

Unique carbon–carbon bond homolysis in 3-alkylcyclohexa-1,4-dienyl-3-carboxylic acid radicals

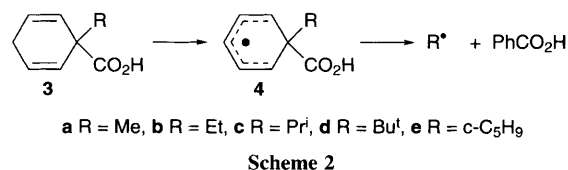
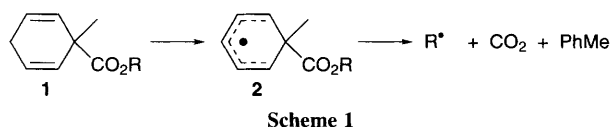
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3-Substituted cyclohexadienyl radicals generated by hydrogen abstraction from 3-alkylcyclohexa-1,4-diene-3-carboxylic acids readily fragment to produce alkyl radicals and benzoic acid; suitably functionalised alkyl groups cyclize in moderate yields.

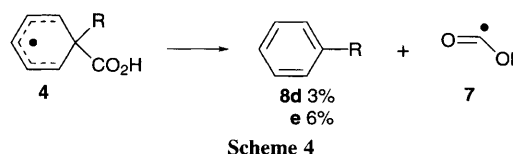
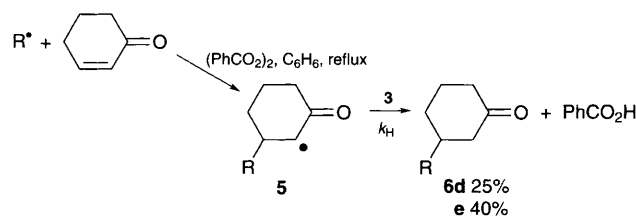
The rapid expansion in the use of free radical methods in organic synthesis has promoted a search for a new generation of initiator compounds capable of producing radicals mildly and selectively. We showed recently that hydrogen abstraction from 3-methylcyclohexa-1,4-diene-3-carboxylates **1** produced cyclohexadienyl radicals **2** which decarboxylated at moderate temperatures to afford alkyl radicals accompanied by in-offensive byproducts (toluene and carbon dioxide, Scheme 1).¹

For comparison purposes, cyclohexadienyl radicals were subsequently generated by hydrogen abstraction from several of the precursor 3-alkylcyclohexa-1,4-diene-3-carboxylic acids **3**. The acids were prepared in good yields by quenching the blue solution, obtained from reduction of benzoic acid with lithium metal in liquid ammonia,^{2–6} with an alkyl iodide (for primary alkyls) or alkyl bromide (for secondary and tertiary alkyls). When solutions of the 3-methyl-**3a** and 3-ethyl-**3b** carboxylic acids with di-*tert*-butyl peroxide in *tert*-butylbenzene were photolysed in the cavity of an EPR spectrometer, spectra due to the corresponding cyclohexadienyl radicals **4a,b** were observed, as expected. Surprisingly however, similar hydrogen abstraction from the 3-isopropyl acid **3c** gave radical **4c** at temperatures below about 300 K, but above this temperature, EPR signals due to the isopropyl radical replaced the original spectrum. On lowering the temperature, the original spectrum of **4c** reappeared. The behaviour of the 3-*tert*-butyl acid **3d** was even more exceptional in that only the *tert*-butyl radical could be observed even down at temperatures as low as 105 K in propane. These spectroscopic observations indicated that homolytic scission of the ring C(3)-to-alkyl bond in radical **4** occurred with great ease for branched alkyl groups and was competitive with radical termination processes even below room temperature (Scheme 2). From the temperatures above which alkyl radicals appeared in the EPR spectra it was evident that the ease of fragmentation was in the order *tert*-alkyl > *sec*-alkyl > *n*-alkyl; *i.e.* the rate of β -scission increased with the thermodynamic stability of the released alkyl radical.



The spectroscopic observations implied that 3-substituted cyclohexadienyl acids **3** might function efficiently as radical sources in chain reactions designed for synthetic purposes. The major byproduct would be benzoic acid which could be easily removed by washing with dilute alkali. Accordingly, individual acids **3**, an alkene (cyclohex-2-ene-1-one, acrylonitrile, vinyl benzoate) and dibenzoyl peroxide were refluxed in benzene for *ca.* 24 h. Moderate amounts of the anticipated adducts **6** were isolated[†] (Scheme 3). When acrylonitrile was used, reaction with **3b** and **3e** proceeded as expected but the adduct was accompanied by significant quantities of oligomers. The reaction of **3e** with vinyl benzoate afforded the cyclopentyl adduct (26%) together with oligomer. To achieve complete conversion of each starting acid it was necessary to use nearly a stoichiometric amount of the peroxide initiator which suggested that hydrogen transfer from **3** to the adduct radical **5** was slow. Apart from benzoic acid, the only significant byproducts were alkylbenzenes **8** which were probably formed by competing loss of hydroxyformyl radicals **7** (Scheme 4) from the intermediate cyclohexadienyl radicals. Loss of carbon dioxide followed by oxidation of the resulting radical **8** plausibly accounts for this side product. Reactions were also carried out in sealed tubes at higher temperatures and with other initiators (di-*tert*-butyl peroxide, *tert*-butyl peroxybenzoate) but the yields of **6** were not significantly improved.

The analogous intramolecular process was found to be more efficient. For example, acid **10**, made by alkylation with cyclohexenyloxyethyl iodide **9**, cyclized on refluxing with an initiator in benzene to afford 2-oxabicyclo[4.3.0]nonane **12** in 55% yield (Scheme 5). This compared favourably with the tributyltin hydride mediated cyclization of **9** which gave **12** in 60% yield. A distinct advantage of using acid **10** was that, because of slow hydrogen transfer from **10**, none of the direct reduction product, 3-ethoxycyclohexene was isolated, as compared with 12% of this byproduct from the organotin route. Reaction of hexenyl acid **14** afforded methylcyclopentane in 62% yield together with minor amounts of hex-1-ene and cyclohexane. From a sealed-tube reaction of **14** (0.88 mol dm^{–3} in *tert*-butylbenzene) at 148 °C the measured ratio of hex-1-ene to methylcyclopentane ([H]/[M]) was 0.0102. It can easily be



shown that the rate constant for hydrogen abstraction from carboxylic acid **14**, $k_H = k_C[M]/[14][H]$, where k_C is the known⁷⁻⁹ rate constant for cyclization of the hex-5-enyl radical and hence $k_H(148\text{ }^\circ\text{C}) \sim 2 \times 10^4 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$. Thus the rate constant for abstraction of a bis(methylene) hydrogen from acid **14** by primary alkyl radicals is about two orders of magnitude

less than the rate constant for hydrogen abstraction from tributyltin hydride ($3 \times 10^6 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ at $37\text{ }^\circ\text{C}$).⁸ This explains the need for high initiator concentrations in the cyclohexadienyl acid reactions, because a small k_H will induce short chains, the negligible amounts of direct reduction products and also the production of oligomers.

In conclusion, 3-alkylcyclohexadienyl-3-carboxylic acids of general type **3** readily fragment at temperatures appropriate for organic synthesis ($< 100\text{ }^\circ\text{C}$) to give primary, secondary or tertiary alkyl radicals. The reaction can be incorporated into short chain processes which show promise for selected cyclizations.

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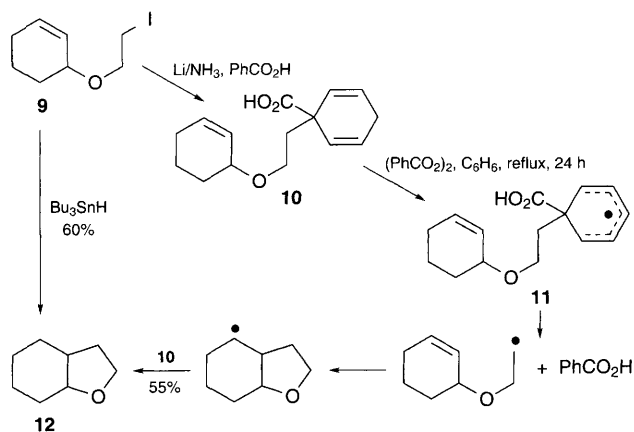
Footnote

† Yields are mol% relative to precursor acid **3**; isolated yield for **6e** estimated from NMR for **6d**.

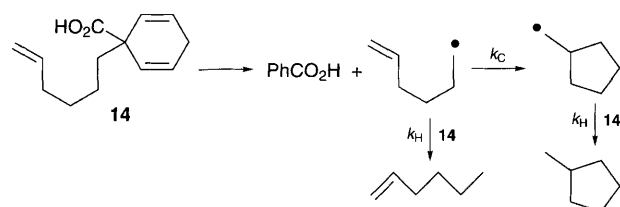
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Scheme 5



Scheme 6