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NUCLEOPHILIC CHARACTER OF BRIDGEHEAD FREE RADICALS

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Abstract—Bridgehead free radicals have been produced in equimolecular mixtures of benzene and *p*-difluorobenzene by the thermal decomposition of the t-butylperoxyesters of 1-adamantyl, 1-bicyclo[2,2,2]octyl and 1-biciclo[2.2.1]heptyl carboxylic acids. The reactivity of *p*-difluorobenzene relative to benzene indicated that bridgehead radicals possess nucleophilic character.

INTRODUCTION

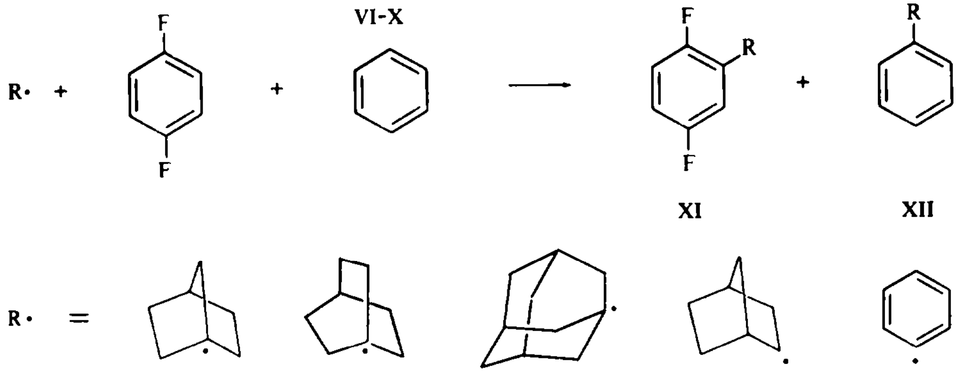
FROM STUDIES of product distribution in homolytic substitution a general correlation has emerged between the polar nature of carbon radicals and the hybridization of the orbital carrying the unpaired electron; thus, it has been established[1] that electrophilicity increases in the series $sp^3 < sp^2 < sp$. Alkyl radicals are in fact nucleophilic and the nucleophilic properties are more pronounced when a radical is produced on a secondary than on a primary carbon atom;[2] tertiary radicals could not be fully investigated because of their tendency to give disproportionation rather than substitution reactions.[2] Recent studies[3] on the alkylation of protonated heteroaromatic bases showed however that tertiary radicals do effect aromatic substitution and are more nucleophilic than secondary radicals.

A particularly interesting case is encountered when a radical is generated at the bridgehead position of a bicyclic or tricyclic system. Because of its structure a tertiary bridgehead radical would be expected to be of higher energy than an aliphatic tertiary radical; moreover the rigidity of the system will block disproportionation. Bridgehead radicals have been largely investigated mainly from the point of view of the ease of their formation as a function of the structure of the cyclic system.[4] Few examples of aromatic substitutions effected by these radicals are reported in the literature; it has been shown that the 1-apocamphyl,[5] the 1-adamantyl[6] and the perchlorohomocubyl[7] radicals, when generated in benzene, can afford the corresponding 1-phenyl derivatives. No substitution product was instead obtained from the decomposition of the ditriptoyl peroxide in benzene.[8] We report here the results of a study intended to investigate the character of bridgehead radicals.

RESULTS AND DISCUSSION

The radicals investigated were the 1-bicyclo[2.2.1]heptyl (I), the 1-bicyclo[2.2.2]-octyl (II) and the 1-adamantyl (III); 2-bicyclo[2.2.1]heptyl (IV) and phenyl (V) radicals were also studied for comparison. Radicals I–V were all produced by the thermal decomposition of the t-butylperoxyesters (VI–X) of the corresponding carboxylic acids. The experimental method employed to explore the nature of these radicals was that of generating them in equimolecular mixtures of *p*-difluorobenzene and benzene and of measuring the relative amounts of the substitution products (XI and XII). The use of *p*-difluorobenzene as a reference substrate was suggested by the fact that the two fluorine atoms, while presenting a small steric effect, produce a pronounced deactivation of the nucleus towards electrophilic attacks. The ratio of the two substitution products XI and XII, which represents the reactivity of the *p*-difluorobenzene relative to benzene ${}^{C_6H_4F_2}_{C_6H_6}K_{R\cdot}$, can thus be taken as an indication of the polar nature of the substituting radical R·. Quantitative determinations of the relative reactivities were carried out by gas chromatography; pure samples of the substitution products XI and XII, necessary as standards, were obtained from the decompositions of the peroxyesters in *p*-difluorobenzene and benzene alone and separated by conventional methods. The results of these experiments are summarized in the scheme; the values of the relative reactivities are the average of at least two independent runs.

$$R\text{-}CO_3CMe_3 \rightarrow R\cdot + CO_2 + Me_3CO\cdot$$



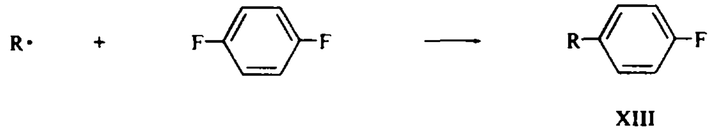
XI XII

I II III IV V

${}^{C_6H_4F_2}_{C_6H_6}K_{R\cdot}$ =	I	II	III	IV	V
	2·35	2·75	3·1	3·4	0·85

The relative reactivity of 0·85 determined in this way for the phenyl radical is in agreement with its practically neutral[1] character. All three bridgehead radicals investigated presented a relative reactivity considerably higher than unity. This clearly indicates the preference for these species to effect substitution in regions of relatively low electron density; in other words radicals I–III behave as nucleophiles. It thus seems that the production of a radical in a bridgehead position does not greatly influence its reactivity, in the sense that it still presents the nucleophilic character expected on the basis of the sp^3 character of the orbital occupied by the odd electron. On quantitative grounds, however, it can be seen that, despite their being tertiary radicals, the nucleophilicity is less pronounced than in the corresponding secondary radicals; this result is particularly evident when one compares the relative reactivity of the 1-bicyclo[2.2.1]heptyl (I) with that of the 2-bicyclo[2,2,1]heptyl (IV) radical. Along the series of the three bridgehead radicals an increase in relative reactivity is progresively encountered on passing from I to III; the reasons for these differences are at present being investigated with other aromatic substrates in order to correlate relative reactivities with isomer distributions.

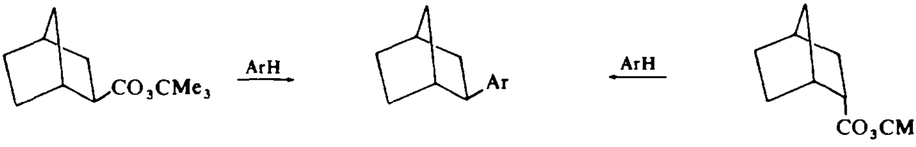
A side reaction which was encountered in this work was the replacement of a halogen atom of the *p*-difluorobenzene to give a *p*-fluorophenyl derivative (XIII): this reaction, however, under the reaction conditions employed takes place to a very small extent and does not give complications in the determination of the relative reactivities reported above. This halogen substitution reaction is characteristic of nucleophilic radicals and has already been observed and studied in detail with the cyclohexyl radicals.[9]



XIII

R• = I, II, III, IV.

Finally, a point of some interest is concerned with the production and the reactivity of radical IV, because of the possible existence of two *exo*-*endo* isomers. The decomposition of both the *exo*- (IXa) and *endo*- (IXb) t-butylperoxyesters of the 2-bicyclo-[2.2.1]heptyl carboxylic acids in benzene and *p*-difluorobenzene afforded no traces of the *endo*-isomer indicating that attack on the aromatic substrates can only take place from the less hindered *exo*-position.



IXa IXb

Ar = C_6H_5, $C_6H_3F_2$

EXPERIMENTAL

The t-butylperoxyesters of 1-bicyclo[2.2.1]heptyl (VI),[10] 1-bicyclo[2,2,2]octyl (VII),[10] 1-adamantyl (VIII,[10] 2-*exo*-(IXa) and *endo*-bicyclo[2.2.1]heptyl (IXb)[11] carboxylic acids were prepared as described in the literature. Commercial (BDH) t-butyl perbenzoate (X) was used without further purification.

Decomposition of peresters VI–X *in benzene.* Solutions of the peroxyesters VI–X (1 g) in benzene (100 ml) were refluxed for 4 days; solvent was evaporated and the residue chromatographed through a silica gel column using light petroleum as eluant. The first 200 ml of solvent contained the desired products ($\simeq$ 0·3 g); the following substitution products (XII), were prepared: 1-*phenyladamantane*, m.p. 86–8° (lit.[12] 87–9°); 1-*phenylbicyclo*[2.2.2]*octane*, m.p. 79–80° (MeOH). (Found: C, 90·20; H, 10·0. Calc. for $C_{14}H_{18}$: C, 90·25; H, 9·75%). NMR (CS_2): 1·71 δ (bs, 13H); 7·09 δ (bs, 5H); 1-*phenylbicyclo*[2.2.1]*heptane*, b.p. 128–30°/16 mm (lit.[13] 124–8°/16 mm); 2-exo-*phenylbicyclo*[2.2.1]*heptane*, b.p. 78–80°/1 mm (lit.[14a] 102°/3 mm). The same product was obtained both from the *exo*- and the *endo* peroxyesters (IX). The *exo* structure was assigned on the basis of the NMR spectrum (see below); no trace of the *endo*-isomer could be detected by NMR.

Decomposition of peroxyesters VI–X *in* p-*difluorobenzene*. Solutions of the peroxyesters VI-X (1 g) in difluorobenzene (100 ml) were refluxed for 5 days and worked up as described above for the decompositions in benzene. The following substitution products (XI) were prepared: *2,5-difluorobiphenyl*, b.p. 92–4°/1 mm (Found: C, 75·9; H, 4·25. Calc. for $C_{12}H_8F_2$: C, 75·8; H, 4·25%). NMR (CS_2): 6·92 δ (m, 3H); 7·3 δ (bs, 5H); *1-(2,5-difluoro)phenyladamantane*, m.p. 85–6° (Found: C, 77·5; H, 7·4. Calc. for $C_{16}H_{18}F_2$: C, 77·4; H, 7·3%). NMR (CS_2): 1·80 δ (bs, 6H); 2·02 δ (bs, 9H); 6·7 (m, 3H); *1-(2,5-difluoro)phenylbicyclo*[2.2.2]*octane*, m.p. 60–1°. (Found: C, 75·9; H, 7·3. Calc. for $C_{14}H_{16}F_2$: C, 75·65; H, 7·25%). NMR (CS_2): 1·77 δ (bs, 13H); 6·72 δ (m, 3H); *1-(2,5-difluoro)phenylbicyclo*[2.2.1]*heptane*, b.p. 86–7/1 mm. (Found: C, 75·1; H, 4·80. Calc. for $C_{13}H_{14}F_2$: C, 74·95; H, 4·85%). NMR (CS_2): 1·71 δ (m, 10H); 2·28 δ (bs, 1H); 6·78 δ (m, 3H); 2-exo-*(2,5-difluoro)phenylbicyclo*[2.2.1]*heptane*, b.p. 83–4°/0·8 mm. (Found: C, 75·05; H, 4·9. Calc. for $C_{13}H_{14}F_2$: C, 74·95; H, 4·85%). NMR (CS_2): 1–2 δ (m, 8H); 2·30 δ (bs 2H); 2·87 δ (t, 1H); 6·78 (m, 3H).

The same product was obtained both from the *exo*- and *endo*-peroxyesters (IX). The *exo*-structure was assigned to this compound on the basis of its NMR spectrum which is similar to that of the 2-*exo*-phenylbicyclo[2.2.1]heptane reported.[14b] The benzylic proton signals for *exo* and *endo* isomer differ both in respect to multiplicity and band position;[15] when the Ph group is *endo* the proton at C-2 appears[14b] as a complex multiplet from 3 to 3·5 δ, when the Ph group is *exo* the corresponding signal appears as a skewed triplet from 2·6 to 2·9 δ.

Analysis by GLC of the mixtures from the decomposition of peroxyesters VI–IX, before work up, showed the presence of a few percent of a second component which was identified as the *p*-fluorophenyl-derivative (XIII) by comparison with authentic compounds prepared independently.[16]

Competitive experiments. Solutions (0·1 M) of the peroxyesters VI–X in equimolecular mixtures of benzene and *p*-difluorobenzene (2 ml) were kept at 100° for 5 days. The mixtures were directly analyzed by GLC using a Varian 1520 gas chromatograph equipped with a 5% LAC 728 on Aeropak 30 column (3 m.). Calibrations for area response differences between XI and XII was effected for each reaction using an internal standard. Two or three independent experiments were carried out and the averaged values thus determined are collected in the scheme.

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