Reductive free-radical alkylations and cyclisations mediated by 1-alkylcyclohexa-2,5-diene-1-carboxylic acids

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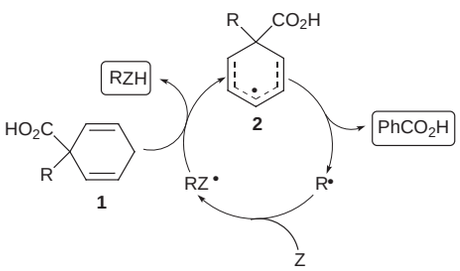
A range of 1-alkylcyclohexa-2,5-diene-1-carboxylic acids were prepared by Birch reduction–alkylation of benzoic acid and their efficiency as mediators of alkyl radical chain addition and cyclisation processes was investigated. Reductive alkylations were respectably successful, even with only one or two equivalents of alkene, for secondary, tertiary and benzylic radicals. Reaction of 1-[2-(cyclohex-2-enyloxy)ethyl]cyclohexa-2,5-diene-1-carboxylic acid yielded the product of *exo-trig*-cyclisation, *i.e.* 7-oxabicyclo[4.3.0]nonane, in a yield comparable to that obtained from the tributyltin hydride induced cyclisation of 3-(2′-iodoethoxy)-cyclohexene. This, together with the isolation of both *exo*- and *endo*-cyclisation products from 1-[2-(6,6-dimethylbicyclo[3.1.1]hept-2-en-2-ylmethoxy)ethyl]cyclohexa-2,5-diene-1-carboxylic acid established that ring closures could also be satisfactorily mediated with these reagents. Preparations were completely free of metal contaminants and direct reduction of the alkyl radicals, prior to addition or cyclisation, was completely absent. However, the desired products were accompanied by alkylbenzenes, together with by-products from the initiator decompositions, and this complicated work-up. Failure to obtain 1-[2-(prop-2-yn-1-yloxy)cyclohexyl]cyclohexa-2,5-diene-1-carboxylic acid in Birch reductive alkylations with *trans*-1-iodo-2-(prop-2-yn-1-yloxy)cyclohexane (and the corresponding bromide) indicated a limitation on precursor synthesis. The Birch reduction–alkylation was not of universal applicability and was suppressed for alkyl halides having β-substituents.

Introduction

Homolytic disconnections are gradually taking their place, alongside more familiar ionic disconnections, as useful tools for synthetic planning. Currently, organotin reagents dominate the field of free radical synthetic methodology, but they suffer from several serious disadvantages. Tin residues are difficult to completely remove from reaction products and this, coupled with the fact that many organotin compounds are neurotoxins, makes them unacceptable co-reagents in preparations of compounds intended for human use. Organotin hydrides are fast hydrogen donors so that premature reduction of non-final intermediates can also be a problem. A potential means of avoiding tin depends on arranging *hydrogen* abstraction from a suitable reagent as the first step of chain propagation, rather than halogen or chalcogen transfer as with tin reagents. Carbon-centred radicals are unselective in H-abstractions, which leads to problems with regioselectivity in propagation steps. However, several series of 'pro-aromatic' cyclohexadienyl and related compounds deliver the required selectivity by means of bisallylic activation of hydrogen, simultaneously taking advantage of re-aromatisation as the driving force for extrusion of some desired initial radical.[1,2] For example, alkyl 1-methylcyclohexa-2,5-diene-1-carboxylates afforded cyclohexadienyl radicals which mainly underwent β-scission above *ca.* 80 °C to produce toluene and alkoxycarbonyl radicals. The latter radicals subsequently extruded CO_2 to generate the corresponding alkyl radicals which could be trapped with moderate efficiency by halogen donors or alkenes. However, loss of a methyl radical from the intermediate cyclohexadienyl radical to afford an alkyl benzoate was a significant competing β-scission.[1,2]

During the course of this work, EPR spectroscopic observations of the paramagnetic intermediates led to the accidental discovery that the related acids, *i.e.* 1-alkylcyclohexa-2,5-diene-1-carboxylic acids **1**, also functioned as sources of alkyl radicals.[3] This implied that acids **1** might act as reductive chain propagation reagents, and hence as replacements for organotin hydrides, under certain circumstances. The key propagation steps of the application envisaged for them are summarised in Scheme 1. Selective H-abstraction from the bisallylic site of acid **1** will generate delocalised radical **2** which will fragment to produce benzoic acid and the desired radical R$^{\bullet}$. This reacts with an added alkene Z to produce an adduct radical which undergoes chain transfer with more **1** to afford the alkylated product RZH and continue the chain. Potential advantages are that benzoic acid would be the only by-product, which could easily be removed by an alkaline extraction, and that the H-transfer step will be slower than for organotin hydrides, thus allowing time for intermediate radical R$^{\bullet}$ to complete intermolecular addition, or cyclisation for suitably unsaturated R$^{\bullet}$. To examine the viability and range of applicability of this methodology a representative series of acids was prepared and examined under free radical conditions.



Scheme 1

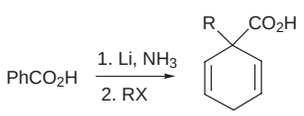
Results and discussion

One pot Birch reduction–alkylation of benzoic acid affords 1-alkylcyclohexa-2,5-diene acids of type **1** in moderate to good yields.[4–6] The method is most efficient for primary and secondary alkyl substituents and has been exploited by several groups for the preparation of intermediates in natural product syntheses.[7–12] 1-Alkyl acids **3**–**5** were obtained in various yields by means of a modification of the procedure due originally to Birch[4,5] (Scheme 2). The low yield of *tert*-butyl acid **4** was

Table 1 Product yields[a] from the peroxide initiated reactions[b] of 1-alkylcyclohexa-2,5-dienecarboxylic acids **1** with alkenes

		Yield (%)		
Acid	Alkene	RZH	RZ_2H	RPh
3	cyclohexenone	59 (31)	0	9
4	cyclohexenone	58	0	22
5	cyclohexenone	(52)	0	3
3	acrylonitrile[c]	14[d]	14[d,e]	3
3	vinyl benzoate	36	21	21

[a] Product yields (mol%) determined by ^{1}H NMR; parentheses denote yields of isolated products. $PhCO_2H$ and biphenyl were produced in each reaction. [b] Reactants refluxed in C_6H_6 for *ca.* 48 h. [c] Initiated with di-*tert*-butyl peroxide at *ca.* 120 °C. [d] Acid **3** conversion was 30%, hence RZH + RZ_2H yield = 92% based on **3** consumed. [e] Trimer (3%) was also detected.



	3	**4**	**4**	**5**
R	*c*-C_5H_9	Bu^t	Bu^t	$PhCH_2$
X	Br	Br	I	Cl
Yield (%)	71	18	29	99

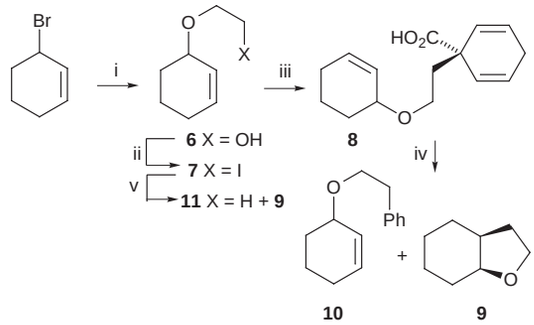
Scheme 2

understandable because both atoms of the newly formed carbon–carbon bond are quaternary. A slightly higher yield was achieved when *tert*-butyl iodide was used instead of the bromide, but chromatographic separation was required to obtain acid **4** free of benzoic and 1,4-dihydrobenzoic acids. As expected, the 1-benzyl acid **5** was prepared in virtually quantitative yield.

The usefulness of 1-alkyl acids **3–5** in intermolecular homolytic alkylations of the type shown in Scheme 1 was tested by reacting each with cyclohexenone. Hydrogen donation by **1** is comparatively slow[3] and hence significant amounts of dibenzoyl peroxide were needed to ensure complete conversion of **1**. In each case benzoic acid and a 3-alkylcyclohexanone (RZH) were the major products and moderate yields of the latter were isolated (Table 1). Each adduct was accompanied by a minor amount of the corresponding alkylbenzene (RPh), probably formed by loss of the hydroxyformyl radical (formate radical, $^{\bullet}CO_2H$) from intermediate **2**. Minor quantities of biphenyl and 3-phenylcyclohexanone, from side reactions of the initiator, were also identified in most cases. Reactions were carried out at higher temperatures in 2-methylbutan-2-ol as solvent, and with other initiators, but with only a minor effect on the products and their proportions. The final two rows of Table 1 show that cyclopentyl radicals from acid **3** also added satisfactorily to acrylonitrile and vinyl benzoate, although appreciable quantities of oligomers were formed.

Table 1 demonstrates that acids of type **1** can be used with moderate efficiency for intermolecular alkylations completely free of toxic metal by-products. Premature reduction of R$^{\bullet}$, before addition to Z, was not a problem but the main drawback to this method was the competing loss of $^{\bullet}CO_2H$ from **2** and production of alkylbenzenes as by-products. Intramolecular reactions are generally more efficient than their intermolecular analogues and therefore we examined a series of acids designed to establish limits of applicability in radical cyclisations.

Acid **8** was chosen to test the efficiency of a radical *exo-trig* ring closure leading to formation of a bicyclic ether. The synthesis of **8** was achieved in three steps from 3-bromocyclohexene as indicated in Scheme 3. Alcohol **6** was readily prepared from the latter and ethylene glycol, and converted to iodide **7** *via* the toluene-*p*-sulfonate (tosylate). The conditions



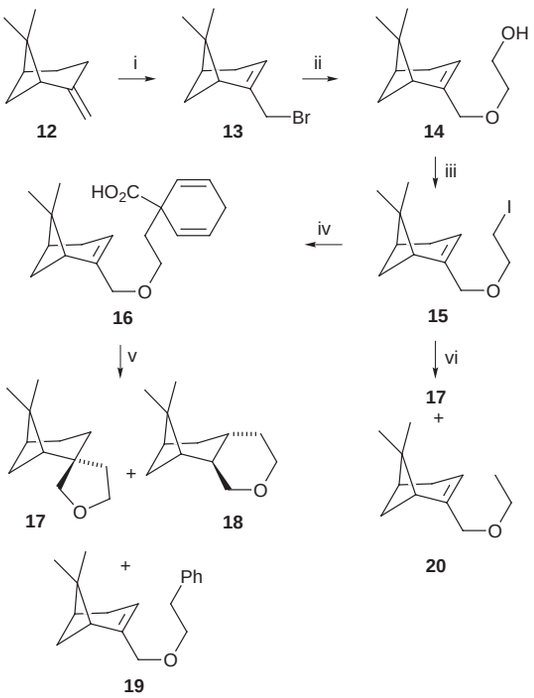
Scheme 3 *Reagents and conditions*: i, $HO(CH_2)_2OH$, Na, THF reflux, 80%; ii, TsCl, pyridine, then NaI, acetone, 65%; iii, Li, $PhCO_2H$, NH_3, 42%; iv, $(PhCO_2)_2$, C_6H_6, 24 h, 83% (**9**:**10** = 1.3:1); v, Bu_3SnH, C_6H_6, **9** 60%, **11** 13%

of the Birch reduction–alkylation step were varied to improve the yield of **8** and to reduce the amount of unreacted benzoic and 1,4-dihydrobenzoic acids, which were difficult to remove by column chromatography. Varying the number of equivalents of iodide **7** had no significant effect on the outcome of the reaction and therefore the iodide was subsequently used in a 1:1 ratio with benzoic acid. Use of distilled and dried NH_3 did not improve the yield. However, if the initial steps in the Birch reduction were carried out in the usual manner, but a delay of 30 min was introduced before quenching with the iodide, as suggested by Mander,[10] this resulted in a more efficient reaction and the product was isolated by column chromatography in an improved yield of 42%.

Carboxylic acid **8** was dissolved in benzene, to which dibenzoyl peroxide was added. The mixture was refluxed for 30 h and the benzoic acid was removed by an alkaline wash. The two main products were the expected 7-oxabicyclo[4.3.0]nonane **9** and an aromatic compound identified as 3-(2′-phenylethoxy)-cyclohexene **10**. This demonstrated that the reaction proceeded by a mechanism analogous to that shown in Scheme 1. The formation of the aromatic product **10** was due to competitive loss of a hydroxyformyl radical from cyclohexadienyl radical **2**. Better conversion of **8** and higher product yields (**9**, 55%) were achieved when the reaction was performed over a three day period, with portionwise addition of one equivalent of dibenzoyl peroxide. The observed coupling constant between hydrogens H^1 and H^6 of **9** (7.8 Hz) was consistent with a *cis* ring junction, as expected for an *exo-trig* hex-5-enyl type cyclisation. The comparatively high yield of **10** (*cf.* RPh yields in Table 1) implied that, as might be expected, the unwanted loss of $^{\bullet}CO_2H$ from intermediate **2** competed more effectively with *primary* alkyl radical loss (from **8**). In reactions of **8** carried out at 103 °C, in 2-methylbutan-2-ol as solvent, the **9**:**10** ratio worsened from 1.3:1 to 0.9:1, but the reaction time was considerably shortened. Reductive cyclisation of iodide **7** with tributyltin hydride afforded bicyclic ether **9** in comparable yield (60%) accompanied by the direct reduction product, 3-ethoxycyclohexene (**11**, 13%).

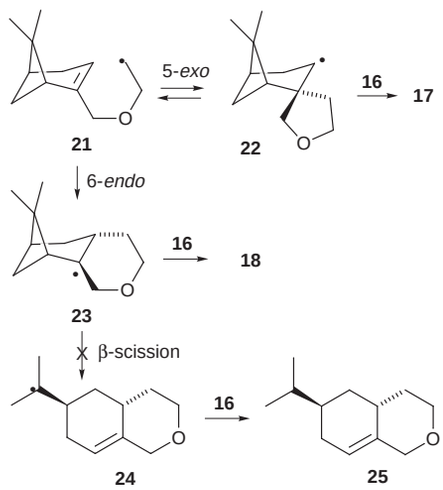
The presence of the carboxylic acid group in **1** conferred solubility in aqueous alkali and hence these acids were potential sources of carbon-centred radicals in environmentally friendly aqueous solvents. To evaluate this possibility, acid **8** was dissolved in aqueous KOH and the reaction was initiated with persulfate at 70 °C. However, under these conditions, 3-(2′-phenylethoxy)cyclohexene **10** was the sole product (63% isolated) and bicyclic ether **9** was undetectable; similar results were obtained with H_2O_2 as initiator. This is most easily explained if the delocalised radical derived from the carboxylate anion of **8** loses the formate anion radical ($CO_2^{\bullet -}$) much more readily than the neutral radical ($^{\bullet}CO_2H$) is lost from radical **2**. There is ample precedent for rapid $CO_2^{\bullet -}$ loss from alkylcarboxylates.[13] Clearly acids **2** are not viable sources of R$^{\bullet}$ under alkaline conditions.

A more severe test was provided by acid **16**. 5-*exo* Cyclisation of the radical derived from this *i.e.* **21** will be disfavoured because it involves intramolecular addition at a quaternary carbon to produce spirocyclic ether **17**. We hoped that the slower rate of hydrogen donation from **16**, in comparison with an organotin hydride, would enable this spirocyclisation to take place *before* reduction of the initial radical. Bromination of β-pinene **12** with NBS afforded myrtenyl bromide **13** which was converted to alcohol **14** with sodium and ethylene glycol and hence to iodide **15** *via* the tosylate (Scheme 4). 1-[2-(6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-ylmethoxy)ethyl]cyclohexa-2,5-diene-1-carboxylic acid **16** was obtained in yields up to 80% by use of the Birch procedure described above. Acid **16** was a viscous oil which also contained small amounts of benzoic and 1,4-dihydrobenzoic acids. Although **16** could be purified by dry-flash chromatography, the majority of the product co-eluted with a small amount of benzoic acid, and it was therefore used in this state in the radical fragmentation reaction. This was considered to be acceptable because the amount of benzoic acid present was insignificant and the radical reaction itself yields benzoic acid.



Scheme 4 *Reagents and conditions*: i, NBS, CCl_4, reflux 4 h, 59%; ii, $HO(CH_2)_2OH$, Na, THF, reflux 24 h, 99%; iii, TsCl, pyridine, then NaI, acetone, 96%; iv, $PhCO_2H$, Li, NH_3, 80%; v, $(PhCO_2)_2$, C_6H_6, reflux, 24 h, 22%; vi, Bu_3SnH, C_6H_6, reflux, *hv*, 3 h, **17** 31%, **20** 8%

When **16** was refluxed with dibenzoyl peroxide in benzene, GC–MS analysis of the reaction mixture disclosed three compounds, in addition to benzoic acid, which were identified as the desired spiro ether **17**, the aromatic ether **19** and the bicyclic ether **18**. The structure of spiro ether **17** was confirmed by its displaying identical GC–MS and ^{1}H NMR data to those observed from the tin hydride mediated cyclisation of iodide **15**. The structure of the aromatic product was assigned on the basis of its NMR spectra, MS and retention time (t_R). The structure of compound **18**, the product of a 6-*endo* cyclisation, is however tentative. Its MS and ^{13}C NMR spectra were consistent with structure **18** and it had a similar, but not identical, t_R to the product (**20**) of the organotin mediated reduction of iodide **15** (Scheme 4). However, its ^{1}H NMR spectrum was badly overlapped by that of spiro ether **17**, from which it could not be separated by chromatography, and this prevented confirmation. We also considered the rearranged product **25** formed by β-scission of the *endo*-radical **23** (Scheme 5), but there was no evidence for the formation of this product by ^{1}H NMR. The isomeric spiro ether, resulting from ring closure of **21** on the opposite face of the alkene was also discounted because we felt this would also have been observed in the tin hydride reaction, had such a cyclisation taken place. We have therefore assigned the third compound from this radical cyclisation reaction to be the product of 6-*endo* ring closure, *i.e.* **18**. The formation of cyclic ether **17** implies that the initial radical **21** underwent 5-*exo* cyclisation on the least hindered side of the double bond to produce secondary radical **22** (Scheme 5). Radical **22** could

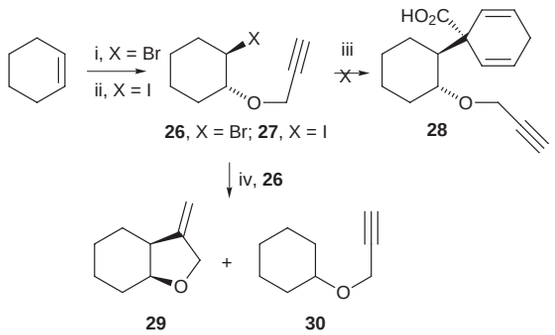


Scheme 5

then either abstract a hydrogen atom from carboxylic acid **16** to give the kinetic product **17**, or undergo reverse ring opening back to radical **21**. Reversal relieves the steric strain at the newly formed quaternary centre present in radical **22**. Radical **21** may also ring close in the 6-*endo* mode forming the more thermodynamically stable compound **18**, after hydrogen atom abstraction. The product mixture was separated by column chromatography and two main fractions were obtained. The first contained aromatic ether **19** followed by co-elution of compounds **17** and **18** in yields of 7%, 10% and 5% respectively.

Iodide **15** was reductively cyclised with tributyltin hydride and analysis by GC–MS, ^{1}H and ^{13}C NMR proved that cyclic ether **17** and the direct reduction product **20** had formed (Scheme 4). The structure of **20** was confirmed by spectral comparisons with authentic material synthesised in a separate experiment. The tin residues were partly removed using potassium fluoride, and the cyclised product **17** and the directly-reduced product **20** were obtained by distillation in yields of 31% and 8% respectively. The low yields in the reactions of **16** and **15** may have been due to difficulties encountered in the cyclisation step, or to the susceptibility of the substrates to polymerisation/decomposition under the reaction conditions. The 6-*endo* product **18** was not produced in the tin hydride mediated reduction of iodide **15**. Probably radical **21** abstracted hydrogen from tin hydride too rapidly for the 6-*endo* closure to be competitive.

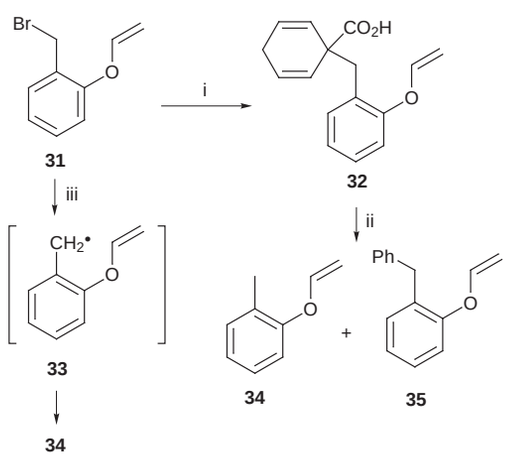
Primary carbon-centred radicals were produced from acids **8** and **16** by fragmentation of the intermediate cyclohexadienyl radicals **2**. However, secondary, tertiary and benzyl radicals are generated with greater ease in analogous fragmentations,[3] and with less competition from alkylbenzene formation. Our next target acid was therefore **28**, designed to yield a secondary cyclohexyl radical capable of 5-*exo* ring closure onto its alkynyloxy side chain (Scheme 6). *trans*-1-Bromo-2-(2-propyn-1-yloxy)-cyclohexane **26** was made from cyclohexene by a literature procedure.[14] Conversion to the corresponding iodide **27** by halogen exchange with NaI in acetone failed. However, vicinal alkoxy-iodoalkanes have been prepared from alkenes by means of copper(II) acetate, iodine and the appropriate alcohol. For



Scheme 6 *Reagents and conditions*: i, $HCCCH_2OH$, NBS, DCM, 68%; ii, $HCCCH_2OH$, I_2, $Cu(OAc)_2{\cdot}H_2O$, 23%; iii, NH_3, $PhCO_2H$, Li; iv, Bu_3SnH, *hv*, PhH, 8 h, rt, 63%

example, the reaction of cyclohexene, iodine and methanol in the presence of copper(II) acetate monohydrate resulted in the formation of *trans*-1-iodo-2-methoxycyclohexane in excellent yield.[15] We prepared vicinal alkynyloxyiodoalkane **27** by a similar procedure although, not unexpectedly, the yield was moderate and the desired iodide had to be separated from unwanted diiodides by chromatography. Reductive alkylations of benzoic acid were attempted with both **26** and **27** but none of the target acid was obtained. It appears that steric hindrance from the vicinal substituent suppresses the nucleophilic substitution step. Although our attempts to prepare carboxylic acid **28** were fruitless, bromide **26** was reductively cyclised with tributyltin hydride to afford bicyclic ether **29** in good yield, accompanied by prop-2-ynyloxycyclohexane **30**.

Our final target 1-[2-(ethenyloxy)benzyl]cyclohexa-2,5-diene-1-carboxylic acid **32** was designed to generate a 2-ethynyloxy-substituted benzyl radical **33**. Formation of this radical from intermediate **2** was expected to be efficient because of its resonance stabilisation. In 2D radical **33** appears capable of a facile



Scheme 7 *Reagents and conditions*: i, $PhCO_2H$, Li, NH_3, 50%; ii, $(PhCO_2)_2$, PhH, reflux; iii, Bu_3SnH, PhH, *hv*, 6 h, rt, **34** 90%

5-*exo* cyclisation. However, models show that approach of the benzyl radical centre from directly above the α-C-atom of the double bond can only occur if the benzyl methylene twists completely out of conjugation with the aromatic ring. All resonance stabilisation would be lost and hence 5-*exo* cyclisation should be disfavoured. Similarly, 6-*endo* approach requires significant twisting of the benzyl methylene. Because of the comparatively slow rate of hydrogen donation by the acids, the occurrence of one or other of these difficult cyclisations seemed within the bounds of possibility. Bromide **31** was prepared in four steps from salicylaldehyde.[16] As expected, organotin hydride mediated reaction of **31** afforded essentially only the direct reduction product **34** and *none* of the cyclised product was detected. The usual Birch reduction–alkylation sequence with **31** provided a moderate yield of **32**, but extensive decomposition occurred in solution over a period of 5 days.

The radical induced fragmentation of acid **32** afforded 1-(ethenyloxy)-2-methylbenzene **34** and 1-(ethenyloxy)-2-benzylbenzene **35** as the main products (Scheme 7), in addition to minor amounts of 1-(ethoxy)-2-methylbenzene and 1-(ethoxy)-2-benzylbenzene. It proved difficult to isolate **34** and **35**, due to the presence of polymeric material, and they were obtained in yields of only 4% and 3% respectively. This proves that, even on generation from **32**, the difficult ring closure of the alkenyloxybenzyl radical can still not compete with its alternative intermolecular reactions.

We conclude that 1-alkylcyclohexa-2,5-diene-1-carboxylic acids function with moderate efficiency as alkyl radical sources. Satisfactory yields from straightforward 5-*exo* ring closure reactions and from alkylations of olefins can be obtained. It is normal in free radical alkylations to use a large excess of olefin, but in this work one equivalent (occasionally two) was used, and the yields in Table 1 should be evaluated in the light of this restriction. The advantages of this pro-aromatic acid methodology are that preparations are completely free of metal contaminants and that direct reduction of the alkyl radicals, prior to addition or cyclisation, are not significant. However, the desired products are accompanied by alkylbenzenes, together with by-products from the initiator decompositions, and this complicates work-up. Our unsuccessful attempts to make acid **28** indicate a limitation on precursor synthesis. The Birch reduction–alkylation is not of universal applicability and is suppressed for alkyl halides having β-substituents.

Experimental

^1H NMR spectra were recorded at 200 or 300 MHz and ^{13}C NMR spectra at 75 MHz, in $CDCl_3$ solution with tetramethylsilane ($\delta_H = \delta_C = 0$) as reference. Coupling constants are expressed in Hz. Ether refers to diethyl ether. Light petroleum refers to the fraction boiling in the range 40–60 °C. EI mass spectra were obtained with 70 eV electron impact ionisation and CI spectra with isobutane as the target gas on a VG Autospec spectrometer. GC–MS analyses were run on a Finnigan Incos 50 quadrupole instrument coupled to a Hewlett Packard HP 5890 chromatograph fitted with a 25 m HP 17 capillary column (50% phenyl methyl silicone). For the calculation of yields from GC data, the detector response was calibrated with known amounts of authentic materials (or close analogues) and *n*-dodecane, *n*-heptane or 3,3-dimethylbutan-2-one was added as a standard. Chromatographic purifications were carried out using either Sorbsil C60 40/60A or BDH 40–63 μm silica gel eluting with the given solvent mixture. Ammonia was obtained from BOC and used directly from the cylinder; drying and distillation had no perceptible effect on the yields.

1-Cyclopentylcyclohexa-2,5-diene-1-carboxylic acid 3

Ammonia (600 cm^3) was added to benzoic acid (10 g, 82 mmol) with careful stirring. To this, Li (1.6 g, 0.231 mmol) was added portionwise until a permanent blue colour persisted, followed by dropwise addition of bromocyclopentane (25 cm^3, 0.233 mol). The reaction mixture was left for 1 h whilst the NH_3 evaporated and ice was added to the remaining solid followed by dilute H_2SO_4. The product was extracted with ether (3 × 150 cm^3) and the combined ethereal extracts were dried ($MgSO_4$) and the solvent was evaporated leaving a solid which was recrystallised in light petroleum, yielding **3** as fine white crystals (11.4 g, 71%), mp 115 °C (lit.,[6] 96 °C) (Found: C, 75.28; H, 8.58. Calc. for $C_{12}H_{16}O_2$: C, 74.95; H, 8.40%); δ_H 1.2–1.4 (2 H, m, methylene-H, cyclopentyl ring), 1.4–1.7 (6 H, m, methylene-H, cyclopentyl ring), 2.3–2.5 (1 H, q, *J* 8, *tert*-H, cyclopentyl ring), 2.6–2.7 (2 H, s, allylic-H), 5.7–6.0 (4 H,

m, olefinic-H); δ_C 25.7, 26.5, 27.2 (5 × methylene-C), 47.8 (*tert*-C), 49.8 (quaternary-C), 125.9, 126.4 (4 × olefinic-C), 180.2 (CO).

1-*tert*-Butylcyclohexa-2,5-diene-1-carboxylic acid 4

Prepared by essentially the same procedure as above, except that the reaction mixture was quenched with *tert*-butyl bromide. Purification by dry flash chromatography, eluting with 20% ethyl acetate in light petroleum yielded **4** as white crystals (2.6 g, 18%), mp 101 °C (lit.,[6] 105 °C) (Found: C, 73.47; H, 9.35. Calc. for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95%); δ_H 1.00 (9 H, s, *tert*-butyl-H), 2.57–2.63 (2 H, s, allylic-H), 5.88–6.10 (4 H, m, olefinic-H); δ_C 26.0 (3 × methyl-C), 26.2 (allylic-C), 38.6 (quaternary-C), 52.9 (quaternary-C), 125.5, 126.2 (4 × olefinic-C), 180.4 (CO). In a similar preparation the blue ammonia solution was quenched with *tert*-butyl iodide eventually yielding **4** (29%) after flash chromatography.

1-Benzylcyclohexa-2,5-diene-1-carboxylic acid 5

This was prepared by essentially the same procedure as described above, except that the reaction was quenched with benzyl chloride. Acid **5** was obtained in pure form after recrystallisation from cyclohexane (14.9 g, 85%), mp 76–77 °C (lit.,[17] 76 °C) (Found: C, 78.17; H, 6.67. Calc. for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59%); δ_H 2.27–2.63 (2 H, m, allylic-H), 3.03 (2 H, s, benzylic-H), 5.80–5.90 (4 H, m, olefinic-H), 7.11–7.29 (5 H, m, arom-H); δ_C 25.0 (allylic-C), 46.1 (benzylic-C), 48.8 (quaternary-C), 126.5, 126.7, 127.9, 130.7, 136.1 (10 × olefinic, arom-C), 179.7 (CO). [Similar reaction on a 1 g rather than the above 10 g scale yielded acid **5** (99%).]

Radical reaction of carboxylic acid 3 and cyclohexenone; 3-cyclopentylcyclohexanone

1-Cyclopentylcyclohexa-2,5-diene-1-carboxylic acid **3** (1 g, 5.2 mmol), cyclohexenone (0.5 g, 5.2 mmol) and *tert*-butyl peroxybenzoate (0.1 g, 10% wt) were dissolved in benzene (5 cm^3) and refluxed for 1 week, during which a further 4 portions of initiator were added (0.55 g, 55% wt overall). Analysis of the reaction mixture by GC–MS indicated the presence of unreacted cyclohexenone, 3-cyclopentylcyclohexanone and phenylcyclopentane.† The reaction contents were diluted with ether (50 cm^3) and washed with NaOH (2 M, 3 × 25 cm^3). The alkaline extracts were combined, washed with light petroleum and the organic fractions were combined, dried ($MgSO_4$) and the solvent was evaporated yielding an oil (0.91 g; 59% 3-cyclopentylcyclohexenone and 9% phenylcyclopentane). The mixture was purified by column chromatography using 5% ethyl acetate in light petroleum, yielding 3-cyclopentylcyclohexenone as a colourless oil (0.27 g, 31%) (lit.,[18] bp 82 °C at 1 mmHg); δ_H 1.02–1.22 (2 H, m, methylene-H, γ to carbonyl), 1.34–1.44 (1 H, m, methylene-H, β to carbonyl), 1.45–1.80 (9 H, m; 8 H, methylene-H, cyclopentyl ring and 1 H, β to carbonyl), 1.87–2.00 (1 H, m, *tert*-H, cyclohexyl ring), 2.00–2.13 (2 H, m, methylene-H, α to carbonyl), 2.20–2.42 (2 H, m, methylene-H, α to carbonyl), 2.43–2.54 (1 H, m, *tert*-H, cyclopentyl ring); δ_C 25.2, 25.4, 30.3, 30.4, 30.7, 41.5 (7 × CH_2), 45.0, 46.2 (2 × CH), 47.5 (CH_2), 212.4 (CO); *m/z* 166 (M^+, 27%), 148 (10), 123 (38), 108 (53), 97 (100), 81 (18), 69 (40), 67 (42), 55 (48) (Found: M^+, 166.1364. $C_{11}H_{18}O$ requires *M*, 166.1358). The acids were regenerated using H_2SO_4, extracted with ether, dried ($MgSO_4$) and the solvent was evaporated yielding benzoic acid (1.12 g) as the only product. Dibenzoyl peroxide and *tert*-butyl peroxybenzoate were both found to be appropriate initiators.

Radical reaction of carboxylic acid 4 and cyclohexenone; 3-*tert*-butylcyclohexanone

1-*tert*-Butylcyclohexa-2,5-diene-1-carboxylic acid **4** (1.0 g, 6 mmol), cyclohexenone (0.54 g, 6 mmol) and dibenzoyl peroxide (0.5 g, 50% wt) were refluxed in benzene (5 cm^3) for 24 h. Analysis of the reaction mixture by GC–MS and ^{1}H NMR indicated the presence of 3-*tert*-butylcyclohexanone, *tert*-butylbenzene, biphenyl, benzoic acid, unreacted cyclohexenone, unreacted starting acid and traces of 3-phenylcyclohexanone. The product mixture was extracted with NaOH (2 M, 5 cm^3) and the alkaline fraction was extracted with benzene (2 × 10 cm^3). The aqueous fraction was acidified with excess acid and extracted with ether (3 × 25 cm^3), the ethereal extracts were combined, dried ($MgSO_4$) and the solvent was evaporated yielding a solid (0.54 g) which was a mixture of benzoic acid and also some unreacted acid **4**. The original benzene fractions were combined, dried ($MgSO_4$) and the solvent was evaporated to yield an orange oil (0.55 g). An attempt to isolate the adduct by flash chromatography resulted in poor recovery of material. The yields were estimated from the ^{1}H NMR of the mixture which indicated 25% of the title compound and 3% of *tert*-butylbenzene. In a repeat experiment, in a mixture of benzene and cyclohexane, yields were 58% adduct, 22% *tert*-butylbenzene and 28% biphenyl, based on acid **4** consumed.

Radical reaction of carboxylic acid 5 and cyclohexenone; 3-benzylcyclohexanone

1-Benzylcyclohexa-2,5-diene-1-carboxylic acid **5** (2.5 g, 12 mmol), cyclohexenone (1.13 g, 12 mmol) and dibenzoyl peroxide (0.25 g, 10% wt) were refluxed in benzene (20 cm^3) under an atmosphere of N_2 for 5 days, during which a further 0.75 g (40% wt overall) of initiator was added. Analysis of the reaction mixture by GC–MS indicated the presence of cyclohexenone, diphenylmethane, 3-benzylcyclohexanone and benzoic acid. The reaction contents were diluted with ether (50 cm^3) and extracted with NaOH (2 M, 3 × 10 cm^3). The combined alkaline extracts were washed with light petroleum (20 cm^3), neutralised with excess HCl and extracted with ether (3 × 50 cm^3). The ether solution was dried ($MgSO_4$) and the solvent was evaporated yielding a brown solid (2.08 g; 1.11 g unreacted starting acid **5**; 0.96 g benzoic acid). The original ether fraction was combined with the petroleum washing, dried ($MgSO_4$) and the solvent was evaporated yielding an oil (1.42 g). This was purified by column chromatography yielding the title compound as a pale yellow oil (0.64 g, 52%, based on the amount of acid reacted); δ_H(lit.,[20]) 1.35–2.50 (9 H, m, methylene, methine-H), 2.60–2.67 (2 H, d, *J* 6.2, benzylic-H), 7.10–7.40 (5 H, m, arom-H); δ_C(50 MHz), 25.3, 31.0 (2 × methylene-C), 41.0, 41.6, 43.1, 48.0 (3 × CH_2, 1 × CH), 126.3 (*p*-arom-C), 128.5, 129.2 (4 × arom-C), 139.5 (*ipso*-arom-C), 211.8 (CO).

Radical reaction of carboxylic acid 3 and acrylonitrile

1-Cyclopentylcyclohexa-2,5-diene-1-carboxylic acid **3** (0.5 g, 2.6 mmol), acrylonitrile (Z) (0.138 g, 2.6 mmol), di-*tert*-butyl peroxide (0.1 g, 20% wt) and benzene (5 cm^3) were added to a test tube which was degassed using the 'freeze, pump and thaw' method, sealed and heated in an oven at 100 °C for 7 h. GC–MS; *peak no. 151*, 3-cyclopentylpropionitrile, *m/z* (relative intensity), 122 (9), 108 (7), 95 (54), 82 (35), 69 (38), 55 (100), 41 (66), 27 (21); *peak no. 200*, phenylcyclopentane, 146 (M^+), 117 (100), 104 (83), 91 (58), 77 (21), 39 (29); *peak no. 238*, benzoic acid; *peak no. 325* (RZ_2H), 135 (54), 122 (18), 108 (22), 95 (35), 82 (40), 68 (48), 55 (84), 41 (100), 27 (22); *peak no. 479* (RZ_3H), 221 (16), 188 (7), 147 (51), 23 (44), 105 (50), 95 (30), 83 (48), 77 (53), 73 (94), 41 (100), 54 (64), 28 (59), 36 (41). NaOH (2 M, 30 cm^3) was added and the layers were separated. The alkaline fraction was extracted with benzene (10 cm^3) and the combined organic extracts were dried ($MgSO_4$) and the solvent was evaporated leaving a yellow oil (0.29 g); δ_H 1.5 (m, methylene-H, cyclopentyl ring), 1.6–2.0 (m, methylene-H, aliphatic chain), 2.25 (t, *J* 8.5, *tert*-H), 2.5 (m, adduct). Unfortunately it was not possible to determine the yield of the adduct from this spectrum. The acid compounds were regenerated using H_2SO_4,

† Identified by comparison with an authentic sample prepared by the procedure of Denton *et al.*[19]

extracted with ether, the combined extracts were dried ($MgSO_4$) and evaporated to give a white solid (0.35 g), shown by ^1H NMR to contain benzoic acid and unreacted starting acid.

Radical reaction of carboxylic acid 3 and vinyl benzoate

1-Cyclopentylcyclohexa-2,5-diene-1-carboxylic acid **3** (0.5 g, 2.6 mmol), vinyl benzoate (0.385 g, 2.6 mmol) and dibenzoyl peroxide (50 mg, 10% wt) were refluxed in benzene (5 cm^3) for 5 days, during which a further 100 mg of dibenzoyl peroxide was added portionwise (4 × 25 mg). Analysis of the reaction mixture by GC–MS indicated the presence of unreacted vinyl benzoate, phenylcyclopentane, benzoic acid, biphenyl, 2-cyclopentylethyl benzoate and another compound which was not identified from its mass spectrum. NaOH (2 M, 30 cm^3) was added to the mixture, the layers were separated and the aqueous fraction was extracted with benzene (10 cm^3). The combined organic fractions were dried ($MgSO_4$) and the solvent was evaporated to yield a brown oil (0.39 g;‡ 2-cyclopentylethyl benzoate 36%, double addition product 21%, phenylcyclopentane 21%); δ_H 1.0–1.25 (m, aliphatic-H, adduct, double addition product, phenylcyclopentane), 3.1 (1 H, quintet, *J* 10, phenylcyclopentane), 4.3–4.6 (3 H, m; 2 H, methylene-H α to O, adduct and 1 H, methine-H α to O, double addition product), 4.7–4.8 (1 H, dd, *J* 6.2, 1.8, olefinic-H, vinyl benzoate), 5.0–5.2 (1 H, dd, *J* 14.0, 1.8, olefinic-H, vinyl benzoate), 5.3–5.6 (broad multiplet, unidentified), 7.0–7.7 (m, arom-H, vinyl benzoate, adduct, double addition product and 1 H, olefinic-H, vinyl benzoate), 7.8–8.2 (m, arom-H, vinyl benzoate, adduct, double addition product). The acid compounds were regenerated using excess H_2SO_4, extracted with ether (2 × 50 cm^3), the ethereal fractions were combined, dried ($MgSO_4$) and the solvent was evaporated leaving a white solid (0.52 g) which was shown by ^1H NMR to be a mixture of benzoic acid (0.38 g) and unreacted **3** (0.12 g).

3-(2′-Hydroxyethoxy)cyclohexene 6

Ethylene glycol (6.16 g, 99 mmol) was added to dry THF (50 cm^3) and to this sodium wire (0.3 g, 12.4 mmol) was added and this mixture was refluxed overnight. 3-Bromocyclohexene (2 g, 12.4 mmol) was added to the reaction mixture and this was left refluxing for a further 12 h. The THF was evaporated and ether (100 cm^3) and H_2O (100 cm^3) were added to the residue. The layers were separated and the aqueous layer was extracted with ether (100 cm^3). The ethereal extracts were combined, dried ($MgSO_4$) and the solvent was evaporated to afford **6** as a clear, colourless liquid after distillation (1.56 g, 88%), bp 68 °C at 0.7 mmHg; δ_H 1.40–2.10 (6 H, m), 2.50 (1 H, m, hydroxy-H), 3.50–3.75 (4 H, m), 3.85–3.95 (1 H, m, *tert*-H), 5.70–5.90 (2 H, m, olefinic-H); δ_C(50 MHz) 19.6, 25.7, 28.7, 62.5, 69.7 (5 × CH_2), 73.7 (CH), 128.0, 131.6 (2 × CH); *m*/*z* 143 (MH^+, 6%), 119 (3), 81 (100), 55 (44), 44 (43), 42 (24), 41 (58) (Found: MH^+, 143.1065. $C_8H_{15}O_2$ requires *M*, 143.1072).

3-(2′-Tosylethoxy)cyclohexene

3-(2′-Hydroxyethoxy)cyclohexene **6** (10 g, 70 mmol) was dissolved in pyridine (80 cm^3) and to this toluene-*p*-sulfonyl chloride (20 g, 0.105 mol) was added at −10 °C. The resulting mixture was left stirring for 24 h at 0 °C. The reaction contents were added to H_2O (200 cm^3) and the product was extracted with ethyl acetate (2 × 100 cm^3). The organic extracts were combined, dried ($MgSO_4$) and the solvent was evaporated to yield the title compound as an orange liquid (16 g, 77%); δ_H 1.40–2.10 (6 H, m), 2.40 (3 H, s, methyl-H), 3.55–3.77 (2 H, m), 3.80 (1 H, m, *tert*-H), 4.10–4.20 (2 H, t, *J* 5.6), 5.60–5.90 (2 H, m, olefinic-H), 7.25–7.40 (2 H, d, *J* 8.1, arom-H), 7.75–7.85 (2 H, d, *J* 8.2, arom-H); δ_C(50 MHz) 22.2 (CH_3), 19.5, 25.6, 28.6, 65.9, 70.2 (5 × CH_2), 73.8 (CH), 127.6, 128.5, 130.3, 131.8, 133.4, 145.3 (8 × CH).

‡ Yield based on mass of starting acid reacted.

3-(2′-Iodoethoxy)cyclohexene 7

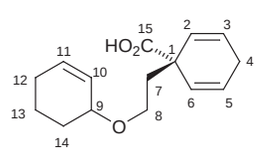
The tosylate (5 g, 17 mmol) was dissolved in AnalaR acetone (70 cm^3) to which sodium iodide (15 g, 0.1 mol) was added and the resulting mixture was refluxed for 20 h. The acetone was evaporated and ethyl acetate (100 cm^3) was added to the residue. This was washed with aqueous sodium thiosulfate (100 cm^3), brine (100 cm^3), dried ($MgSO_4$) and the solvent was evaporated to afford **7** as a clear, colourless liquid after distillation (3.6 g, 84%), bp 68–71 °C at 0.2–0.3 mmHg (Found: C, 38.20; H, 5.18. Calc. for $C_8H_{13}OI$: C, 38.11; H, 5.20%); δ_H 1.50–2.15 (6 H, m), 3.15–3.30 (2 H, t, *J* 7.0), 3.65–3.80 (2 H, m), 3.85–4.00 (1 H, m, *tert*-H), 5.70–6.00 (2 H, m, olefinic-H); δ_C(50 MHz) 4.4, 19.6, 25.7, 28.8, 69.6, 73.6, 127.8, 132.0.

3-(2′-Bromoethoxy)cyclohexene

Bromocyclohexene (2.6 g, 16 mmol), 2-bromoethanol (25 g, 0.2 mol) and dry THF (40 cm^3) were stirred at room temp. and to this mixture was added sodium wire (0.92 g, 0.04 mol). The resulting mixture was refluxed for 24 h, the NaBr precipitate was filtered off and the THF was evaporated. To the residue H_2O (100 cm^3) and cyclohexane (50 cm^3) were added. The layers were separated and the aqueous layer was extracted with more cyclohexane (2 × 50 cm^3). The combined organic extracts were dried ($MgSO_4$) and the solvent was evaporated to yield a brown liquid. The title compound was obtained as a clear, colourless liquid by distillation (1.84 g, 56%), bp 44–46 °C at 0.1–0.2 mmHg (Found: C, 47.14; H, 6.40. Calc. for $C_8H_{13}OBr$: C, 46.85; H, 6.39%); δ_H 1.44–2.12 (6 H, m), 3.42–3.47 (2 H, t, *J* 6.5), 3.75–3.86 (2 H, m), 3.87–3.95 (1 H, m, *tert*-H), 5.72–5.93 (2 H, m, olefinic-H); δ_C 19.5, 25.6, 28.7, 31.3, 68.7, 73.9, 127.9, 132.1.

1-[2-(Cyclohex-2-enyloxy)ethyl]cyclohexa-2,5-diene-1-carboxylic acid 8

Ammonia (250 cm^3) was added to benzoic acid (1.3 g, 10.7 mmol) followed by the portionwise addition of Li (0.24 g, 34 mmol) causing the solution to turn blue. This mixture was allowed to stir for 25 min before the addition of 3-(2′-iodoethoxy)cyclohexene **7** (3.23 g, 12.8 mmol) dissolved in dry THF (5 cm^3), causing an exothermic reaction and a colour change to yellow. The NH_3 was left to evaporate and NaOH (2 M, 70 cm^3) and ether (100 cm^3) were added to the resulting residue. The layers were separated and the organic fraction was extracted with aqueous NaOH (70 cm^3). The alkaline fractions were combined, washed with light petroleum and neutralised with excess HCl. The product was extracted with ether (3 × 100 cm^3), the ethereal extracts were combined, dried ($MgSO_4$) and the solvent was evaporated yielding an oil (2.07 g; 1.76 g, 67% **8** and 0.31 g, 24% unreacted benzoic acid). The mixture was purified by column chromatography using 10% ethyl acetate in light petroleum yielding **8** as a viscous oil (1.12 g, 42%); δ_H(300



8

MHz) 1.40–1.80 (4 H, m, 13,14-H), 1.85–2.10 (4 H, m; 2 H, 12-H and 2 H, t, *J* 7.1, 7-H), 2.60–2.70 (2 H, m, 4-H), 3.40–3.55 (2 H, dt, *J* 9.7, 7.2, 8-H), 3.75–3.85 (1 H, m, 9-H), 5.70–5.95 (6 H, m, olefinic 2,3,5,6,10,11-H); δ_C 19.6 (13-C), 25.7, 26.5, 28.7 (4,12,14-C), 39.6 (7-C), 46.5 (1-C), 64.7 (8-C), 73.6 (9-C), 126.5, 127.0 (2,3,5,6-C), 128.0, 131.4 (10,11-C), 180.6 (15-C); *m*/*z* 248 (M^+, 2%), 204 (5), 168 (6), 151 (17), 149 (20), 123 (25), 121 (13), 117 (2), 105 (55), 97 (20), 91 (26), 81 (100), 79 (15) (Found: M^+, 248.1412. $C_{15}H_{20}O_3$ requires *M*, 248.1421).

Radical fragmentation of carboxylic acid 8

Carboxylic acid **8** (1.21 g, 4.9 mmol) was dissolved in benzene (5 cm^3) to which dibenzoyl peroxide (0.6 g, 50% wt) was added and this mixture was refluxed for 30 h. GC–MS; *peak no. 239*, 7-oxabicyclo[4.3.0]nonane, *m*/*z* (relative intensity), 126 (M^+) (13), 83 (100), 67 (17), 55 (50), 41 (51), 39 (54), 29 (41), 27 (49); *peak no. 362*, benzoic acid; *peak no. 396*, biphenyl; *peak no. 474*, 3-(2′-phenylethoxy)cyclohexene, 202 (M^+, 1), 105 (36), 97 (15), 91 (25), 81 (100), 65 (18), 53 (22), 41 (37), 27 (28). Ether (20 cm^3) was added to the reaction mixture and this was washed with NaOH (2 × 20 cm^3). The alkaline fractions were neutralised with excess acid, extracted with ether (2 × 50 cm^3), dried ($MgSO_4$) and the solvent was evaporated to yield benzoic acid (0.8 g) and unreacted acid **8** (0.61 g). The original organic fraction was dried ($MgSO_4$) and the solvent was removed by distillation at atmospheric pressure yielding an orange liquid containing mainly 7-oxabicyclo[4.3.0]nonane **9** (0.17 g, 47%§) and 3-(2′-phenylethoxy)cyclohexene **10** (0.21 g, 36%); δ_H 1.20–2.10 (17 H, m; 11 H, **9** and 6 H, **10**), 2.85–3.00 (2 H, t, *J* 7.5, **10**), 3.65–3.78 (2 H, m, **10**), 3.78–3.92 (3 H, m; 2 H, **9** and 1 H, *tert*-H, **10**), 3.92–4.05 (1 H, q, *J* 7.8, *tert*-H, **9**), 5.75–5.92 (2 H, m, olefinic-H, **10**), 7.20–7.68 (5 H, m, arom-H, **10**). A small amount of **9** (0.2 g, 34%§) was isolated in pure form using a micro-distillation kit; δ_H 1.15–1.30 (2 H, m), 1.35–1.75 (6 H, m), 1.84–2.10 (3 H, m), 3.75–3.90 (2 H, dt, *J* 4.5, 8.6), 3.90–4.05 (1 H, q, *J* 7.8, *tert*-H); δ_C(50 MHz) 21.0, 24.1, 27.5, 28.1, 32.0 (5 × CH_2), 37.6 (CH), 66.0 (CH_2), 77.1 (CH).

In a separate experiment acid **8** (1.60 g, 6.4 mmol) in benzene (6 cm^3) containing dibenzoyl peroxide (0.8 g, 50% wt) was refluxed for 3 days during which a further 0.8 g of initiator was added. Ether (20 cm^3) was added to the reaction mixture and benzoic acid was removed with NaOH (2 M, 2 × 20 cm^3). Work-up of the alkaline fraction gave benzoic acid only. The ether and benzene were removed by atmospheric distillation yielding a liquid (1.30 g) containing 7-oxabicyclo[4.3.0]nonane **9** (55%) and **10** (40%).

Tin hydride mediated cyclisation of 3-(2′-iodoethoxy)cyclohexene 7

Iodide **7** (1 g, 4 mmol), tributyltin hydride (1.3 g, 4 mmol) and benzene (5 cm^3) were irradiated using a medium pressure 125 W Hg lamp for 6 h at 70 °C. GC–MS analysis; *peak no. 244*, 3-ethoxycyclohexene **11**, *m*/*z* (relative intensity), 126 (M^+) (14), 83 (100), 67 (12), 55 (30), 41 (28), 39 (24), 29 (17), 27 (24); *peak no. 213*, 7-oxabicyclo[4.3.0]nonane (MS as above). To the reaction mixture ether (10 cm^3) and saturated aqueous KF were added. The resulting mixture was left stirring for 24 h and polymeric tin fluoride was filtered off. The layers were separated, the ether layer was washed with H_2O (2 × 10 cm^3), dried ($MgSO_4$) and the solvent was removed by atmospheric distillation. The resulting residue was distilled to yield the two products (0.36 g) identified above (**9**, 60% and **11**, 13%); δ_H 1.15–2.10 (20 H, m; 11 H, **9** and 9 H, **11**), 3.45–3.62 (2 H, m, **11**), 3.76–3.88 (3 H, m; 2 H, **9** and 1 H, *tert*-H, **11**), 3.89–4.06 (1 H, q, *J* 8, *tert*-H, **9**), 5.75–5.88 (2 H, m, olefinic-H, **11**).

Radical fragmentation of carboxylic acid 8 in D_2O; 3-(2′-phenylethoxy)cyclohexene 10

Carboxylic acid **8** (0.18 g, 0.7 mmol) was dissolved in D_2O (800 μl) containing KOH (0.045 g, 0.8 mmol). This mixture was added to an NMR tube containing potassium persulfate (98 mg, 0.36 mmol). The contents of the tube were irradiated using a medium pressure 125 W Hg lamp for 7 h at 70 °C. $CDCl_3$ was added to the NMR tube and the layers were separated. The aqueous fraction was washed with a further portion of chloroform and then neutralised with excess HCl. The aqueous layer was extracted with ether, the ethereal extracts were combined, dried ($MgSO_4$) and the solvent removed giving an oil (0.044 g, 25%) which was shown by ^{1}H NMR spectroscopy to be unreacted acid **8**. The chloroform extracts were combined, dried using molecular sieves and the mixture was filtered, yielding **10** in $CDCl_3$ (63%¶); δ_H 1.50–2.10 (6 H, m), 2.85–3.00 (2 H, t, *J* 7.5), 3.60–3.80 (2 H, m), 3.80–3.95 (1 H, m, *tert*-H), 5.75–5.91 (2 H, m, olefinic-H), 7.2–7.4 (5 H, m, arom-H); δ_C 19.2, 25.2, 28.3, 36.9, 69.3, 73.0, 126.2, 128.0, 128.4, 129.1, 130.9, 139.3; *m*/*z* (relative intensity), 202 (M^+, 1), 173 (1), 105 (29), 97 (15), 91 (14), 81 (100), 65 (10), 53 (15), 41 (26), 27 (23), 18 (12) (Found: M^+, 202.1349. $C_{14}H_{18}O$ requires *M*, 202.1358).

2-Bromomethyl-6,6-dimethylbicyclo[3.1.1]hept-2-ene (myrtenyl bromide) 13

β-Pinene **12** (60 g, 0.44 mol) and NBS (30 g, 0.167 mol) were refluxed in CCl_4 (250 cm^3) containing dibenzoyl peroxide (0.3 g) for 4 h. The succinimide was filtered off and the solvent and unreacted pinene were evaporated yielding a brown liquid. The title compound was obtained as a clear, colourless liquid by fractional distillation using a Vigreux column (21 g, 59%), bp 64–68 °C at 0.5 mmHg (lit.,[21] bp 52–58 °C at 0.6 mmHg); δ_H(300 MHz) 0.83 (3 H, s, methyl-H), 1.09–1.12 (1 H, d, *J* 8.7, methylene-H), 1.31 (3 H, s, methyl-H), 2.06–2.13 (1 H, m), 2.21–2.32 (3 H, m), 2.32–2.40 (1 H, dt, *J* 9, 5.4, methylene-H), 3.96 (2 H, s, allylic-H), 5.69 (1 H, s, olefinic-H); δ_C 21.0, 25.9, 31.2, 31.4, 37.6 (quaternary-C), 37.8, 40.2, 44.7, 123.0, 144.0.

6,6-Dimethyl-2-(2-hydroxyethoxymethyl)bicyclo[3.1.1]hept-2-ene 14

Ethylene glycol (39.3 g, 0.663 mol) was added to dry THF (250 cm^3) and to this mixture sodium wire (2.2 g, 0.095 mol) was added. The mixture was refluxed overnight followed by the addition of myrtenyl bromide **13** (15 g, 79 mmol) dissolved in dry THF (20 cm^3) and the resulting mixture was refluxed for 10 h. The NaBr was filtered off and the THF was evaporated. To the residue H_2O (100 cm^3) and ether (100 cm^3) were added and the layers were separated. The aqueous fraction was extracted with ether (2 × 100 cm^3), the organic extracts were combined and washed with H_2O (100 cm^3). The resulting organic fraction was dried ($MgSO_4$) and the solvent was evaporated to yield **14** as a pale yellow liquid (13.7 g, 99%) (Found: C, 72.60; H, 10.75. Calc. for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27%); δ_H 0.85 (3 H, s, methyl-H), 1.19–1.21 (1 H, d, *J* 9, methylene-H), 1.32 (3 H, s, methyl-H), 2.09–2.43 (5 H, m), 3.50–3.57 (2 H, m), 3.70–3.73 (2 H, t, *J* 4.5, methylene-H), 3.94 (2 H, s, allylic-H), 5.51 (1 H, s, olefinic-H); δ_C 21.5, 26.6, 31.6, 31.9, 38.4 (quaternary-C), 41.3, 43.7, 62.3, 71.2, 74.4, 120.7, 145.7.

6,6-Dimethyl-2-(2-tosylethoxymethyl)bicyclo[3.1.1]hept-2-ene

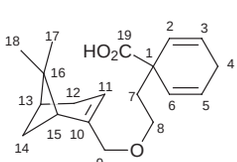
The alcohol **14** (14 g, 71 mmol) was dissolved in pyridine (100 cm^3) and toluene-*p*-sulfonyl chloride (19 g, 100 mmol) was added at −10 °C and this mixture was stirred for 16–20 h at −10 °C to 5 °C. The reaction contents were poured into ice–water (200 cm^3) and the product was extracted with ethyl acetate (3 × 200 cm^3) and the combined organic extracts were washed with H_2O (100 cm^3), dried ($MgSO_4$), and the solvent was evaporated to yield the title compound (24.5 g, 96%); δ_H 0.78 (3 H, s, methyl-H), 1.07–1.11 (1 H, d, *J* 8.4, methylene-H), 1.25 (3 H, s, methyl-H), 2.00–2.48 (8 H, m), 3.52–3.57 (2 H, t, *J* 4.8, methylene-H), 3.78 (2 H, s, allylic-H), 4.10–4.15 (2 H, t, *J* 4.8, methylene-H), 5.38–5.45 (1 H, m, olefinic-H), 7.26–7.30 (2 H, m, arom-H), 7.76–7.80 (2 H, d, *J* 8.2, arom-H); δ_C 21.1, 21.8, 26.3, 31.4, 31.6, 38.1 (quaternary-C), 40.9, 43.2, 67.0, 69.5, 74.1, 120.6, 128.1, 130.0 (× 2), 133.1, 144.9.

§ Yield based on amount of acid reacted.

¶ Yield based on the amount of **8** reacted, using benzyl alcohol as a standard.

6,6-Dimethyl-2-(2-iodoethoxymethyl)bicyclo[3.1.1]hept-2-ene 15
The tosylate of **14** (24.5 g, 70 mmol) was dissolved in AnalaR acetone (250 cm^3) and to the mixture NaI (64.5 g, 0.43 mol) was added. The mixture was stirred at room temperature for 5 h and refluxed overnight. The precipitate was filtered off and the acetone was removed under reduced pressure. Dichloromethane (200 cm^3) and H_2O (200 cm^3) were added to the residue, the layers were separated and the aqueous layer was extracted with dichloromethane (2 × 100 cm^3). The organic fractions were combined, washed with saturated aqueous sodium thiosulfate (2 × 150 cm^3), dried ($MgSO_4$) and the solvent was evaporated to give **15** (21.8 g, 100%) as a dark red liquid which was distilled using the Kugelrohr to yield a clear colourless liquid, bp 80–100 °C at 0.1 mmHg; δ_H 0.83 (3 H, s, methyl-H), 1.14–1.19 (1 H, d, *J* 8.9, methylene-H), 1.28 (3 H, s, methyl-H), 2.03–2.49 (5 H, m), 3.22–3.29 (2 H, t, *J* 6.8, methylene-H), 3.62–3.69 (2 H, t, *J* 6.8, methylene-H), 3.89 (2 H, s, allylic-H), 5.46–5.52 (1 H, m, olefinic-H); δ_C 3.1, 20.9, 26.1, 31.2, 31.4, 37.9 (quaternary-C), 40.7, 43.1, 70.1, 73.5, 120.3, 150.0; *m/z* 306 (M^+, 12%), 191 (14), 185 (13), 155 (14), 151 (15), 136 (37), 135 (100), 121 (10), 107 (22), 93 (55), 91 (27), 79 (61), 57 (10) (Found: M^+, 306.0467. $C_{12}H_{19}OI$ requires *M*, 306.0481).

1-[2-(6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-ylmethoxy)ethyl]-cyclohexa-2,5-diene-1-carboxylic acid 16
Ammonia (500 cm^3) was added to benzoic acid (2.5 g, 20.4 mmol) to which Li (0.45 g, 65.2 mmol) was added portionwise causing the solution to turn blue. This mixture was left stirring for 30 min followed by the addition of 6,6-dimethyl-2-(2-iodoethoxymethyl)bicyclo[3.1.1]hept-2-ene **15** (7.5 g, 24.5 mmol) dissolved in dry THF (5 cm^3), causing the solution to turn brown. The NH_3 was allowed to evaporate, ice was added to the residue followed by aqueous NaOH (2 M, 100 cm^3) and dichloromethane (100 cm^3). The layers were separated and the dichloromethane fraction was extracted with NaOH (100 cm^3), the alkaline fractions were combined and neutralised with excess HCl. The product was extracted with ether (3 × 100 cm^3), the ethereal extracts were combined, dried ($MgSO_4$) and the solvent was evaporated yielding a dark oil (5.18 g; 4.56 g, 74%, **16** and 0.28 g, 11% dihydrobenzoic acid and 0.34 g, 14% unreacted benzoic acid); δ_H (signals for **16** only) 0.81 (3 H, s,



16

methyl-H), 1.10–1.16 (1 H, d, *J* 8.4, 14-H), 1.24 (3 H, s, methyl-H), 1.90–2.05 (2 H, t, *J* 7.2, 7-H), 1.95–2.43 (5 H, m), 2.59–2.75 (2 H, m, 4-H), 3.34–3.44 (2 H, t, *J* 7.3, 8-H), 3.75–3.83 (2 H, m, 9-H), 5.40–5.50 (1 H, m, 11-H), 5.80–5.98 (4 H, m, 2,3,5,6-H). A small amount of the title compound was isolated after two successive purification steps by column chromatography, to give essentially pure material as a viscous oil; δ_C 21.0, 26.0, 26.2 (3 × 4,17,18-C), 31.3, 31.5 (2 × 12,14-C), 38.0 (16-C), 38.7 (7-C), 41.0, 41.3 (2 × 13,15-C), 46.1 (1-C), 66.0 (8-C), 73.8 (9-C), 119.7 (11-C), 126.0, 126.6 (4 × 2,3,5,6-C), 145.4 (10-C), 180.2 (19-C); *m/z* 302 (M^+, 2%), 195 (4), 151 (28), 134 (58), 119 (36), 107 (39), 105 (68), 93 (51), 92 (52), 91 (100), 79 (64), 77 (46) (Found: M^+, 302.1884. $C_{19}H_{26}O_3$ requires *M*, 302.1882).

Radical fragmentation of carboxylic acid 16
Carboxylic acid **16** (2.12 g, 7.0 mmol) was refluxed in benzene for 5 days with portionwise addition of dibenzoyl peroxide (3 × 0.2 g, 30% wt overall). GC–MS; *peak no. 297*, (tentatively identified as the 6-*endo* product **18**; see Results and discussion), *m/z* (relative intensity), 150 (1), 135 (6), 117 (4), 107 (43), 91 (37), 79 (100), 77 (46), 65 (18), 53 (18), 51 (70), 45 (22), 39 (55), 29 (35), 27 (44); *peak no. 338*, benzoic acid; *peak no. 375*, 6,6-dimethylbicyclo[3.1.1]heptane-2-spiro-3′-oxacyclopentane **17**, 180 (M^+) (1), 165 (3), 154 (5), 137 (9), 107 (21), 95 (25), 91 (28), 82 (28), 79 (37), 77 (29), 67 (43), 55 (39), 41 (100), 39 (53), 29 (28), 27 (44); *peak no. 540*, 6,6-dimethyl-2-(2-phenylethoxymethyl)bicyclo[3.1.1]hept-2-ene **19**, 195 (3), 136 (11), 119 (16), 105 (79), 91 (100), 79 (35), 77 (36), 65 (17), 55 (12), 41 (46), 27 (23). The benzene was evaporated and the resulting solid was dissolved in ether (50 cm^3) and extracted with NaOH (2 M, 2 × 20 cm^3). The ether was evaporated to yield a liquid (1.03 g) from which the cyclised and aromatic products were isolated by column chromatography eluting with 5% ethyl acetate in light petroleum, to yield two main fractions (0.19 g; 10% **17**, 5% **18** and 0.14 g, 7.4% **19**). 6,6-Dimethylbicyclo[3.1.1]heptane-2-spiro-3′-oxacyclopentane **17**; δ_H 0.88 (3 H, s, methyl-H), 1.14–1.25 (4 H; methyl-H and 1 H, methylene-H), 1.65–1.93 (8 H, m), 2.15–2.25 (1 H, m), 3.45–3.80 (4 H, m); *m/z* 181 (MH^+, 100%), 167 (45), 103 (18), 151 (13), 139 (11), 123 (16), 105 (6), 95 (5), 57 (45) (Found: MH^+, 181.1586. $C_{12}H_{21}O$ requires *M*, 181.1592). Tricyclic ether **18**; the ^1H NMR of **18** was badly overlapped by that of **17** and, except for the two methyl singlets at 0.79 and 1.33 ppm, could not be distinguished with any confidence; δ_C 20.9, 25.8 (2 × CH_3), 31.3, 32.3 (2 × CH_2), 37.7 (C), 40.2, 40.7, 40.9, 51.3 (4 × CH), 53.4, 66.7, 80.4 (3 × CH_2). 6,6-Dimethyl-2-(2-phenylethoxymethyl)bicyclo[3.1.1]hept-2-ene **19**; δ_H 0.85 (3 H, s, methyl-H), 1.15–1.20 (1 H, d, *J* 8.6, methylene-H), 1.30 (3 H, s, methyl-H), 2.10–2.48 (5 H, m), 2.86–2.98 (2 H, t, *J* 7.2), 3.57–3.67 (2 H, t, *J* 7.3), 3.89 (2 H, s, allylic-H), 5.45–5.52 (1 H, s, olefinic-H), 7.20–7.40 (5 H, m, arom-H); δ_C 21.0, 26.2 (2 × CH_3), 31.5, 31.2, 36.4 (3 × CH_2), 38.0 (quaternary-C), 40.9, 43.3 (2 × CH), 70.8, 73.7 (2 × CH_2), 119.6 (olefinic-C), 126.1, 127.2, 128.3, 128.7, 128.9 (6 × arom-C), 145.5 (olefinic-C); *m/z* 257 (MH^+, 10%), 239 (12), 213 (5), 195 (14), 181 (27), 167 (24), 155 (9), 135 (100), 123 (10), 105 (23), 93 (40), 79 (10), 58 (54), 56 (38) (Found: MH^+, 257.1913. $C_{18}H_{25}O$ requires *M*, 257.1905). The alkaline fractions were neutralised with excess acid and the mixture was extracted with ether to give benzoic acid (1.21 g).

Tin hydride mediated cyclisation of iodide 15
6,6-Dimethyl-2-(2-iodoethoxymethyl)bicyclo[3.1.1]heptane **15** (0.5 g, 1.63 mmol) and tributyltin hydride (0.52 g, 1.8 mmol) were dissolved in benzene (5 cm^3) and added to a 1 cm diameter ^{13}C NMR tube. The tube was capped and irradiated with light from a 125 W medium pressure Hg lamp for 2.5 h at room temperature and 3.5 h at 70–90 °C. Analysis of the reaction mixture by GC–MS indicated that all the iodide had been consumed; *peak no. 306*, 2-(ethoxymethyl)-6,6-dimethylbicyclo-[3.1.1]hept-2-ene **20**, *m/z* (relative intensity), 136 (12), 119 (29), 105 (16), 93 (33), 92 (46), 91 (100), 79 (31), 77 (52), 59 (82), 41 (69), 31 (49), 29 (46), 27 (43), 18 (19); *peak no. 373*, 6,6-dimethylbicyclo[3.1.1]heptane-2-spiro-3′-oxacyclopentane **17** (MS as above). The reaction contents were transferred to a round-bottomed flask and saturated aqueous KF (10 cm^3) was added and the mixture was stirred for 3 days. The polymeric tin fluoride was filtered off and the layers were separated. The aqueous layer was extracted with ether and the ethereal extracts were combined, dried ($MgSO_4$) and the solvent was evaporated yielding an orange liquid which, when analysed by ^1H NMR, still contained some tin residues. The liquid was distilled using a Kugelrohr (80–100 °C, 1 mmHg) giving a clear colourless liquid (0.114 g, 8% **20**, 31% **17**); δ_H 0.83 (3 H, s, methyl-H, **20**), 0.86 (3 H, s, methyl-H, **17**), 1.12–1.30 (11 H, m; 4 H, **17** and 7 H, **20**), 1.70–1.94 (8 H, m, **17**), 2.02–2.45 (6 H, m; 1 H, **17** and 5 H, **20**), 3.38–3.75 (6 H, m; 4 H, **17** and 2 H, **20**), 3.78–3.82 (2 H, m, allylic-H, **20**), 5.40–5.50 (m, 1 H, olefinic-H, **20**); δ_C 23.5, 25.1, 27.2, 28.7, 28.9, 38.8 (quaternary-C), 40.4, 43.4, 47.9 (quaternary-C), 51.2, 66.2, 80.4 (minor signals due to **20** were

present and corresponded almost exactly with the pure sample prepared as described below).

2-(Ethoxymethyl)-6,6-dimethylbicyclo[3.1.1]hept-2-ene 20

Myrtenyl bromide **13** (1 g, 4.65 mmol) was added to a mixture of sodium (0.13 g, 5.6 mmol) and ethanol (1.72 g, 37 mmol) in dry THF (20 cm^3) which had been stirring for 15 min. The resulting mixture was stirred for 0.5 h. The solution was filtered, the solvent was evaporated leaving a residue to which H_2O (30 cm^3) and ether (50 cm^3) were added. The layers were separated and the aqueous fraction was washed with ether (2 × 20 cm^3). The ethereal extracts were combined, dried ($MgSO_4$) and the solvent was evaporated yielding a yellow oil. Compound **20** was obtained as a clear, colourless liquid after Kugelrohr distillation (0.68 g, 81%), bp 50–60 °C at 0.5 mmHg (lit.,[22] bp 30 °C at 0.2 mmHg); δ_H 0.85 (3 H, s, methyl-H), 1.17–1.20 (4 H; 3 H, t, *J* 7.1, methyl-H and 1 H, methylene-H), 1.28 (3 H, s, methyl-H), 2.06–2.44 (5 H, m), 3.41–3.48 (2 H, q, *J* 7.0), 3.72–3.82 (2 H, m, allylic-H), 5.40–5.50 (1 H, s, olefinic-H); δ_C 15.2, 21.0, 26.2, 31.3, 31.6, 38.0 (quaternary-C), 41.0, 43.4, 65.2, 73.4, 119.2, 145.7.

***trans*-1-Bromo-2-(prop-2-yn-1-yloxy)cyclohexane 26**

Cyclohexene (19 g, 0.23 mol), prop-2-ynyl alcohol (38.9 g, 0.69 mol) and dichloromethane (20 cm^3) were stirred at −20 °C under an atmosphere of N_2. *N*-Bromosuccinimide (50 g, 0.28 mol) was added over the course of 40 min and the resulting mixture was stirred at the same temperature for 2 h and then at room temperature for a further 15 h. To the resulting mixture H_2O (75 cm^3) was added and the product was extracted with dichloromethane (3 × 25 cm^3). The combined organic extracts were washed with $NaHSO_3$ (1 M, 75 cm^3), K_2CO_3 (1 M, 75 cm^3) and H_2O (75 cm^3), dried ($MgSO_4$) and the solvent removed. The title compound was obtained as a clear, colourless liquid by distillation (31.9 g, 64%), bp 70–75 °C at 10–12 mmHg; δ_H(lit.,[14]) (300 MHz) 1.25–1.45 (3 H, m), 1.65–1.95 (3 H, m), 2.15–2.25 (1 H, m), 2.25–2.40 (1 H, m), 2.42–2.45 (1 H, t, *J* 2.3, alkyne-H), 3.52–3.60 (1 H, td, *J* 8.4, 4.4, *tert*-H), 3.95–4.04 (1 H, ddd, *J* 10, 8.2, 4.3, *tert*-H), 4.29–4.32 (2 H, dd, *J* 2.3, 1.3, prop-2-ynyl-H); δ_C 23.0, 25.0, 30.6, 35.3 (4 × CH_2), 54.9 (CH), 57.0 (CH_2), 74.0 (CH), 79.9 (C), 80.8 (CH); *m*/*z* (relative intensity), 218 (M^+) (1), 216 (1), 162 (1), 119 (5), 107 (9), 95 (32), 82 (100), 81 (72), 79 (31), 67 (43), 55 (19), 39 (29).

***trans*-1-Iodo-2-(prop-2-yn-1-yloxy)cyclohexane 27**

Iodine (21.6 g, 85 mmol) was added over the course of 0.5 h to a mixture of cyclohexene (9.35 g, 0.114 mol), $Cu(OAc)_2 \cdot H_2O$ (11.4 g, 57 mmol) and prop-2-ynyl alcohol (100 cm^3) under N_2. This mixture was stirred mechanically for 15 h. The reaction contents were filtered, the filtrate was washed with H_2O (2 × 200 cm^3), dried ($MgSO_4$) and the solvent was evaporated to yield an orange liquid (24.64 g); GC–MS: *peak no. 362*, 2,3-diiodoprop-2-en-1-ol; *peak no. 388*, 1,2-diiodocyclohexane; *peak no. 399*, *trans*-1-iodo-2-(prop-2-yn-1-yloxy)cyclohexane **27**. A 7 g portion of the mixture was purified by chromatography, eluting with 10% ethyl acetate in light petroleum, yielding a yellow liquid. The title compound was then obtained as a clear colourless liquid after Kugelrohr distillation (1.92 g, 23%‖), bp 80 °C at 0.15 mmHg (Found: C, 40.77; H, 5.09. Calc. for $C_9H_{13}OI$: C, 40.93; H, 4.96%); δ_H(300 MHz) 1.20–1.50 (3 H, m), 1.50–1.70 (1 H, m), 1.75–1.90 (1 H, m), 1.92–2.05 (1 H, m), 2.16–2.3 (1 H, m), 2.34–2.40 (1 H, m), 2.42–2.46 (1 H, t, *J* 2.4, alkyne-H), 3.53–3.62 (1 H, td, *J* 8.6, 4.3, *tert*-H), 4.04–4.14 (1 H, ddd, *J* 10.4, 8.6, 4.2, *tert*-H), 4.27–4.30 (2 H, t, *J* 2.3, prop-2-ynyl-H); δ_C 23.6, 27.0, 31.2 (3 × CH_2), 34.8 (CH), 37.7 (CH_2), 56.9 (CH_2), 74.4 (CH), 80.1 (C), 81.9 (CH); GC–MS *peak no. 399*, *m*/*z* (relative intensity) 137 (26), 127 (8), 109 (5), 91 (8), 69 (48), 55 (16), 39 (46).

‖ Yield based on the proportion of product purified.

Attempted preparation of 1-[2-(prop-2-yn-1-yloxy)cyclohexyl]-cyclohexa-2,5-diene-1-carboxylic acid 28

Benzoic acid (5 g, 41 mmol) was dissolved in ammonia (300 cm^3) to which Li (0.8 g, 0.12 mol) was added portionwise, causing the solution to turn deep blue. *trans*-1-Bromo-2-(prop-2-yn-1-yloxy)cyclohexane **26** (5 g, 23 mmol) dissolved in dry ether (50 cm^3) was added dropwise, causing the solution to turn yellow. After the NH_3 had evaporated, NaOH (150 cm^3) was added. This was washed with dichloromethane (2 × 100 cm^3), the carboxylic acids were regenerated by adding excess HCl, extracted with ether (2 × 200 cm^3), dried ($MgSO_4$) and the solvent was evaporated, yielding a solid (5.93 g) shown by ^1H NMR to be a mixture of benzoic acid and 1,4-dihydrobenzoic acid. The combined dichloromethane extracts were dried ($MgSO_4$) and the solvent removed to give a liquid (2.91 g) which was shown by ^1H NMR to contain mainly the bromide **26** and the corresponding alcohol. Birch reduction–alkylation with iodide **27** gave similar results.

Tin hydride mediated cyclisation of bromide 26; 9-methylene-7-oxabicyclo[4.3.0]heptane 29

trans-1-Bromo-2-(prop-2-yn-1-yloxy)cyclohexane **26** (2 g, 9.2 mmol), tributyltin hydride (2.91 g, 10 mmol) and benzene (5 cm^3) were added to a 1 cm diameter ^{13}C NMR tube and irradiated using a medium pressure 125 W Hg lamp for 8 h at room temperature. A sample of the reaction mixture was analysed by GC–MS; *peak no. 253*, prop-2-yn-1-yloxycyclohexane, *m*/*z* (relative intensity), 138 (M^+) (4), 109 (9), 95 (54), 82 (95), 81 (100), 79 (18), 67 (72), 55 (75), 41 (49), 39 (74); *peak no. 264*, 9-methylene-7-oxabicyclo[4.3.0]heptane **29**, 138 (M^+) (27), 120 (26), 109 (61), 95 (86), 81 (95), 79 (68), 68 (56), 67 (100), 41 (47), 39 (45). The benzene was removed by distillation at room temperature and the product was distilled using a Kugelrohr (0.2 mmHg) and collected in a liquid nitrogen trap (0.78 g, 61%); δ_H(300 MHz) 1.10–1.20 (8 H, m), 2.50–2.60 (1 H, m, *tert*-allylic-H), 3.95–4.00 (1 H, qd, *J* 7.8, 1.4, *tert*-H), 4.25–4.32 (1 H, dquintet, *J* 12.5, 1.4, methylene allylic-H), 4.42–4.50 (1 H, dq, *J* 12.3, 1.9, methylene allylic-H), 4.82–4.85 (1 H, q, *J* 2.0, olefinic-H), 4.88–4.91 (1 H, q, *J* 2.0, olefinic-H); δ_C 21.2, 23.0, 27.0, 27.6, 43.3, 69.6, 77.8, 102.4, 152.6; *m*/*z* 138 (M^+, 27%), 137 (55), 124 (10), 119 (13), 109 (30), 95 (40), 91 (29), 82 (63), 79 (50), 67 (100), 55 (57) (Found: M^+, 138.1049. $C_9H_{14}O$ requires *M*, 138.1045).

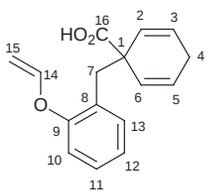
1-(Bromomethyl)-2-(ethenyloxy)benzene 31

To a solution of triphenylphosphine (22 g, 84 mmol) in DMF (300 cm^3) was added at 0 °C carbon tetrabromide (27.8 g, 84 mmol). To this mixture 2-(ethenyloxy)benzyl alcohol[16] (9 g, 60 mmol) was added and stirred at 0 °C for 15 min followed by 90 min at room temperature. The mixture was diluted with ice and water (500 cm^3), extracted with pentane (4 × 75 cm^3), these fractions were combined, dried ($CaCl_2$) and the solvent was evaporated to give an orange liquid (24.16 g). This was purified by column chromatography eluting with 2% ethyl acetate in light petroleum yielding the clear, colourless bromide **31** (5.7 g, 44%); δ_H 4.48–4.52 (1 H, dd, *J* 6.0, 1.7, olefinic-H), 4.56 (2 H, s, benzylic-H), 4.70–4.85 (1 H, dd, *J* 13.4, 1.8, olefinic-H), 6.60–6.70 (1 H, dd, *J* 13.6, 6.4, olefinic-H), 6.95–7.03 (1 H, dt, *J* 1.4, 7.1, arom-H), 7.07–7.11 (1 H, dd, *J* 7.6, 1.2, arom-H), 7.26–7.34 (1 H, dt, 2.0, 7.8, arom-H), 7.35–7.43 (1 H, dd, *J* 1.8, 7.4, arom-H); δ_C(50 MHz) 28.1, 95.5, 116.9, 123.7, 127.9, 130.3, 131.3, 148.2, 154.7.

1-[2-(Ethenyloxy)benzyl]cyclohexa-2,5-diene-1-carboxylic acid 32

Ammonia (250 cm^3) was added to benzoic acid (2.6 g, 21.4 mmol) to which Li (0.47 g, 68.2 mmol) was added portionwise causing the solution to turn blue. After 30 min the solution was quenched with 1-(bromomethyl)-2-(ethenyloxy)benzene **31** (5 g, 23.5 mmol) causing the solution to turn red. The NH_3 was

evaporated using a water bath, ice was added to the residue followed by aqueous NaOH (2 M, 50 cm^3) and ether (100 cm^3). The ether layer was extracted with aqueous NaOH (30 cm^3), the alkaline fractions were combined, washed with ether (100 cm^3) and neutralised with excess HCl. The product was extracted with ether (3 × 100 cm^3), the ethereal extracts were combined, dried ($MgSO_4$) and the solvent was evaporated yielding a yellow oil (3.25 g; 2.75 g, 50%, **32** and 0.5 g, unreacted benzoic acid). Recrystallisation from cyclohexane yielded pure **32** as white



32

crystals (1.37 g, 25%), mp 99–101 °C (Found: C, 74.76; H, 6.34. Calc. for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29%); δ_H 2.15–2.60 (2 H, m, 4-H), 3.13 (2 H, s, 7-H), 4.37–4.40 (1 H, dd, *J* 6.1, 1.6, 15-H), 4.67–4.72 (1 H, dd, *J* 13.8, 1.6, 15-H), 5.73–5.98 (4 H, m, 2,3,5,6-H), 6.50–6.56 (1 H, dd, *J* 13.7, 6.1, 14-H), 6.88–7.22 (4 H, m, arom-H); δ_C 25.8 (4-C), 39.0 (7-C), 48.8 (1-C), 94.7 (15-C), 116.1, 122.5 (10,12-C), 126.1, 126.4 (2,3,5,6-C), 126.4 (8-C), 127.9, 132.6 (11,13-C), 148.5 (14-C), 155.4 (9-C), 180.1 (16-C).

Radical fragmentation of carboxylic acid 32

1-[2-(Ethenyloxy)benzyl]cyclohexa-2,5-diene-1-carboxylic acid **32** (1 g, 3.91 mmol) and dibenzoyl peroxide (0.25 g, 25% wt) were dissolved in benzene (10 cm^3) and refluxed for 2 days under nitrogen, during which a further portion of initiator (0.20 g) was added. A sample of the reaction mixture was submitted for GC–MS analysis; *peak no. 231*, 1-(ethenyloxy)-2-methylbenzene **34**, *m*/*z* (relative intensity), 134 (M^+) (60), 119 (27), 105 (37), 91 (100), 77 (59), 65 (57), 51 (43), 39 (78), 27 (61), 18 (47); *peak no. 264*, 1-ethoxy-2-methylbenzene, 136 (M^+) (46), 108 (100), 107 (83), 90 (37), 79 (48), 77 (53), 65 (18), 51 (26), 39 (29), 27 (46), 18 (35); *peak no. 356*, benzoic acid; *peak no. 474*, 1-(ethenyloxy)-2-benzylbenzene **35**, 210 (M^+) (34), 195 (32) 181 (29), 165 (68), 152 (26), 115 (40), 105 (29), 91 (79), 77 (81), 63 (38), 51 (67), 39 (61), 27 (100), 18 (96); *peak no. 564*, 1-ethoxy-2-benzylbenzene, 212 (M^+) (5), 184 (7), 163 (8), 106 (7), 105 (100), 91 (9), 78 (65), 77 (56), 51 (33), 39 (31), 27 (16), 18 (24). The mixture was passed down a column of silica gel which resulted in one fraction which gave a well-resolved ^{1}H NMR spectrum (60 mg; 11 mg, 3%, **34**; 36 mg, 4%, **35**; 13 mg, biphenyl) δ_H 2.36 (3 H, s, methyl-H, **34**), 3.98 (2 H, s, benzylic-H, **35**), 4.37–4.40 (2 H, m, olefinic-H, **34**, **35**), 4.58–4.70 (2 H, m, olefinic-H, **34**, **35**), 6.57–6.671 (2 H, m, olefinic-H, **34**, **35**), 6.95–7.70 (23 H, m, arom-H, **34**, **35**, biphenyl).

Tin hydride mediated reduction of bromide 31; 1-(ethenyloxy)-2-methylbenzene 34

1-(Bromomethyl)-2-(ethenyloxy)benzene **31** (1 g, 4.7 mmol) and tributyltin hydride (1.5 g, 5.2 mmol) were dissolved in benzene (10 cm^3) and irradiated using a medium pressure 125 W Hg lamp for 6 h. The reaction was monitored by TLC until all the bromide had been consumed. GC–MS: *peak no. 231*, 1-(ethenyloxy)-2-methylbenzene **34**, *m*/*z* (relative intensity), 134 (M^+) (36), 119 (25), 105 (23), 91 (65), 77 (53), 65 (63), 51 (47), 39 (100), 27 (78); *peak no. 260*, 1-(ethoxy)-2-methylbenzene. Saturated aqueous KF (10 cm^3) was added, the resulting mixture was stirred for 24 h and the tin residues were filtered off. The solvent was evaporated to yield slightly impure **34** as an orange liquid (0.57 g, *ca*. 92%); δ_H 2.36 (3 H, s, methyl-H), 4.31–4.39 (1 H, dd, *J* 6.2, 2.0, olefinic-H), 4.57–4.64 (1 H, dd, *J* 13.6, 2.0, olefinic-H), 6.56–6.66 (1 H, dd, *J* 13.5, 6.4, olefinic-H), 6.90–7.32 (4 H, m, arom-H).

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