Radical-chain Decomposition of Cyclohexa-1,4-diene-3-carboxylates and 2,5-Dihydrofuran-2-carboxylates

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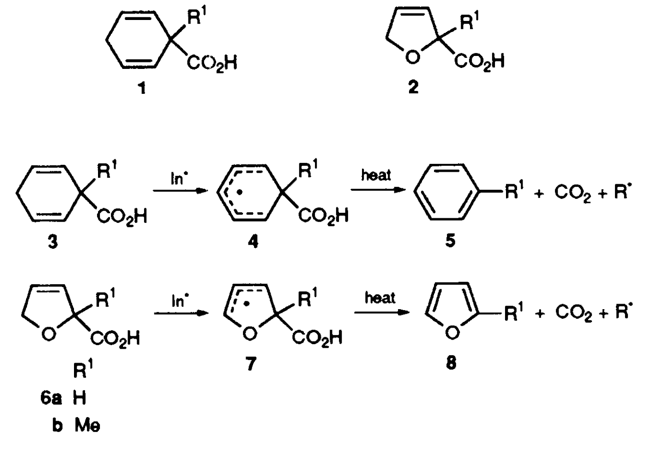
3-Methylcyclohexa-1,4-diene-3-carboxylates and 2-methyl-2,5-dihydrofuran-2-carboxylates decompose to generate free alkyl radicals which have been incorporated into chain reactions producing alkyl bromides, alkene adducts and ring-closure products.

Demand for flexible free radical chain reactions, suitable for synthetic applications under a wide range of experimental conditions, has expanded greatly in the last few years. The majority of recent syntheses of this type rely either on organotin hydrides or on Barton thiohydroxamic acid esters.[1] The main difficulties with these, and related reagents, are either their toxicity, or the formation of undesirable side products; there is therefore a clear need for the development of versatile alternatives. We have investigated the radical chain decompositions of esters of cyclohexa-1,4-diene-3-carboxylic acids **1** and 2,5-dihydrofuran-2-carboxylic acids **2**.

The esters of both molecules contain allylic, or bisallylic, hydrogens which are highly labile towards transfer by carbon- and oxygen-centred radicals so that an intermediate cyclohexadienyl **4** or dihydrofuranyl radical **7** will be formed with high selectivity (Scheme 1). Formation of the aromatic product **5** or **8** will provide the driving force for decarboxylation. The alkyl radical R· produced in this step could take part in intra- or inter-molecular reactions before continuing the chain by reacting with another molecule of **3** or **6**. The attractive feature of this scheme is that in each case the aromatic by-product, **5** or **8**, is easily removed because of its volatility, and is comparatively benign (apart from **5a**).

The precursor carboxylic acids were readily accessed by Birch reduction of benzoic or furoic acid. The substituents R^1 were introduced with high regioselectivity by quenching the metal/ammonia solution with an alkyl bromide or iodide, instead of the usual ammonium chloride.[2,3] Initially, the simplest esters with R^1 = H (**3a**, **6a**) were investigated. Reaction of **3a**, R = $PhCH_2$, with *N*-bromosuccinimide (NBS) in refluxing tetrachloromethane did indeed give benzyl bromide and benzene; benzyl bromide was also formed in the reaction of **6a**, R = $PhCH_2$ with NBS. Thus, the expected chain sequences (Scheme 1) took place, but the yields were low and additional side products were encountered. The reason for this was revealed by an examination of the intermediate radicals by EPR spectroscopy. When a *tert*-butylbenzene solution of **3a** (R = $PhCH_2$ or Bu^t) and di-*tert*-butylperoxide was photolysed in the cavity of an EPR spectrometer the spectrum showed the presence of two cyclohexadienyl radicals, **9** and **10**, in comparable amounts. Evidently the hydrogen abstraction from **3** by *tert*-butoxyl radicals took place with little or no selectivity. Cyclohexadienyl radical **10** could not decarboxylate and hence the reactions became complex and low yielding. EPR spectra showed a similar production of both possible dihydrofuranyl radicals from **6a** (R = $PhCH_2$ or Bu^t).



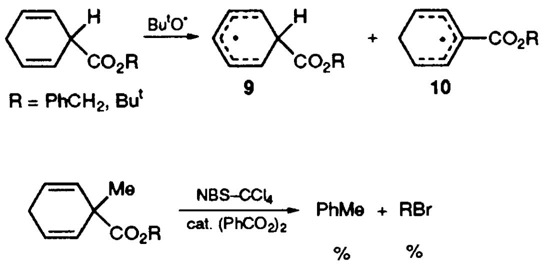
Scheme 1 In· = initiator radical

To circumvent this problem esters **3b** and **6b** in which the second site was blocked by a methyl group were prepared. Hydrogen abstraction from **3b** with *tert*-butoxyl radicals under EPR conditions gave rise to clean spectra of single cyclohexadienyl radicals of type **9** [*e.g.* the cyclohexadienyl derived from **3bi** had: g = 2.003 ± 0.001, a(1H) = 1.33, a(2H) = 0.93, a(2H) = 0.27 mT at 220 K]. In hydrocarbon solutions the cyclohexadienyl spectrum persisted up to *ca.* 330 K, which indicated that decarboxylation was still slow on the EPR timescale at this temperature.

Several inter- and intra-molecular chain reactions of **3b** and **6b** were examined. Refluxing the ester with NBS in tetrachloromethane gave moderate yields of the corresponding alkyl bromide, RBr. It proved difficult to ensure complete consumption of the reactant esters under these conditions, particularly with esters of primary and secondary alcohols but, by adding a second equivalent of NBS after *ca.* 10 h and continuing the reflux for a further 6 h, good conversion of secondary, tertiary and benzylic esters was achieved. The yields (mol% by GC) shown in Scheme 2 indicate that bromide formation was best for esters of tertiary and benzyl alcohols, some polybrominated material was also formed. The intermediate cyclohexadienyl radicals **4** probably decarboxylate more readily at 80 °C when comparatively stabilised tertiary or benzyl radicals are ejected.

Similar results were obtained for the corresponding 2-methyl-2,5-dihydrofuran-1-carboxylates, **6bii** and **6biii**. An interesting and unexpected feature of the reaction of the primary ester **3bi** was the formation of *ca.* 2% *n*-hexyl benzoate **12** (R = n-C_6H_{13}). This is evidently formed by loss of a methyl radical from the intermediate radical **9**, *i.e.* methyl loss competes to some extent with decarboxylation at this temperature.

Participation of esters **3b** in intermolecular chain additions was examined in reactions with acrylonitrile, thermally initiated



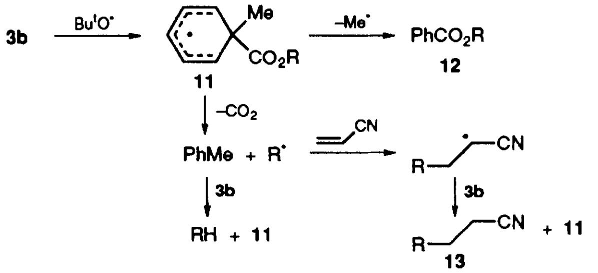
		PhMe %	RBr %
3b	i, R = n-C_6H_{11}[a]	7	3
	ii, R = Bu^t	47	40
	iii, R = $PhCH_2$	–	63[b]

[a] Incomplete consumption of ester. [b] Isolated yield

Scheme 2

at 140 °C with di-*tert*-butylperoxide. The product range from reactions in *tert*-butylbenzene (also benzene) in sealed tubes included the expected adducts **13** together with reduction products (RH) and significant amounts of benzyl esters **12** (Scheme 3). The sizable amounts of RH formed showed that the alkyl radicals R· abstracted hydrogen from **3b** almost as readily as they added to the alkene; the proportion of adduct could obviously be increased by using more alkene, although this would also promote oligomerisation, which was already significant in some experiments. The significant yields of benzoic acid esters **12** show that, as expected, methyl radical loss is more important at higher temperatures.

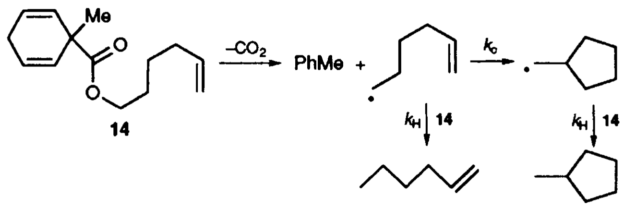
The hex-5-enyl ester **14** decomposed at 140 °C in *tert*-butylbenzene solvent to give toluene, the product of intramolecular addition, *i.e.* methylcyclopentane, together with minor amounts of hex-1-ene, cyclohexane, and hex-5-enylbenzoate (Scheme 4). From the ratio of methylcyclopentane to hex-1-ene, and the known concentration of **14**, the ratio of the rate constants for cyclisation (k_c) to hydrogen abstraction from **14** (k_H) was determined in the usual way[4,5] to be: $k_H/k_c = 1.3 \times 10^{-2}$ dm^3 mol^{-1}. Using the known k_c value at 140 °C[5–7] we find $k_H = 0.82 \times 10^5$ dm^3 mol^{-1} s^{-1} at this temperature. This rate constant is lower than previous estimates of k_H for abstraction from cyclohexa-1,4-diene by primary alkyl radicals (1×10^5 and 2.3×10^5 dm^3 mol^{-1} s^{-1} at 50 °C).[8,9] However, there are four abstractable hydrogen atoms in cyclohexa-1,4-diene compared with only two in **14** so that after statistical correction the agreement is good. Thus, the rate of hydrogen abstraction from **14** by primary alkyl radicals is about an order of magnitude slower than the rate of hydrogen abstraction from tri-*n*-butyltin hydride ($k_H = 2.9 \times 10^6$ at 37 °C)[6] and about an order of magnitude greater than the rate of chlorine abstraction from tetrachloromethane by carbon-centred radicals ($k_{Cl} = 1.8 \times 10^4$ dm^3 mol^{-1} s^{-1} at 37 °C).[10] That the cyclohexa-1,4-dienyl esters are slower hydrogen donors than organotin hydrides may be advantageous in synthetic procedures because the rapid hydrogen transfer by organotin reagents is inconvenient in many applications.



	R	RH	PhMe	13^a	12 %
I	n-C_6H_{11}	30	48	28	48
II	Bu^t	37	49	57	41
III	$PhCH_2$	–	57	26	51

[a] Includes diadduct; note that the conversion of **3b** was *ca.* 50% in each case

Scheme 3



Scheme 4

We have shown that 3-methylcyclohexa-1,4-dienyl-3-carboxylates and 2-methyl-2,5-dihydrofuran-2-carboxylates function effectively as radical sources for chain reactions. For synthetic applications it would be advantageous for decarboxylation to occur under milder conditions without competition from methyl loss. Experiments designed to achieve this are in progress with alternative substituted cyclohexa-1,4-dienyl carboxylates.

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