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The efficiency of alkyl radical generation and hydrogen transfer from 1-alkylcyclohexa-2,5-diene-1-carboxylic acids

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Abstract

A novel EPR spectroscopic technique has been used to determine kinetic data for alkyl radical generation and hydrogen transfer from 1-alkylcyclohexa-2,5-diene-1-carboxylic acids; the implications of these data for preparative chain reactions of these reagents are inferred. © 1999 Elsevier Science Ltd. All rights reserved.

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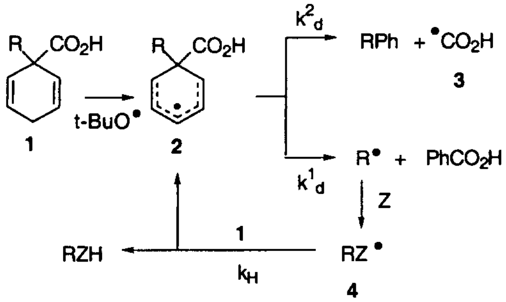
1-Alkylcyclohexa-2,5-diene-1-carboxylic acids **1** can act as reductive chain propagation reagents, and hence as replacements for organotin hydrides, under certain circumstances.[1,2] The key propagation steps are selective H-abstraction from the bisallylic site of acid **1** to generate delocalised radical **2** which fragments in an unusual type of C–C bond scission to produce benzoic acid and the desired radical R$^\bullet$. The latter 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; suitably functionalised R$^\bullet$ may



a, R = Me, **b**, R = Et, **c**, R = n-Pr
d, R = i-Pr, **e**, R = t-Bu

Scheme 1. 1-Alkylcyclohexa-2,5-diene-1-carboxylic acid mediated radical chain alkylation of alkenes (Z)

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cyclise instead. The advantages over organotin reagents are that benzoic acid, which can easily be removed by an alkaline extraction, is the only co-product, and that the H-transfer step is slower. Respectable yields of alkylated olefins were obtained for secondary, tertiary and delocalised alkyl radicals,[2] however, kinetic information on the hydrogen transfer (k_H) and dissociation (k_d) steps was very desirable as a tool for effective synthetic planning.

When cyclohexadienyl radicals **2b–e** were generated in an EPR spectrometer, by means of photolytically produced *t*-butoxyl radicals, *both* radical **2b–e** and the released alkyl radical $R^{\cdot}$ were spectroscopically detectable in a particular temperature range which depended on the nature of R. This suggested that steady-state EPR spectroscopy might provide an option for determining the key rate parameters. Acids **1a–e** were prepared by Birch reduction/alkylation as described previously.[3a–f] The concentrations of **2** and $R^{\cdot}$ were determined by the EPR method[4] from photolyses of known concentrations of **1b–e** with di-*t*-butyl peroxide either neat or in *t*-butylbenzene, or in cyclopropane solution, directly in the EPR resonator. The propagation steps under these conditions were as shown in Scheme 1 and chain termination was by bimolecular reactions of **2** and $R^{\cdot}$ ($2k_t$). Using the Steady State Approximation it can easily be shown that:

$$k^1_d/2k_t + k_H/2k_t\{[1][R^\bullet]/[2]\} = [R^\bullet]^2/[2] + [R^\bullet] \qquad (1)$$

provided the alternative β-scission to the hydroxyformyl radical (**3**) is negligible. Eq. 1 simplifies to the usual expression $\{k^1_d/2k_t=[R^{\cdot}]^2/[2]+[R^{\cdot}]\}$[5] for low concentrations of acid **1** or when k_H is small. From measurements of $[R^{\cdot}]$ and [**2**] at two (or more) different acid concentrations [**1**], simultaneous equations were derived from Eq. 1 and solved for $k^1_d/2k_t$ and $k_H/2k_t$.

$CH_3^{\cdot}$ radical production was not observed from the 1-methyl acid **1a** in the spectroscopically accessible temperature range ($T \leq 380$ K). For the other acids **1b–e** with primary, secondary and tertiary alkyl substituents, alkyl radical generation was smooth and the rate constants obtained by use of Eq. 1, in conjunction with the well established $2k_t$ value of Fischer and co-workers,[6] corrected for changes in solvent viscosity as described previously,[7] are given in Table 1. The extent of the alternative, undesired β-scission producing hydroxyformyl, was appraised from the relative yields of alkylbenzene and benzoic acid determined by GC and NMR. The measured $[PhCO_2H]/[RPh]$ ratios from photolyses at 300 K were found to be: ca. 20, ca. 13, for **1b**, and **1c**, respectively, and no alkylbenzenes could be detected during reactions of **1d** or **1e**. It follows that diversion of cyclohexadienyl radicals **2** down this reaction channel can safely be neglected.

Table 1
Kinetic data for alkyl radical generation (k^1_d, E^1_d) from **2** and hydrogen abstraction from acids **1** by the corresponding alkyl radicals (k_H)

Acid	R	Delocalised radical	$10^{-4}k_H$/ $M^{-1}s^{-1}$ (300K)	$10^{-3}k^1_d$/ s^{-1} (300K)	E^1_d/ kcal mol^{-1}	$E_s(R^\bullet)$/ kcal mol^{-1}
1a	Me	**2a**	—	≤ 0.001	≥ 18	0
1b	Et	**2b**	1.1	0.03	15.7	4.3
1c	n-Pr	**2c**	0.8	0.02	16.0	3.9
1d	i-Pr	**2d**	0.1	1.1	13.7	6.4
1e	t-Bu	**2e**	—	1000	9.6	8.9

The measured k^1_d values confirm that the ease of fragmentation of radicals **2** increases dramatically with the degree of branching of the released alkyl radical; in fact, production of *t*-Bu$^\cdot$ was nearly five orders of magnitude faster than primary alkyl radical production.

The methane-based stabilisation energies of the alkyl radicals [$E_s(R^\cdot)$ in Table 1][8] show linear correlations with $\log k^1_d$ and with the Arrhenius activation energies of the fragmentations (E^1_d). This suggests that the rate of fragmentation increases with the thermodynamic stabilisation of the released alkyl radical. It is probable, however, that increased steric strain in **2d** and **2e**, containing branched alkyl substituents, also enhances the fragmentation rates.

The radical concentrations were significantly affected by 10-fold changes in the initial concentrations of **1b** and **1c** and hence satisfactory k_H values could be determined for H-abstraction by Et$^\cdot$ and *n*-Pr$^\cdot$ radicals (Table 1). For the isopropyl radical the effect was small and the error limits on k_H are high. The k_H values determined by this novel technique for Et$^\cdot$ and *n*-Pr$^\cdot$ agree reasonably well with the few previous accounts[1,9,10] of rate data for primary radicals abstracting hydrogen from cyclohexadiene and derivatives thereof (which report values in the range 10^4 to 10^5 M^{-1} s^{-1}) but tend to support the low end of the range. The lower measured k_H value for the *i*-Pr radical is in accord with expectation because of the smaller *i*-Pr–H bond dissociation energy. No effect on the radical concentrations was observed for different initial concentrations of acid **1e** indicating that, as expected, k_H is even lower for the *t*-butyl radical.

The rate of hydrogen donation by **1** to branched radicals is comparatively slow and hence adduct radicals RZ$^\cdot$ from, for example, 1,1-disubstituted alkenes, will not be able to sustain chain reactions effectively. However, transformations of R$^\cdot$ which produce primary radicals, for example 5-*exo*-cyclisations, should be well suited to this methodology. The most useful cyclohexadienyl acids will contain branched R (high k^1_d) which are transformed to primary cyclised radicals (larger k_H). In no case will premature reduction of R$^\cdot$ to RH be a problem because the k_H values are nearly two orders of magnitude less than for H-donation by organotin hydrides.[11]

Acknowledgements

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