenanthrene		
	% yield	normal/rearr.	% yield	normal/rearr.	Pleiadane
0.1 M	60	94/6	2.6	83/17	0.6
		12		**34**	
0.01 M	26	93/7	4.7	80/20	1.4
		14		**40**	

when dilution increases, which was to be expected, since the idea in diluting was to decrease the immediate scavenging of the newly formed naphthylbutyl radical by the tin hydride. The yield of tetrahydrophenanthrene is nearly doubled by the dilution but is still very small.

Now the scrambling of the label in the naphthylbutane, although small, shows that the reopening of the spiro radical indeed occurs under the reaction conditions. In fact, out of 100 molecules of primary radical ending up as naphthylbutane 12 have been scrambled through Ar_15. This shows that the rate of Ar_15 ring closure is not negligibly small compared with the velocity of the hydrogen transfer step. Since this has been shown by Carlsson and Ingold[33] to have a rate constant of 10^6 l mol^{-1} s^{-1} with 0.1 M Bu_3SnH, the rate constant k_{c_5} will be roughly

$$(12/88)10^6 \times 0.1 = 10^4\ s^{-1}$$

This is in good agreement with the value of 5×10^4 calculated by Kochi and his colleagues[6, 7] for the ring closure of 4-phenylbutyl radical in the presence of cupric salts by comparing the ratio of tetralin with that of naphthylbutene. In that case Ar_15 and Ar_26 were not distinguished but reopening might be expected to be prevented by rapid oxidation of the cyclohexadienyl radical to a carbenium ion (followed by rearrangement; see below). It is somewhat puzzling that the scrambling did not increase very much when dilution increased. In this case, however, the formation of unidentified byproducts increased seriously. These appear not to be scrambled (in n.m.r.).

It might at first sight seem surprising that the amount of scrambling in the tetrahydrophenanthrene (34–40 per cent) was higher than that in the naphthylbutane (12–14 per cent). It should be pointed out, however, that the scrambling in the naphthylbutane reflects (but is not equal to) the ratio of the velocity v_1 of the Ar_15 cyclization step over that of hydrogen transfer (v_H):

$$\frac{v_1}{v_H} = \frac{12}{88} \# \frac{14}{100}$$

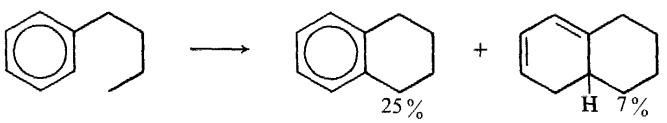
whereas the scrambling in the tetrahydrophenanthrene reflects the ratio of the velocities of Ar_15 and Ar_26 cyclization steps:

$$\frac{v_1}{v_2} = \frac{34}{66} \# \frac{52}{100}$$

The higher scrambling in the second case means that v_2 is smaller than v_H, which is not unexpected. In fact, the ratio 52/14 might reflect in some way the

ratio of these two processes. Moreover the scrambling in the THP is very much the same in this experiment as in the simple pyrolysis of the acyl peroxide—that is, out of 100 molecules ending up as THP about 40 have followed the scrambling route, which means if one considers the loss of scrambled molecules through hydrogen transfer after reopening of Ar_15, that the Ar_15 ring closure is definitely faster than the Ar_26.

The above ratio cannot be considered to be an accurate value of the rate ratio v_1/v_2 for another reason. In the non-identified fractions several cyclohexadienyl derivatives were detected by n.m.r. and g.l.c.–mass spectrometry. Very recently Doyle and his colleagues[8] have isolated such derivatives in the pyrolysis of the homologous peresters in benzene.



A more accurate value of the rate ratio of the Ar_15 and Ar_26 ring closure was obtained when the reopening of cyclohexdienyl radicals was prevented by rapid oxidation[9].

We used lead tetra-acetate oxidation of the isomerically labelled naphthyl valeric acids. It is known that in this sort of reaction a primary radical is not efficiently oxidized by lead(IV), whereas cyclohexadienyl radicals are[10]. It is also known that spiro cyclohexadienyl cations do not open up again but go over to tetralin derivatives[11].

The reaction mixture is much cleaner and contains 46 per cent THP.

Table 2. Oxidation of naphthyl valeric acid with lead tetra-acetate

Naphthylbutane	THP		Pleidane
	%	normal/rearr.	
—	46	65/35 **70**	5

The good yield of tetrahydrophenanthrene and the absence of open chain compound agree with efficient oxidative trapping of the cyclohexadienyl radicals (spiro and tetralinyl) by LTA. We therefore suggest that in this case the proportion of scrambling *is* the ratio of the two rate constants, $v_1/v_2 = 70/30$.

We see that, as in the addition to double bonds, the aromatic cyclization Ar_15 is faster than the Ar_26, the difference in activation energies being about 0.6 kcal/mol.

It must be pointed out that the reactivity of the α position of a naphthalene ring is somewhat higher than that of the β carbon[12], so that the above ratio is somewhat high.

Rough calculation of the relative stabilities of the Ar_15 and Ar_26 radicals shows the first to be about 2.5 kcal less stable and the second 6.2 kcal more stable than the open chain radical.

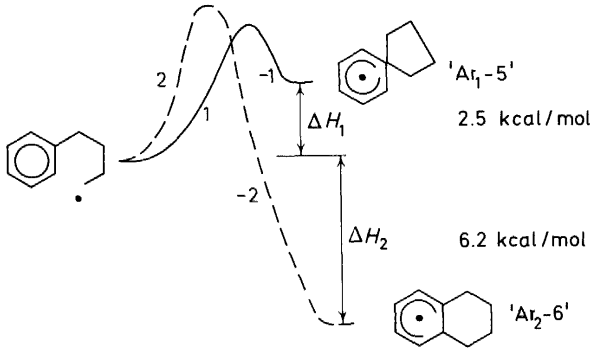


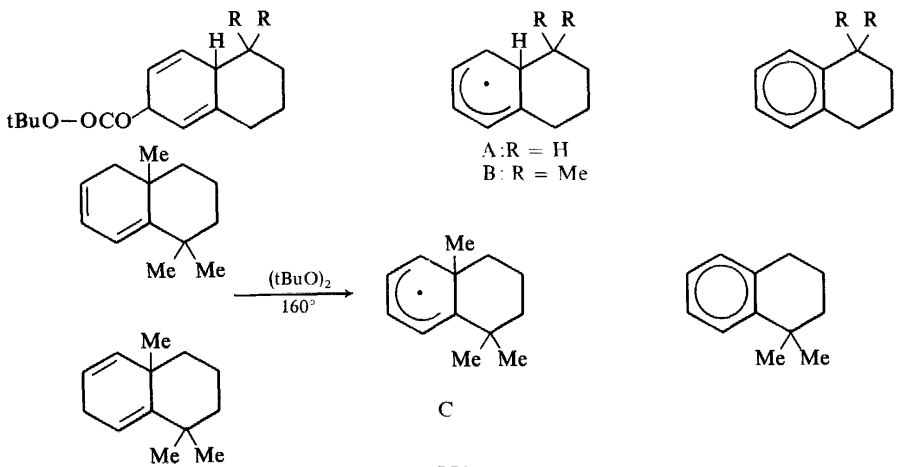
Figure 1. Relative stabilities of $C_6H_5(CH_2)_4$ radicals

The activation energy for the opening of the Ar_26 radical will therefore be appreciably higher than that of the Ar_25 radical, and reaction 2 will be expected to be irreversible under these reaction conditions.

In order to get information on this point we wanted to produce the corresponding Ar_26 cyclohexadienyl radical under the same reaction conditions and find out whether it would open up.

The simple dihydrotetralinyl radical A was produced by 'pyrolysis' of the (unstable) corresponding t-butyl perester; it gave tetralin but no n-butylbenzene. Substitution by two methyl groups in B (prepared in a similar way) would lower the enthalpy of reaction -2 by about 6 kcal, which should be favourable. In this case, however, only dimethyl tetralin but less than 0.5 per cent open chain hydrocarbon was produced. Wondering whether facile aromatization by hydrogen abstraction outweighed the -2 reaction, we then investigated radical C with a methyl group at the ring junction: in this case the ring fission should be favoured over methyl fission by about 7 kcal. Here again, however, aromatization by loss of the methyl group was observed, but no ring opening. A reason for this behaviour might be the stereoelectronic conditions for radical fission.

The conclusion is of course that reaction 2 is irreversible, and the mechanism of these tetralin cyclizations is reasonably understood.



It has been shown that in free radicals having in the δ position either a double bond or a benzene ring the formation of a five-membered ring is kinetically favoured over the formation of the six-membered ring. This behaviour might seem rather puzzling, and various proposals have been made to explain it. It should be pointed out, however, that kinetic preference for cyclization towards a five-membered ring is a common phenomenon in ionic organic chemistry[13]. In the case of hexenyl radical it seemed surprising both because it violates the Kharasch 'rule' of free radical addition on the terminal carbon of an α-olefin and because the analogous carbenium ion does lead to a six-membered ring.

It has been suggested that more conformations are available for five-membered ring formation; this could, however, hardly explain the observed difference[14]. A non-classical radical would require accommodation of an electron on an antibonding orbital; this is quite reasonable with bridging bromine but not with carbon. There is no evidence for participation of the double bond as concluded from the rates of decomposition of heptanoyl and and 6-heptenoyl peroxides[15].

Recently the e.p.r. spectrum of the hexenyl radical has been observed at low temperature where no cyclization takes place[16]. It shows the free radical carbon lying above the double bond.

Beckwith[1a, 17] has pointed out that a free radical adding to a double bond should approach from a direction almost perpendicular to the nodal plane of the olefinic π orbital in order to ensure a good overlap with the antibonding π orbital. This would favour carbon atom No. 5.

A stereochemical factor has been suggested (in a discussion by Prof. N. Le Bel) as hindering the formation of the six-membered ring[18]. Comparison of the transition states leading to cyclopentane or cyclohexane (*Figure 2*) formation shows in the latter a non-bonded interaction between the pseudo-axial hydrogen on carbon atom No. 2 and the H(Z) on carbon atom No. 6. This hydrogen leans towards the centre of the ring. The C_1–C_6 distance in the transition state is unknown, which makes it impossible to evaluate the magnitude of the interaction, but introduction of methyl groups on C_2 has been shown to hinder the cyclization.

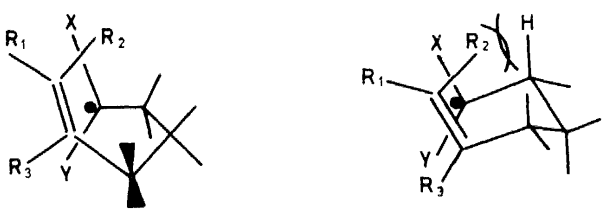


Figure 2. Transition states leading to cyclopentane (*left*) and cyclohexane

Replacing the H(Z) on C_6 by a methyl (for instance) would be expected to increase the interaction and reduce the proportion of cyclohexane derivative in the mixture of products. Since the hexenyl radical gives hardly any cyclohexane, we had to choose a more favourable reference compound.

It had been shown that a methyl group on C_5 very much favoured the formation of six-membered rings[19] in cyanoester cyclization. 5-Methylhexenyl

radical was therefore chosen as the reference and the isomeric 5-methyl 5E (and 5Z) hexenyl radicals were investigated[20]. Reduction of the 5-methyl-hexenyl bromide with tributyltin hydride led (*Table 3*) to a C_6/C_5 ratio of 2.5–2.9. Walling and Cioffari[21] got somewhat different results. The large increase in the rate of six-membered ring formation agrees with the effect of substitution of a double bond on the rates of addition of methyl radicals[22,23].

The effect of a methyl group E or Z on carbon atom No. 6 of 5-hexenyl radical could now be investigated. The results show a marked difference between the two isomers: whereas a methyl group in the *E* stereochemistry has but a small influence on the distribution of products formed, the Z methyl group prevents formation of the six-membered ring.

This result shows that the non-bonded interaction mentioned above does influence the orientation of the cyclization.

(2) CYCLIZATION AS A TOOL IN MECHANISTIC STUDIES

In many mechanistic studies the question arises of the nature of the reactive intermediates involved: carbenium ions, radicals, carbanions. It is now well known that the simple hexenyl carbenium ion cyclizes with formation of a six-membered ring[24], whereas the radical gives a five-membered ring. The carbanion in the cases studied also gives a five-membered ring but much more slowly[25].

When the substrate is so designed as to have a double bond in the δ position to the 'important carbon atom', the size of the ring that is formed will be used as evidence for the nature of the species involved. For instance. free radicals will be detected by the formation of five-membered rings.

This method has been used (a) for the reduction of alkyl halides with sodium naphthalene[26] or with chromium(II) salts[27]; (b) in the oxidation of Grignard derivatives[28]; (c) in the Wittig rearrangement and the reaction of ketyls with alkyl iodides[29]; and (d) in the oxidative cyclization of polyenes with Kochi's reagent ($(BzO)_2$. CuCl)[30].

The cyclization of hexenyl radicals can also be used to measure reaction rates. Carlsson and Ingold made this possible by measuring the absolute rate constant of the reduction of alkyl halides with trialkyltin hydrides[33].

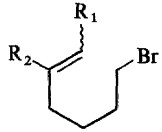
On the other hand, the ratio of the rate constants of cyclization and direct reduction was obtained from the kinetics of the reduction of 5-hexenyl bromide[34]. The first-order rate constant of the cyclization was found to be $10^5\ s^{-1}$ (see also reference 26c).

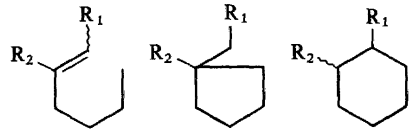
Knowledge of this rate constant allows us now by a competitive technique of the same kind (ref. 33) to measure absolute rate constants for other free-radical reactions.

The velocity of the reduction of a primary radical by naphthalene sodium has thus been measured to be at least $10^8\ l\ mol^{-1}\ s^{-1}$ [26a,c].

In a similar way the rate constant of the oxidation of free radicals by copper (II) by electron transfer was found to be $1.2 \times 10^6\ mol^{-1}\ s^{-1}$ [35] and by ligand transfer $2 \times 10^8\ mol^{-1}\ s^{-1}$ [36].

The reaction we should like to discuss here is the new substitution process that has been recently discovered by Kornblum[31], Russell[32] and others (the

Table 3. Reduction of  by Bu_3SnH (stoichiom.) in benzene; 70°C

Bromides	Bu_3SnH (M)	Reduction products % 			C_6/aliph.	C_5/aliph.	C_6/C_5
$R_1 = R_2 = H$(1)	0.5	53.6	46.5	Traces	0	0.86	0
	0.05	22	78	Traces	0	3.5	0
$R_1 = H$, $R_2 = CH_3$(2)	0.5	84	4.6	11.5	0.13	0.054	2.47
	0.05	55	11.8	33.3	0.60	0.21	2.91
$R_1 = CH_3$, $R_2 = H$ (3E)	0.5	51	49	Traces	0	0.96	0
$R_1 = CH_3$, $R_2 = CH_3$ (4E)	0.5	E 77 Z 2.5	7.5	*cis* 4 *trans* 9	0.16	0.09	1.74
$R_1 = CH_3$, $R_2 = CH_3$ (4Z)	0.5	Z 86 E 2	12	0	0	0.13	0

'Purdue reaction'). The important facts are that the alkylation of ambident anions such as enolates or nitrolates by benzyl halides is very much influenced by a nitro group in the para (or ortho) position of the halide. Thus, 2-nitropropane is alkylated much more rapidly and the proportion of C/O alkylation is much higher with the nitro derivative. This phenomenon is much more pronounced with the chloride than with the bromide. The rationalization involved the competition between straightforward S_N2 reaction, very efficient with the bromide, and a new mechanism involving electron transfer.

The first interpretation suggested involved electron transfer from the anion to the nitro derivative followed by dissociation of chloride ion and coupling of radicals. Later, however, the chain character of the reaction was recognized. The main step of the propagation sequence is coupling of the *p*-nitrobenzyl radical with the anion itself to yield a radical anion which will give up its electron to a new molecule of nitrobenzyl halide. In this way a molecule of end-product is formed and a new cycle is started:

$$O_2NC_6H_4CH_2X + A^- \rightarrow (O_2NC_6H_4CH_2X)^{\cdot -} + A^{\cdot} \quad (1)$$

$$(O_2NC_6H_4CH_2X)^{\cdot -} \rightarrow O_2NC_6H_4CH_2^{\cdot} + X^- \quad (2)$$

$$O_2NC_6H_4CH_2^{\cdot} + A^{\cdot} \rightarrow O_2NC_6H_4CH_2A \quad (3)$$

$$O_2NC_6H_4CH_2^{\cdot} + A^- \rightarrow (O_2NC_6H_4CH_2A)^{\cdot -} \quad (4)$$

$$(O_2NC_6H_4CH_2A)^{\cdot -} + (O_2NC_6H_4CH_2X) \rightarrow O_2NC_6H_4CH_2A + (O_2NC_6H_4CH_2X)^{\cdot -} \quad (5)$$

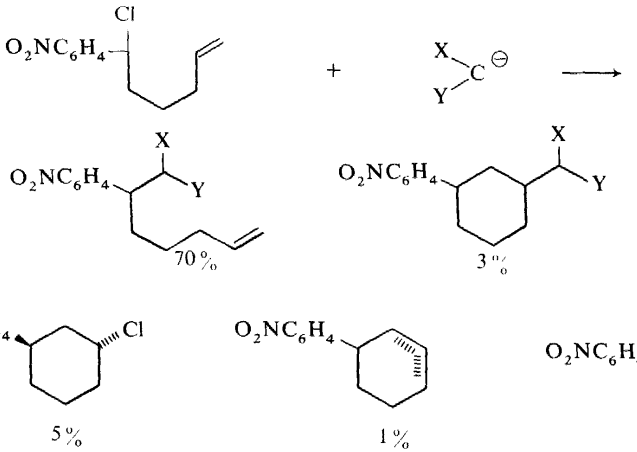
It is clear that in the two mechanisms all the molecules of halide give rise to free radicals, whereas the molecules of anion will give free radicals only in the first mechanism.

We therefore investigated the alkylation by *p*-nitrobenzyl chloride of the anion of ethyl 2-cyano-6-heptenoate. The related radical has been shown to cyclize nicely. Thus, if it is involved in the substitution reaction, we could expect to find not only the 'normal' open chain product but cyclized isomers if the cyclization can compete in rate with the intermolecular bonding step. We could also expect the formation of non-alkylated cyclized products by hydrogen abstraction from the reaction medium.

It has been checked that treatment of the cyanoester in DMF with $(BzO)_2$ did lead to cyclization. The reaction then was run with ethyl cyanoacetate and ethyl phenylacetate with *p*-nitrobenzyl bromide and chloride in DMF or HMPT, and gave large yields of normal alkylation product. No rearranged products could be detected. This could be taken as consistent with the second mechanism and not with the first, but it is negative evidence and therefore to be taken with caution.

The symmetrical reaction was then attempted—that is, alkylation of malonate ion with a *p*-nitrobenzyl halide bearing an unsaturated side chain: *p*-nitrophenylhexenyl chloride in DMF at room temperature.

This gave the results shown.



Much normal alkylation product is formed but a few other interesting products are also present in the reaction mixture. The 'expected' *p*-nitrophenylcyclohexyl malonate was there although in very low yield (3 per cent). Other arylcyclohexane compounds were present—the chloride (5 per cent) isomeric with the starting material and the substituted cyclohexene (1 per cent)—together with some product of dehydrochlorination.

These results were, if not really satisfactory, encouraging in showing that something was happening that was not straightforward S_N2 alkylation.

However, apart from the low yield, the fact that no cyclopentane compounds were formed looked very peculiar, since the 1-phenyl-5-hexenyl radical gives a C_5 to C_6 ratio of about 9[33]. The nitro group was not expected to make such a tremendous difference. We shall confirm this presently. And, finally, isomerizations in free radical reaction are not so common either. It will be noticed that only the *trans* (less stable) isomer of the cyclized halide was formed. The cyclized malonates were shown not to be formed from the cyclized chloride by synthesizing the authentic epimeric halides and heating them with ethyl malonate. The yield (from both epimeric chlorides) is too low to account for the amount isolated.

The free radical was generated by pyrolysis of the corresponding t-butyl perester. In DMF only the open chain (45 per cent) compound was formed; in toluene, however, at 80° the 'hydrocarbons' (40 per cent) were a mixture of open chain (50 per cent), cyclopentane (30 per cent) and cyclohexane (20 per cent) isomers. This is a perfectly reasonable result for such a radical.

It therefore looked as if the cyclized chloride was formed from the radical anion, which would then have several routes opened to it. One would be isomerization followed by electron transfer to give the cyclized chloride. Another would be scission to the *p*-nitrobenzyl radical (and chloride ion) followed by coupling with the radical $A^{\cdot}$ or the anion A^- (with some intervening cyclization). The main path was obviously the formation of the normal product.

In order to characterize the generated intermediate radical we tried to separate it from the anion. We therefore worked in a two-phase system. The necessary anion was produced in an aqueous phase by the action of sodium

hydroxide on a reasonably strong carbon acid (benzyl cyanide was used), and led by a cationic soap (quaternary ammonium halide) to an organic phase, where the nitrobenzyl halide would be dissolved. The newly born radical would not therefore find too many molecules of anion around it.

$$(\equiv N^+)A^- + O_2NC_6H_4CH_2Cl \rightarrow A^{\cdot} + (O_2NC_6H_4CH_2Cl)^{\cdot -}$$

$$(O_2NC_6H_4CH_2Cl)^{\cdot -} \rightarrow O_2NC_6H_4CH_2^{\cdot} + Cl^-$$

$$AH + OH^- \rightleftharpoons A^- + H_2O$$

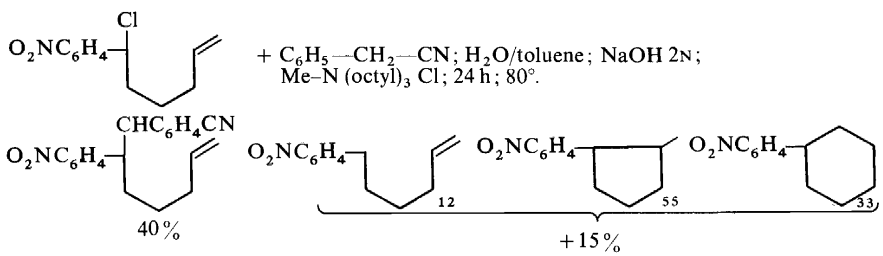
$$\equiv N^+Cl^- + A^- \rightleftharpoons \equiv N^+A^- + Cl^-$$

Table 4. Alkylation of benzyl cyanide with *p*-nitrobenzyl chloride in a two-phase system. $O_2NC_6H_4CH_2X + PhCH_2CN$; H_2O/SH; NaOH2N; MeN (octyl)$_3$Cl; 24 h; 20°C

X	SH	$O_2NC_6H_4CH_2CHPh$–CN	$O_2NC_6H_4CH_3$	$(O_2NC_6H_4CH=)_2$	Dicumyl
Cl	Benzene	40	10	10	
Cl	Cyclohexane	40	15	10	
Br	Benzene	60	1	10	
Br	Cyclohexane	60	2	10	
Cl	Benzene D_2O	40	12 Containing no deuterium		
Cl	Cumene	50	14		8(16)

The results are shown in *Table 4* with *p*-nitrobenzyl chloride itself. Benzene and cyclohexane gave similar results, but the chloride and the bromide behave differently. Only in the first case were reasonable amounts (yields 10–15 per cent) of *p*-nitrotoluene formed, which seems to be good evidence for the *p*-nitrobenzyl radical being an intermediate. It may be recalled that *p*-nitrobenzyl bromide does not react much by the electron transfer process, probably because the normal S_N2 process is too rapid. When the same reaction was run with D_2O/NaOD instead of H_2O/NaOH (with benzene), the nitrotoluene formed did not contain any deuterium. The hydrogen atom is therefore not transferred as a proton. Since the benzyl cyanide is largely labelled under these conditions, the hydrogen does not come from it. It is likely that the cationic soap is the hydrogen source. With cumene as solvent dicumyl was formed (8 mol %) in addition to *p*-nitrotoluene (14 per cent).

The same sort of experiment was then carried out with the unsaturated nitrohalide. The normal alkylation product was formed in a yield of 40 per



cent with 15 per cent of hydrocarbons. These were analysed by g.l.c. and shown to consist of nitrophenyl hexene (12 per cent), nitrophenylmethyl cyclopentane (55 per cent) and nitrophenyl cyclohexane (33 per cent). This now is typically the pattern exhibited in the free radical cyclization above.

Now considering that the cyclization had not been clearly observed in homogeneous solution, but only in the heterogeneous system, it was only fair to reinvestigate the behaviour of the ethylenic anion under those reaction conditions.

As ester groups were rapidly hydrolysed in the aqeuous two-phase system, we treated 2-phenyl-6-heptenonitrile with *p*-nitrobenzyl halide. *p*-Nitrotoluene is formed as before, but only the normal alkylation product could be detected.

This together with the results obtained with the unsaturated halide seems positive evidence for the chain mechanism in the Purdue reaction.

Since more and more cases are uncovered where electron transfer processes[38] compete with straightforward nucleophilic substitution, it is likely that the cyclization method will be of great use in mechanistic and other studies, to show whether free radicals derived from reagent or substrate are involved.

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