Some Intramolecular Reactions of *ortho*-Substituted Aryl Radicals

By **Athelstan L. J. Beckwith** * and **William B. Gara**, Organic Chemistry Department, Univresity of Adelaide, Adelaide, South Australia, Australia

ortho-Substituted aryl radicals have been generated by reduction of arenediazonium salts in aqueous solution by use of a flow cell. The e.s.r. spectra indicate that radicals containing olefinic bonds in the 5,6- or 6,7-positions with respect to the radical centre undergo rapid cyclization by addition at the 5- and 6-positions respectively to give the thermodynamically less stable products. No evidence was obtained for addition to the remote termini of the double bonds. The direction of cyclization is not determined primarily by the ease of approach of the radical centre to the olefinic carbon atoms. Aryl radicals containing saturated *ortho*-substituents undergo rearrangement by 1,5-intramolecular hydrogen atom transfer. The conclusions based on e.s.r. spectroscopic studies have been supported by the isolation of rearranged products from the reduction of suitable arenediazonium salts.

STUDIES of intramolecular reactions are of considerable utility for the investigation of transition state structure. In such reactions the relative dispositions of the reactive centres are constrained within limits defined by the geometry of the molecule and thus can be varied in a predetermined manner by changing the structure of the reactant.

The observation [1-3] that the hex-5-enyl radical (1), like many related species,[4-6] cyclizes under conditions of kinetic control to the thermodynamically *less* stable (2) of the two possible products, (2) and (3), discords with the general rule that competing radical processes involving the same reactants have rate constants related to their standard enthalpy changes, the fastest reaction

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[1] C. Walling, J. H. Cooley, A. A. Ponaras, and E. J. Racah, *J. Amer. Chem. Soc.*, 1966, **88**, 5361.

[2] A. L. J. Beckwith and G. Moad, *J.C.S. Chem. Comm.*, 1974, 472.

[3] C. L. Jenkins and J. K. Kochi, *J. Amer. Chem. Soc.*, 1972, **94**, 843 and references cited therein.

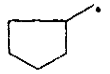
[4] C. Walling and A. Cioffari, *J. Amer. Chem. Soc.*, 1972, **94**, 6059.

[5] A. L. J. Beckwith, I. A. Blair, and G. Phillipou, *Tetrahedron Letters*, 1974, 2251.

[6] For recent reviews of radical cyclization see M. Julia, *Pure Appl. Chem.*, 1967, **15**, 167; *Accounts Chem. Res.*, 1971, **4**, 386; A. L. J. Beckwith, ' Essays in Free-radical Chemistry,' Chemical Society Special Publication No. 24, London, 1970, p. 239; J. W. Wilt in ' Free Radicals,' ed. J. K. Kochi, Wiley–Interscience, New York, 1973, vol. 1, ch. 8.

being that which is most exothermic. Explanations for this unusual behaviour of radical (1) have been based on consideration of entropy,[7] steric,[8] and stereoelectronic [2,9,10] factors. Although no single hypothesis has gained unanimous support, the experimental evidence appears to be incompatible with either a collinear or bridged arrangement of centres in the transition state for alkyl radical addition to an olefinic bond, and there has been some acceptance of the view [9,10] that bond formation in such reactions requires the approach of the radical within the plane of the π orbital and along an axis extending approximately vertically above one of the terminal atoms of the double bond. The basis for this model of the transition state (4) rests on the suggestion [9] that the primary interaction involves overlap of the half-filled orbital of the radical with one lobe of the vacant π^* orbital, a view recently supported by an MO treatment of the addition of methyl radicals to ethylene.[11] If this hypothesis is correct the preferential 1,5-cyclization of hex-5-enyl radical (1) can be rationalized on the grounds that approach of the radical centre to C-5 is less constrained than is its approach to C-6. Other examples of intramolecular free-radical addition, including the cyclization of cyclopentenylethyl radical[12] and of 4-(cyclohex-1-enyl)butyl radical,[9] are consistent with this view.


(1)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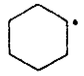
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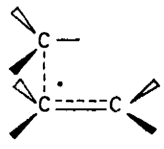
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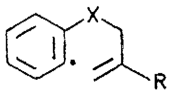
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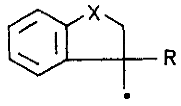
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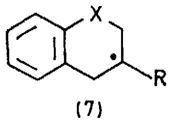
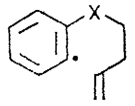

(7)

a; X = CH_2, R = H
b; X = O, R = H
c; X = O, R = Me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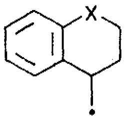
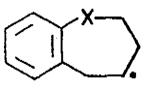

(9)

a; X = CH_2
b; X = O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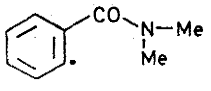
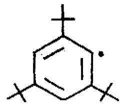

(11)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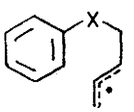
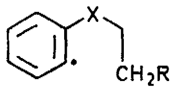

(13) X = CH_2
(14) X = O


(15) X = O; R = H
(16) X = CH_2; R = H
(17) X = CH_2; R = CO_2^-

If the mode of cyclization of an alkenyl radical is determined solely by the relative ease of approach of the radical centre to the two terminal atoms of the double bond, it should be possible to devise structures related to hex-5-enyl radical (1) in which 1,6-cyclization is favoured over 1,5-cyclization. Inspection of models of the *o*-but-3-enylphenyl radical (5a) and the related species (5b and c) reveals that the proposed disposition of reactive centres (4) is more readily attained for 1,6- than it is for 1,5-cyclization. Therefore, one expects that intramolecular addition in the radicals (5a—c) will afford mainly the six-membered cyclic radicals (7a—c).

Similar comparison of models of the substituted aryl radicals (8a and b) with that of hept-6-enyl radical leads to the prediction that the former, like the latter,[2] should preferentially undergo 1,6-cyclization to afford (9a and b) rather than the thermodynamically more stable secondary radicals (10a and b). However, the rate constants for the formation of (9a and b) should be considerably greater than that for cyclization of hept-6-enyl radical.[2]

The radicals (8a and b) are suitably constituted not only for intramolecular addition but also for 1,5-hydrogen atom transfer.[13] Examples of hydrogen atom transfer from carbon to carbon include isomerization of hexyl radical to 1-methylpentyl radical,[14] and the intramolecular hydrogen atom abstractions that lead to chain branching in vinyl polymerization.[15] The isomerization of the substituted aryl radical (11) is very rapid,[16] and 1,4-intramolecular transfer has been detected in 2,4,6-tri-t-butylphenyl radical (12).[17] Due to the resonance stabilization of the products (13) and (14), intramolecular hydrogen atom transfer should occur in (8a and b) with great facility. Our experiments were designed to test these predictions.*

Finally, in order to avoid possible complications arising

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* For a preliminary account of this work see A. L. J. Beckwith and W. B. Gara, *J. Amer. Chem. Soc.*, 1969, **91**, 5689, 5691.

[7] R. D. Rieke and N. A. Moore, *Tetrahedron Letters*, 1969, 2035; *J. Org. Chem.*, 1972, **37**, 413.

[8] M. Julia and M. Maumy, *Bull. Soc. chim. France*, 1969, 2427.

[9] A. L. J. Beckwith, G. E. Gream, and D. L. Struble, *Austral. J. Chem.*, 1972, **25**, 1081.

[10] A. L. J. Beckwith, I. Blair, and G. Phillipou, *J. Amer. Chem. Soc.*, 1974, **96**, 1613.

[11] H. Fujimoto, S. Yamabe, T. Minato, and K. Fukui, *J. Amer. Chem. Soc.*, 1972, **94**, 9205.

[12] J. W. Wilt, S. N. Massie, and R. B. Dabek, *J. Org. Chem.*, 1970, **35**, 2803.

[13] For reviews of intramolecular atom transfer processes see R. Kh. Friedlina, *Adv. Free Radical Chem.*, 1965, **1**, 211; K. Heusler and J. Kalvoda, *Angew. Chem. Internat. Edn.*, 1964, **3**, 525; R. H. Hesse, *Adv. Free Radical Chem.*, 1969, **3**, 83.

[14] K. W. Watkins and L. A. Ostreko, *J. Phys. Chem.*, 1969, **73**, 2080.

[15] S. L. Aggarwal and O. J. Sweeting, *Chem. Rev.*, 1957, **57**, 665.

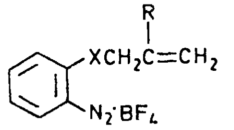
[16] T. Cohen, K. W. Smith, and M. D. Swerdloff, *J. Amer. Chem. Soc.*, 1971, **93**, 4303.

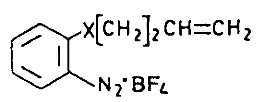
[17] L. R. C. Barclay, D. Griller, and K. U. Ingold, *J. Amer. Chem. Soc.*, 1974, **96**, 3011.

from competing intramolecular transfer and addition processes in radicals such as (8a and b) we have studied reactions of the aryl radicals (15)—(17) which contain saturated *ortho*-substituents.

METHODS

We chose first to employ e.s.r. methods to detect the occurrence of intramolecular addition reactions in suitably constituted aryl radicals. It has been shown previously that arenediazonium salts are readily reduced to the related aryl radicals by treatment with titanium(III) salts at pH 6—9, or by interaction with organic radicals of high reduction potential (*e.g.* $\cdot CO_2H$; $\cdot CH_2OH$) at low pH, and that the adducts formed by intermolecular addition of aryl radicals to suitable olefins can be readily identified by e.s.r. spectroscopy.[18] In the present work the diazonium salts (19), (20), and (22)—(25) were reduced in suitable flow cells, and the spectra were recorded in the usual way.


(18) X = CH_2; R = H
(19) X = O; R = H
(20) X = O; R = Me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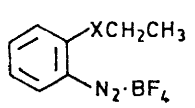
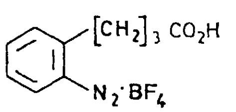
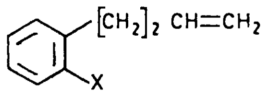
(22) X = O


(23) X = CH_2
(24) X = O


(25)

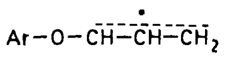

(26) X = CO_2H
(27) X = $CONH_2$
(28) X = NH_2
(29) X = I

Although e.s.r. spectroscopy in conjunction with the flow method is of great value for the qualitative study of homolytic processes, accurate quantitative data cannot readily thus be obtained because the stationary concentrations of the species detected depend not only on their rates of formation but also on their rates of destruction by dimerization and other termination reactions. Therefore, with the aim of developing methods suitable for the quantitative determination of the relative rates of intramolecular addition processes we examined the products from reaction of suitable diazonium salts with some one-electron reducing agents. The crude products were isolated by conventional techniques, and were identified and estimated by g.l.c., using, as reference, authentic compounds synthesized by unambiguous routes.

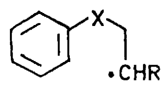
The amines required for the preparation of the diazonium salts (19), (20), and (22)—(25) were readily prepared by standard methods. However, we were unable to obtain the amine (28) in good yield *via* the route (26) ⟶ (27) ⟶ (28) because attempted preparation of the required acid (26) by alkylation of *o*-toluic acid with allyl bromide in the presence of lithium di-isopropylamide[19] gave an intractable mixture of products. Similar difficulties were encountered in the attempted preparation of the homologous amine required as a precursor for the diazonium salt (21). Since separate experiments had meanwhile afforded compounds, *e.g.* (29), suitable for the generation of the radicals (5a) and (8a) by the tin hydride method,[20] further attempts to prepare the salts (18) and (21) were abandoned.

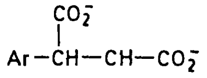
RESULTS AND DISCUSSION

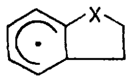
The spectrum recorded when *o*-allyloxybenzenediazonium fluoroborate (19) was reduced in the flow cell of the e.s.r. spectrometer with titanium(III) ion or $CO_2^{\cdot-}$ at pH 8 is shown in Figure 1. Addition to the reactant solutions of ethanol or of ammonium maleate, each of which react rapidly with aryl radicals,[18] neither changed the spectrum nor diminished its intensity. The same spectrum, but at much lower signal strength, was recorded when the diazonium salt (19) was reduced with the radical, $Me_2\dot{C}OH$, derived from isopropanol at pH 2.

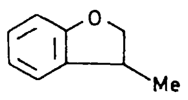

$\mathrm{Ar{-}O{-}CH{-}\dot{C}H{-}CH_2}$
(30)

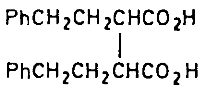
$\mathrm{ArOCH_2\dot{C}HCH_2R}$
(31)

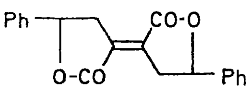

(32) X = O; R = H
(33) X = CH_2; R = H
(34) X = CH_2; R = CO_2^-


$\mathrm{Ar{-}CH(CO_2^-){-}CH{-}CO_2^-}$
(35) Ar = *o*-$EtOC_6H_4$
(36) Ar = *o*-PrC_6H_4

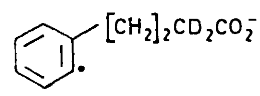

(37) X = CH_2
(38) X = O


(39)


$\mathrm{PhCH_2CH_2CHCO_2H{-}CH(CO_2H)CH_2CH_2Ph}$
(40)


(41)

Ph$[CH_2]_3CO_2H$
(42)


(43)

PhO$[CH_2]_4$OPh
(44)

The multiplicity, hyperfine splitting constants, and *g*

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[18] A. L. J. Beckwith and R. O. C. Norman, *J. Chem. Soc.* (*B*), 1969, 403.

[19] P. L. Creger, *J. Amer. Chem. Soc.*, 1970, **92**, 1396.

[20] H. G. Kuivila, *Accounts Chem. Res.*, 1968, **1**, 299.

value (see Table) of the signal enable the radical responsible for it to be identified as the product (6b) of 1,5-cyclization of *o*-allyloxyphenyl radical (5b). Four other radicals which could possibly be formed in this system, *viz* the aryl radical (5b),[21] the 1,6-cyclization product (7b), the allylic radical (30),[22] and radicals of the general type (31), would each show higher multiplicity.

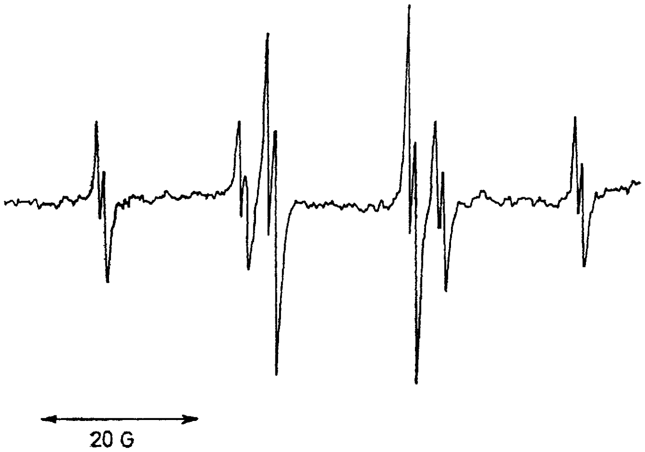

FIGURE 1 E.s.r. spectrum of the radical (6b) generated by reduction of *o*-allyloxybenzenediazonium fluoroborate (19)

Hyperfine splitting constants (G) for radicals formed by rearrangement of *ortho*-substituted aryl radicals

Radical	$a_{\alpha\text{-H}}$	$\alpha_{\beta\text{-H}}$	$a_{\gamma\text{-H}}$	g
(6b)	22·2 (2)	19·0 (1)	1·0 (1)	2·0025
(6c)	20·4 (2)			2·0024
(9b)	21·8 (2)	26·2 (1)		2·0025
(32)	22·1 (2)	27·2 (2)		2·0025
(33)	22·3 (2)	27·2 (2)		2·0025
(34)	20·2 (1)	22·6 (2)		2·0031

The only ambiguity in the spectrum of the radical (6b) concerns the origin of the small doublet splitting, the magnitude of which suggests that it arises from interaction of the free spin with a γ-proton. Examination of models indicates that free rotation about the bond to the radical centre will readily allow the orbital containing the unpaired electron to assume the spatial relationship with the *trans*-C–H bond required for effective homohyperconjugative interaction.[23] The rigid geometry of the cyclic system prevents such interaction with the *cis*-proton.

Reduction of the methylallyloxy-diazonium salt (20) in the e.s.r. flow cell gave a strong signal for product (6c) of 1,5-cyclization of radical (5c). The lines were broad, presumably because of unresolved splitting by γ-protons. Surprisingly, in view of the propensity of 5-substituted hex-5-enyl radicals to undergo 1,6-cyclization,[5] we were unable to detect the signal of high multiplicity expected for radical (7c).

When the butenyloxybenzenediazonium salt (22) was reduced at high pH with titanium(III) ion in the e.s.r. flow cell, the radical formed was unequivocally identified as product (9b) of 1,6-cyclization of (8b). No trace could be detected of the signals of higher multiplicity expected for the allylic radical (14), the product (10b) of 1,7-cyclization, and other possible species. As was the case with the radicals (6b and c), the signal due to the 1,6-cyclization product (9b) was unaltered when ammonium maleate or ethanol was added to the reactant solutions.

Although in the absence of kinetic data for the initiating process an accurate kinetic analysis of the reactions occurring in the e.s.r. flow cell is not possible, the relatively high intensities of the signals detected in our experiments indicate that the cyclization reactions of the aryl radicals (5b), (5c), and (8b) to form the cycloalkylmethyl radicals (6b), (6c), and (9b) respectively, have large rate constants ($>10^4$ s^{-1}). The failure of added maleate ion, or ethanol, to interfere with the cyclization process supports this view, for it is known that these reagents normally react rapidly with aryl radicals.[18]

Because of the limitations of the method, the failure to detect the cycloalkyl radicals (7b), (7c), and (10b) does not necessarily indicate that there is no cyclization onto the remote termini of the olefinic bonds in the aryl radicals (5b), (5c), and (8b). However, the e.s.r. results leave little doubt that in each case it is the formation of the smaller possible ring which proceeds the more rapidly. It appears, therefore, that the simple view, adumbrated in the Introduction, that the direction of cyclization is controlled primarily by the ease of approach of the radical centre to the termini of the double bond, is incorrect, and that other factors must be taken into account. Quantitative work designed to elucidate these factors will be described in a later paper.

Because of our failure to detect product (14) of 1,5-intramolecular hydrogen atom transfer in radical (8b) we examined some related saturated systems (15)—(17), in which competing addition processes are not possible. Reduction of *o*-ethoxybenzenediazonium fluoroborate (24) with aqueous titanium(III) ion at pH 8 gave a strong signal (see Figure 2), the characteristics of which (Table) enable the radical present to be unequivocally identified as product (32) of intramolecular hydrogen atom abstrac-

FIGURE 2 E.s.r. spectrum of the radical (32) generated by reduction of *o*-ethoxybenzenediazonium fluoroborate (24)

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[21] A. L. J. Beckwith, *Intra-science Chem. Rep.*, 1970, **4**, 127.

[22] A. L. J. Beckwith and R. O. C. Norman, *J. Chem. Soc.* (*B*), 1969, 400.

[23] G. R. Underwood and V. L. Vogel, *J. Amer. Chem. Soc.*, 1971, **93**, 1058.

tion in the radical (15). When ethanol was added to the titanium(III) solution, the signal disappeared. Addition of ammonium maleate also caused the disappearance of the signal due to the radical (32), but in this case it was replaced by a new spectrum comprising a doublet of doublets ($a_{\alpha\text{-H}}$ 20·4, $a_{\beta\text{-H}}$ 9·4 G) attributed to product (35) of addition of the aryl radical (15) to the maleate ion.

Reduction of *o*-propylbenzenediazonium fluoroborate (23) gave the rearranged radical (33); addition of ethanol destroyed the signal; and addition of ammonium maleate caused the formation of the adduct (36) ($a_{\alpha\text{-H}}$ 20·2, $a_{\beta\text{-H}}$ 10·45 G). We did not detect the cyclohexadienyl radicals (37) and (38) expected to be formed by cyclization[24] of radicals (33) and (32) respectively.

When the diazonium salt (25) was reduced at pH 8 an intense signal was recorded for the rearranged radical (34) (Figure 3). In this case the spectrum was essentially unaltered by the addition of ethanol or of maleate ion to the reactant solutions.

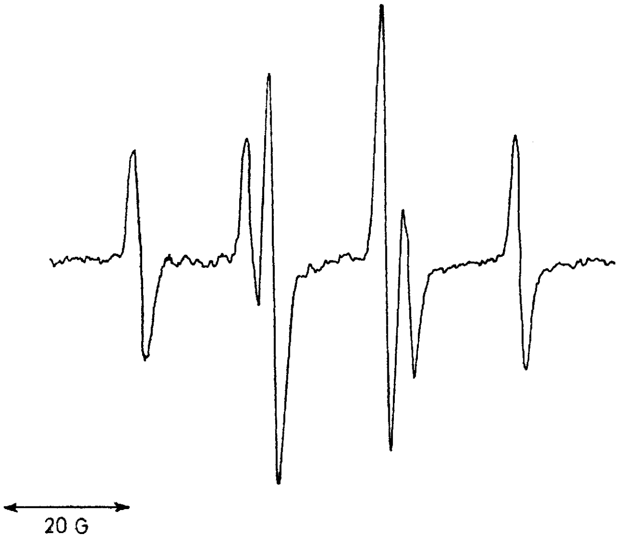

FIGURE 3 E.s.r. spectrum of the radical (34)

These results indicate that 1,5-hydrogen atom transfer from an unactivated saturated C–H position to an aryl radical centre occurs readily in suitably substituted aryl radicals. The strengths of the signals show that the rate constants are at least of moderate magnitude ($k > 10^2$ s^{-1}) but in the case of the rearrangement of the radicals (15) and (16) are not sufficiently large as to allow intramolecular hydrogen atom transfer to compete effectively with the rapid intermolecular reactions with ethanol or maleate ion. The presence of the carboxylate substituent clearly enhances the rate of formation of (34) in comparison with possible intermolecular processes. Presumably, stabilization of the radical centre in (34) by the adjacent CO_2^- group increases the exothermicity of the rearrangement process; polar effects may also be important. Finally, it appears that our failure to detect intramolecular hydrogen atom transfer in radical (8b) containing an unsaturated side chain was due not to any inherent impediment to the formation of the allylic radical (14) but to the much greater rate of the addition process (8b) ⟶ (9b).

Various exploratory experiments were carried out with the aim of confirming the e.s.r. results and of developing suitable quantitative methods for determining the relative rates of rearrangement processes in suitably constituted aryl radicals. Reduction of *o*-allyloxybenzenediazonium fluoroborate (19) at low pH failed to afford reasonable yields of identifiable products. However, reduction with titanium(III) ion in aqueous methanol at pH 8 or by Bunnett's procedure[25] gave both allyl phenyl ether, and the cyclization product, 3-methyl-2,3-dihydrobenzofuran (39). Significantly, in no case was chroman, the product of 1,6-cyclization, detected. These results provide strong support for the e.s.r. evidence that aryl radicals containing appropriately unsaturated *ortho*-substituents rapidly undergo intramolecular cyclization to afford the thermodynamically less stable products containing primary radical centres exocyclic to the newly formed rings. However the reduction methods described here are clearly unsuitable for quantitative studies. Later experiments, to be described in a separate paper, showed that such studies can be conveniently conducted by making use of the free-radical reaction of aryl iodides with tributylstannane.

Reduction of the diazonium salt (25) with titanium(III) ion at pH 8 in a flow system similar to that used for e.s.r. experiments afforded a dicarboxylic acid, m.p. 164—165°, identified as 2,3-diphenethylsuccinic acid (40) on the basis of its n.m.r. and mass spectra. When prepared by hydrogenation of Pechmann's dye (41), a method which is expected to afford the racemic form, 2,3-diphenethylsuccinic acid has m.p. 185°.[26] We conclude, therefore, that the compound isolated from our experiments is the *meso*-form. As a general rule racemic disubstituted succinic acids have higher m.p.s than their *meso*-isomers. The reduction of the diazonium salt (25) also gave a mixture of monocarboxylic acids from which 4-phenylbutyric acid (42) was isolated by chromatography.

The formation of the dicarboxylic acid (40) must involve dimerization of the rearranged radical (34). However, 4-phenylbutyric acid (42) could arise either directly from the aryl radical (17) by reduction followed by protonation, or intermolecular hydrogen atom transfer, or from the rearranged radical (34), by reduction, disproportionation, or atom transfer. Evidence supporting the latter route was obtained when the dideuterio-radical (43) was generated from the appropriately deuteriated diazonium salt. Examination of the peaks at *m/e* 91 and 92 in the mass spectrum of the 4-phenylbutyric acid produced showed that at least 75% of the sample contained a deuterium atom on the aromatic ring. A separate experiment with an authentic specimen showed that

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[24] R. Perrey, Thesis, University of Paris, 1969 (quoted in M. Julia, *Accounts Chem. Res.*, 1971, **4**, 386).

[25] J. F. Bunnett and H. Takayama, *J. Amer. Chem. Soc.*, 1968, **90**, 5173; *J. Org. Chem.*, 1968, **33**, 1924.

[26] C. S. Fang and W. Bergmann, *J. Org. Chem.*, 1951, **16**, 1231.

2,2-dideuterio-4-phenylbutyric acid does not undergo scrambling to give a greatly enhanced peak at *m/e* 92 in its mass spectrum.

When the dideuterio-radical (43) was generated by Bunnett's method in methanol,[25] no dicarboxylic acid (40) was obtained, and the mass spectrum of the monomeric product (42) showed that only 6% of it arose from the rearranged radical. Apparently, under these conditions intermolecular hydrogen atom transfer from methanol to the aryl radical centre competes effectively with the intramolecular transfer process. Finally, when the product of the reduction of the ethoxy-diazonium salt (24) was examined by g.l.c. it was found to contain a small amount of the dimer (44) of the rearranged radical (32). The major component was phenetole. These results verify those obtained by e.s.r. methods, and highlight the importance of e.s.r. spectroscopy as an exploratory tool for the study of intramolecular radical processes.

EXPERIMENTAL

Instruments and Apparatus.—I.r. spectra were recorded with a Perkin-Elmer 237 spectrophotometer for Nujol mulls unless otherwise specified. Mass spectra were measured with an Hitachi–Perkin-Elmer RMU-6D instrument operating at 70 eV. N.m.r. spectra were taken on a Varian HA60 spectrometer in CCl_4 unless otherwise specified and are reported in p.p.m. relative to tetramethylsilane (internal standard).

For the recording of e.s.r. spectra a Varian E9 spectrometer with 100 kHz modulation and an X-band klystron was employed in conjunction with mixing chambers [27] which allowed the mixing of two, or three, reactants *ca.* 0·02 s before the solution entered the cavity. The *g* factors and splitting constants were measured by comparison with the signal for Fremy's salt added to one of the reactant solutions. The general conditions used for the generation of aryl radicals have been previously described.[18]

Analytical g.l.c. was conducted on a Perkin-Elmer 881 instrument and preparative g.l.c. on an Aerograph Autoprep 705. The carrier gas (N_2) flow rate in analytical work was 30 ml min^{-1}. Compounds were identified by retention times under standard conditions and by 'spiking' with authentic samples. Relative peak areas were obtained by triangulation or by use of a Perkin-Elmer 194B printing integrator, and amounts of compounds were then estimated with the aid of calibration curves prepared by submitting mixtures of authentic compounds and internal standard to g.l.c. Details of the columns used are as follows: (A) 10% Carbowax 20M on 100—120 Aeropak 30, 20 ft × 1/8 in stainless steel; (B) 3% PDEAS on 100—120 Aeropak 30, 14 ft × 1/8 in glass; (C) 10% SE-52 on 100—120 Aeropak 30, 6 ft × 1/8 in stainless steel.

Materials and Reference Compounds.—Chroman,[28] *o*-allyloxyaniline,[29] 1,4-diphenoxybutane (44),[30] and allyl phenyl ether were prepared by known methods.

o-*Allyloxybenzenediazonium fluoroborate* (19). Sodium nitrite (4·4 g) in water (9 ml) was added dropwise to a stirred solution of *o*-allyloxyaniline in 21% aqueous fluoroboric acid (54 ml) whilst the mixture was maintained at 10°. The mixture was then cooled to −20°, and the precipitate was collected by filtration, washed with cold 5% aqueous fluoroboric acid (20 ml), and with water, and allowed to dry in the air at room temperature. The solid was then washed with ether, dissolved in acetone, and reprecipitated by addition of dry ether. The required *diazonium fluoroborate* was obtained as a colourless powder (12·7 g, 76%), $\nu_{max.}$ 3100, 2275, 1055, 1035, 980, 925, and 760 cm^{-1}.

o-(2-*Methylallyloxy*)*aniline*. Reduction of *o*-(2-methylallyloxy)nitrobenzene [31] with tin(II) chloride for 18 h by the usual procedure [32] afforded the required *amine* (77%) as a colourless liquid, b.p. 96° at 1·4 mmHg (Found: C, 73·4; H, 8·1; N, 8·3. $C_{10}H_{13}NO$ requires C, 73·6; H, 8·0; N, 8·6%), *m/e* 163 (M^+), δ 1·80 (3H, s, CMe), 3·6 (2H, s, NH_2), 4·33 (2H, s, OCH_2), 4·9—5·4 (2H, m, CH_2=C), and 6·3—6·8 (4H, m, ArH). The compound showed one peak on g.l.c. [column (B); 120°].

o-(2-*Methylallyloxy*)*benzenediazonium fluoroborate* (20). Diazotization of the foregoing aniline by the method described above gave the required *diazonium salt* as a colourless powder (80%), $\nu_{max.}$ 3100, 2275, 1055, 1035, 975, 920, and 755 cm^{-1}.

o-(*But*-3-*enyloxy*)*nitrobenzene*. A stirred mixture of *o*-nitrophenol (7 g), 4-bromobut-1-ene (7·4 g), sodium carbonate (3·2 g), and water (20 ml) was boiled under reflux for 2 days. The mixture was then diluted with water and extracted with chloroform. The organic layer was washed, dried, and distilled to afford the required *ether* as a pale yellow liquid (7·8 g, 81%), b.p. 102° at 0·07 mmHg (Found: C, 62·5; H, 5·5; N, 7·5. $C_{10}H_{11}NO_3$ requires C, 62·2; H, 5·7; N, 7·3%), *m/e* 193 (M^+), δ 2·3—2·8 (2H, m, CCH_2C), 4·10 (2H, t, *J* 6·5 Hz, OCH_2), 4·9—5·4 (2H, m, C=CH_2), 5·6—6·2 (1H, m, C–CH=C), and 6·8—7·8 (4H, m, ArH).

o-(*But*-3-*enyloxy*)*aniline*. Reduction of the foregoing nitro-compound with tin(II) chloride in ethanol for 18 h [32] gave o-(*but*-3-*enyloxy*)*aniline* (75%) as a liquid, b.p. 96—98° at 0·8 mmHg (Found: C, 73·3; H, 8·0; N, 8·5. $C_{10}H_{13}NO$ requires C, 73·6; H, 8·0; N, 8·6%), *m/e* 163 (M^+), δ 2·1—2·7 (2H, m, CCH_2C), 3·60 (2H, s, NH_2), 3·90 (2H, t, *J* 6·5 Hz, OCH_2), 4·8—5·3 (2H, m, C=CH_2), 5·5—6·0 (1H, m, C–CH=C), and 6·3—6·8 (4H, m, ArH). The compound gave one peak on t.l.c. [column (B); 120°].

o-(*But*-3-*enyloxy*)*benzenediazonium fluoroborate* (22). Treatment of the foregoing aniline in aqueous fluoroboric acid with sodium nitrite as described above gave the required *diazonium salt* (60%) as a colourless powder, $\nu_{max.}$ 3100, 2275, 1055, 1035, 980, 930, and 760 cm^{-1}.

o-*Ethoxybenzenediazonium fluoroborate* (24). Diazotization of redistilled *o*-phenetidine in fluoroboric acid afforded the required diazonium salt (65%) as a cream powder, $\nu_{max.}$ 2275, 1055, 1035, and 760 cm^{-1}.

o-*Propylbenzenediazonium fluoroborate* (23). When *o*-propylaniline, prepared by reduction with tin and hydrochloric acid of *o*-nitropropylbenzene,[33] was diazotized in aqueous fluoroboric acid with sodium nitrite, the required diazonium salt (55%) was obtained as a heavy colourless oil, which was insoluble in ether and sparingly soluble in water.

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[33] G. Baddeley and J. Kenner, *J. Chem. Soc.*, 1935, 303.

It was purified by washing with ether, was quickly dried *in vacuo*, and was then used immediately for e.s.r. experiments.

4-(o-*Aminophenyl)butyric acid hydrochloride*. Sodium azide (7·8 g) was added in small portions with shaking to a mixture of 1-tetralone (20 g) and polyphosphoric acid (190 g). After the addition, the mixture was stirred at 50° for 8·5 h, then poured onto crushed ice (1 kg). Sufficient cold aqueous sodium hydroxide was added to neutralize the mixture which was then extracted repeatedly with chloroform. Evaporation of the chloroform solution, and crystallization of the residue from water afforded the dihydro-1-benzazepin-2-one (17·3 g, 78%), m.p. 143—145° (lit.,[34] m.p. 141—142°).

A sample (10 g) of the lactam was heated with concentrated hydrochloric acid (40 ml) for 3 h. The cooled mixture was then filtered, and the residue of the amine hydrochloride (12·3 g, 90%) was washed with ether and dried over phosphorus pentoxide.

o-(3-*Carboxypropyl)benzenediazonium fluoroborate* (25). Sodium nitrite (3·9 g) in water (8 ml) was added dropwise to a cold (0—5°), stirred solution of the foregoing amine hydrochloride (12 g) and sodium borofluoride (8 g) in water (20 ml) and concentrated hydrochloric acid (10·5 ml). After the addition, the mixture was stirred for a further 15 min, then filtered. After being washed with cold water, cold ethanol, and ether, the required *diazonium salt* was obtained as a cream powder (10·2 g, 65%), $\nu_{\text{max.}}$ 2275, 1670, and 760 cm^{-1}.

3-*Methyl*-2,3-*dihydrobenzofuran* (39). A reaction vessel was constructed comprising two 100 ml round bottom flasks, connected at the 50 ml mark by means of a short glass tube, with their respective ground joints parallel. Bulb A was fitted with a reflux condenser carrying a drying tube, while bulb B was fitted with a ground glass stopper. Sodium (2·0 g) was introduced into bulb B, and 3-methylbenzofuran [35] (1·0 g) in absolute ethanol (5 ml) was placed into bulb A. The reaction vessel was placed into a boiling water-bath with both necks vertical. When the sodium was molten, the boiling solution in bulb A was tipped into bulb B, and the resulting mixture was heated under reflux in the water-bath until the mixture became viscous. The apparatus was then brought back to its original position and ethanol (5 ml) was introduced through the condenser into bulb A, brought to the boil and tipped into bulb B. The reaction mixture was again heated under reflux until it became viscous. This last procedure was repeated several times until all the sodium had reacted. The mixture was then poured into water (150 ml) and extracted with ether. The organic layer was washed with brine, dried, concentrated, and distilled, to give 3-methyl-2,3-dihydrobenzofuran as a colourless liquid (0·88 g, 88%), b.p. 78° at 12 mmHg (lit.,[36] b.p. 86—87° at 16 mmHg), $\nu_{\text{max.}}$ 1460, 1225, and 745 cm^{-1}, δ 6·6—7·3 (4H, m, ArH), and 4·60 (1H), 4·00 (1H), 3·45 (1H), and 1·30 (3H) as an ABXY$_3$ system (O–CH$_2$–CH–CH$_3$) with J_{AB} 8·5, J_{AX} 9·0, J_{BX} 7·0, and J_{XY_3} 7·0 Hz. G.l.c. [column (A); 130°] showed the compound to contain <1% of 3-methylbenzofuran.

2,2-*Dideuterio*-4-*phenylbutyric acid*. Sodium (0·70 g) was dissolved in D$_2$O (3 ml), phenylbutyric acid (0·40 g) was added, and the mixture was heated under reflux in a bath at 150° for 48 h. The cooled mixture was then diluted with water and shaken with ether. The aqueous layer was then acidified and extracted with ether, and the residue obtained by evaporation of the extract was recrystallized from water to give the dideuteriated acid, m.p. 52°, δ 1·95 (2H, t, *J* 9 Hz, CCH$_2$CD$_2$), 2·35 (0·3H, m, CHCO$_2$), 2·65 (2H, t, *J* 9 Hz, ArCH$_2$), and 7·2 (5H, m, ArH); *m/e* 167 (2·5%), 166 (21), 165 (6·7), 164 (0·6), 105 (39), 104 (100), 92 (7·3), and 91 (44). On the basis of the spectral evidence the sample was calculated to contain 74% dideuteriated, 24% monodeuteriated, and 2% undeuteriated acid. The mass spectrum of phenylbutyric acid shows the ratio of peaks at *m/e* 91 and 92 as 44 : 5.

o-(3,3-*Dideuterio*-3-*carboxypropyl)benzenediazonium fluoroborate*. A solution of sodium deuterioxide formed from sodium (1·0 g) in D$_2$O (20 ml) was added to dihydro-1-benzazepin-2-one (6 g) and the mixture was heated in a stainless steel bomb at 150° for 3 h. The cooled mixture was then poured into cold concentrated hydrochloric acid (30 ml), and the precipitate of the hydrochloride of the deuteriated acid (5·5 g, 68%) was collected, washed with small amounts of cold water and ether, and dried. A sample of the hydrochloride was taken up in water and aqueous sodium acetate was added. Extraction of the mixture with ethyl acetate, and evaporation of the extract *in vacuo* afforded 2,2-dideuterio-4-(*o*-aminophenyl)butyric acid, which crystallized from chloroform–light petroleum in plates, m.p. 125° (lit.,[37] m.p. 125°). The n.m.r. spectrum of the sodium salt in D$_2$O showed resonances at δ 1·8 (2H, t, *J* 9 Hz, CCH$_2$CD$_2$), 2·3 (0·2H, m, CHCO$_2$), 2·75 (2H, t, *J* 9 Hz, ArCH$_2$), and 7·3 (4H, m, ArH). When warmed with acetic anhydride–pyridine the amino-acid afforded deuteriated benzazepinone, δ 2·2 (2H, t, *J* 7 Hz, CCH$_2$CD$_2$), 2·8 (2H, t, *J* 7 Hz, ArCH$_2$), 7·1 (4H, m, ArH), and 8·2 (1H, s, NH); *m/e* 164 (3·5%), 163 (34), 162 (6·5), 161 (<1), 120 (3·5), 119 (4·5), 118 (4·5), 107 (12·5), and 106 (100). On the basis of the spectra the sample was calculated to contain 85% of the dideuteriated compound.

The major portion of the hydrochloride of the dideuteriated amino-acid was converted into the diazonium salt in the usual way.

Reduction of o-*Allyloxybenzenediazonium Fluoroborate* (19). —(*a*) A deaerated solution of titanium(III) chloride (10 ml; 15% w/v), disodium ethylenediaminetetra-acetate (24 g), and potassium carbonate (4·0 g) in water (500 ml) and methanol (500 ml) was mixed in a flow cell over 15 min with a cold solution of the diazonium salt (1·0 g) in water (500 ml) and methanol (500 ml). The effluent was extracted thrice with pentane, and the combined pentane extracts were dried and evaporated. G.l.c. analysis [column (A); 130°] of the residue (0·71 g) indicated the presence of allyl phenyl ether (0·010 g, 2%) and 3-methyl-2,3-dihydrobenzofuran (0·061 g, 11%). Chroman was not detected.

(*b*) The diazonium salt (0·25 g) was added with stirring under nitrogen to a 2M solution of sodium methoxide in methanol (10 ml) at 0°. After the mixture had been heated under reflux for 5 min, it was cooled and poured into water (20 ml). The mixture was then extracted with ether, and the ether layer, after drying, was evaporated. G.l.c. analysis of the residue indicated the presence of allyl phenyl ether (5%) and 3-methyl-2,3-dihydrobenzofuran (31%).

Repetition of this experiment in 2M-sodium isopropoxide in propan-2-ol (10 ml) afforded allyl phenyl ether (7·0%) and 3-methyl-2,3-dihydrobenzofuran (1·5%). In neither experiment was chroman formed in detectable amounts.

(*c*) An aqueous solution of titanium(III) chloride (23·5 ml; 2·25% w/v) was added dropwise with stirring to a solution

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of the diazonium salt (1·0 g) in acetone (50 ml) and water (10 ml) at $-10°$ under nitrogen. The mixture was then stirred for 5 min at $-10°$, for 75 min at 0°, and for 15 min at 10°. After dilution with water, the mixture was extracted with methylene chloride, and the extract was subjected to short-path distillation. G.l.c. of the distillate (0·26 g) showed it to contain a negligible quantity of monomeric products.

(*d*) The diazonium salt (1·0 g) in iced water (150 ml) was added dropwise with stirring during 25 min to a solution of titanium(III) chloride (0·54 g) in water and ethanol (5 ml) at 0° under nitrogen. After a further 30 min at 0° the mixture was worked up as in (*c*). The yield of monomeric products was $<5\%$. Similarly unfruitful experiments were carried out using chromous sulphate and potassium ferrocyanide as reducing agents under the same conditions.

Reduction of o-*(3-Carboxypropyl)benzenediazonium Fluoroborate* (25).—(*a*) A deaerated solution of titanium(III) chloride (20 ml; 15% w/v), disodium ethylenediaminetetraacetate (18 g), and concentrated aqueous ammonia (20 ml) in water (2 l) was mixed in a flow cell during 20 min with a solution of the diazonium salt (4·1 g) in water (2 l). The mixture was washed with ethyl acetate, then acidified with dilute sulphuric acid. Extraction of the mixture with ethyl acetate gave a crude acid fraction (2·5 g) which was separated by chromatography on silica gel into 4-phenylbutyric acid (0·69 g), and meso-2,3-*diphenethylsuccinic acid* (0·37 g), which crystallized from ethanol in prisms, m.p. 164—165° (Found: C, 73·9; H, 6·95. $C_{20}H_{22}O_4$ requires C, 73·6; H, 6·8%), $\nu_{max.}$ 1685, 1238, and 780 cm^{-1}, δ (sodium salt in D_2O) 1·9 (4H, m, CCH_2C), 2·5 (2H, m, $CHCO_2$), 2·5 (4H, t, *J* 7 Hz, $ArCH_2$), and 7·5 (10H, m, ArH), *m/e* 326 (M^+, 22), 308 ($M - H_2O$, 100), 222 ($M - PhCH{=}CH_2$, 38), 204 ($M - H_2O - PhCH{=}CH_2$, 62), 159 ($PhC_4H_6CO^+$, 48), 118 ($PhC_3H_5^+$, 26), 105 ($PhCH_2CH_2^+$, 46), 104 ($PhCH{=}CH_2^+$, 46), and 91 ($C_7H_7^+$, 35).

When the experiment was repeated with a sample of the dideuterio-diazonium salt, the mass spectrum included peaks at *m/e* 91 (32%) and 92 (100), from which it was calculated that the sample included 75% of phenylbutyric acid containing one aromatic deuterium atom.

(*b*) The dideuterio-diazonium salt (0·60 g) was added with stirring under nitrogen to a 2M solution of sodium methoxide in methanol (20 ml) at 0°, and the mixture was then heated under reflux for 10 min. After cooling, and dilution with water (50 ml), the mixture was washed with ether, and acidified with dilute sulphuric acid. Extraction with ether afforded crude 4-phenylbutyric acid (0·46 g) which was purified by chromatography on silica gel. The mass spectrum included peaks at *m/e* 91 (100%) and 92 (23), from which it was calculated that the sample included 6% of material containing one aromatic deuterium atom.

Reduction of o-*Ethoxybenzenediazonium Fluoroborate* (24).—The diazonium salt (3·6 g) was reduced with titanium(III) chloride in alkaline aqueous solution by the flow method as described above. Extraction of the mixture with light petroleum afforded a dark oil (2·1 g) which was shown by g.l.c. [column (C); 120°] to contain 1,4-diphenoxybutane (2%), phenetole (*ca.* 30%), and other unidentified materials.

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