Homolytic Reactions of Ligated Boranes. Part 12.[1] Amine–Alkylboranes as Polarity Reversal Catalysts for Hydrogen-atom Abstraction by t-Butoxyl Radicals

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E.s.r. spectroscopy has been used to show that abstraction of electron-deficient hydrogen atoms from α-C–H groups in esters, ketones, and acetic anhydride by electrophilic t-butoxyl radicals is catalysed by amine–alkylboranes, in particular by trimethylamine–thexylborane ($Me_3N{\rightarrow}BH_2Thx$; Thx = $-CMe_2CMe_2H$) (**2**). The single-step abstraction by $Bu^tO^\bullet$ is replaced by a two-step catalytic cycle in which $Bu^tO^\bullet$ first abstracts electron-rich hydrogen from the amine–alkylborane to give a nucleophilic amine–alkylboryl radical, which subsequently abstracts with high regioselectivity the electron-deficient α-hydrogen from the carbonyl compound. Both steps of this catalytic cycle are promoted by favourable polar effects, while such effects militate against direct α-hydrogen abstraction by $Bu^tO^\bullet$. The rate coefficient for hydrogen abstraction from (**2**) by $Bu^tO^\bullet$ to give the amine–alkylboryl radical $Me_3N{\rightarrow}\dot{B}HThx$, has been estimated to be 4.7×10^7 dm^3 mol^{-1} s^{-1} at 189 K in cyclopropane. Relative reactivities of carbonyl compounds towards α-hydrogen-atom abstraction by amine–alkylboryl radicals have been determined in competition experiments at 189 K and shown to depend on enthalpic, polar, and steric factors. Towards $Me_3N{\rightarrow}\dot{B}HThx$, the relative molar reactivities of $MeCO_2Et$, $MeCH_2CO_2Et$, and Me_2CHCO_2Et are 1 : 4.5 : 0.4, while towards the less bulky $Me_3N{\rightarrow}\dot{B}HMe$ they are 1 : 6.7 : 7.3, showing the importance of steric effects in determining the rate of hydrogen abstraction. *Ab initio* molecular-orbital calculations have been carried out at the MP3/6-31G**//HF/6-31G** level for $H_3N{\rightarrow}BH_2Me$ and $H_3N{\rightarrow}\dot{B}HMe$ and the strengths of the B–H and B–C bonds in ammonia–methylborane are estimated to be 432 and 404 kJ mol^{-1}, respectively.

The influence of polar factors on the reactions of uncharged free radicals has been recognised for over forty years.[2] A striking illustration of the operation of polar effects can be seen in the phenomenon of alternating radical copolymerisation. This is the property of certain monomer pairs, for example styrene and maleic anhydride, to form a copolymer in which the monomer units tend to alternate along the chain.[2]

It is also well established that polar factors play an important role in determining the chemo- and regio-selectivities of hydrogen-atom transfer reactions of the type (1).[2–5] In valence

$$A^\bullet + H\text{–}B \longrightarrow A\text{–}H + B^\bullet \qquad (1)$$

bond terms, the transition state for direct atom transfer may be represented as a hybrid of the canonical structures (**1a–d**) and its stability will increase with increasing contributions from the ionic structures (**1c**) or (**1d**). As a result, the activation energies

$$\underset{\textbf{(1a)}}{[A^\bullet\ H\text{–}B]} \longleftrightarrow \underset{\textbf{(1b)}}{[A\text{–}H\ B^\bullet]} \longleftrightarrow \underset{\textbf{(1c)}}{[A^+H^\bullet\ B^-]} \longleftrightarrow \underset{\textbf{(1d)}}{[A^-H^\bullet\ B^+]}$$

for a series of similarly exothermic hydrogen-atom abstraction reactions would be expected to decrease as the properties of the attacking and departing radicals become more mutually conducive to the participation of charge-transfer structures of the types (**1c**) or (**1d**). Thus, if El$^\bullet$ and Nuc$^\bullet$ represent electrophilic and nucleophilic radicals, respectively, the hydrogen abstractions (2) and (3) will be favoured because of charge transfer in the transition state, while reactions (4) and (5) will not.† The same predictions result from consideration of the interactions between the frontier molecular orbitals of the reactants.[6]

$$El^\bullet + H\text{–}Nuc \longrightarrow H\text{–}El + Nuc^\bullet \qquad (2)$$

$$Nuc^\bullet + H\text{–}El \longrightarrow H\text{–}Nuc + El^\bullet \qquad (3)$$

$$El^{1\bullet} + H\text{–}El^2 \longrightarrow H\text{–}El^1 + El^{2\bullet} \qquad (4)$$

$$Nuc^{1\bullet} + H\text{–}Nuc^2 \longrightarrow H\text{–}Nuc^1 + Nuc^{2\bullet} \qquad (5)$$

The preceding analysis points to the concept of polarity reversal catalysis (PRC),[7–9] whereby the sluggish single-step processes (4) or (5) are replaced by the pairs of consecutive reactions (6) and (7) or (8) and (9), respectively. Both steps of each catalytic cycle now are facilitated by favourable polar effects. Ideally, the exothermicity of the overall process should be divided roughly equally between the two steps which replace it. We may refer to the molecules H–Nuc and H–El as *donor* and *acceptor* catalysts, respectively.‡

$$El^{1\bullet} + H\text{–}Nuc \longrightarrow H\text{–}El^1 + Nuc^\bullet \qquad (6)$$

$$Nuc^\bullet + H\text{–}El^2 \longrightarrow H\text{–}Nuc + El^{2\bullet} \qquad (7)$$

$$Nuc^{1\bullet} + H\text{–}El \longrightarrow H\text{–}Nuc^1 + El^\bullet \qquad (8)$$

$$El^\bullet + H\text{–}Nuc^2 \longrightarrow H\text{–}El + Nuc^{2\bullet} \qquad (9)$$

† The descriptions 'electrophilic' and 'nucleophilic' are relative terms. In general, whether a radical A$^\bullet$ behaves as a net electrophile [structure (**1d**) more important than (**1c**)] or a net nucleophile [structure (**1c**) more important than (**1d**)] in reaction (1) must depend on the nature of B$^\bullet$ (*i.e.* on the electronegativity difference between A$^\bullet$ and B$^\bullet$).

‡ In 1953 Barrett and Waters[10] reported that thiols catalyse the radical chain decarbonylation of aldehydes. In the published discussion of this paper, Mayo[11] explained this effect of thiols in terms of what we refer to here as polarity reversal catalysis. We thank Professor Cheves Walling for drawing our attention to this early work.

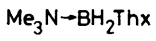
The t-butoxyl radical is an easily generated electrophilic radical, the elementary reactions of which may be readily monitored by e.s.r. spectroscopy.[12] In accord with predictions based on consideration of polar effects, t-butoxyl radicals readily abstract hydrogen from a C–H group attached to oxygen in an alcohol or an ether, while analogous abstraction from an α-C–H group in a nitrile or an ester proceeds more slowly under the same conditions.[13] For example, although reactions (10) and (11) are both exothermic[14–16] by *ca.* 50 kJ mol^{-1}, the former proceeds more rapidly than the latter.

$$Bu^tO^\bullet + CH_3OBu^t \xrightarrow{k_{10}} Bu^tOH + {}^\bullet CH_2OBu^t \quad (10)$$

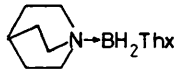
$$Bu^tO^\bullet + CH_3CN \longrightarrow Bu^tOH + {}^\bullet CH_2CN \quad (11)$$

Using the standard competition method with detection by e.s.r. spectroscopy,[17] we find in this work that t-butoxyl radicals abstract hydrogen from CH_3OBu^t at least 50 times faster than from CH_3CN at 245 K in di-t-butyl peroxide (DTBP) solvent. We have previously[18] determined the activation energy for reaction (10) to be 12.6 ± 2.0 kJ mol^{-1} and, assuming equal *A*-factors, the activation energy for reaction (11) must be ≥ 20.6 kJ mol^{-1}.

We have reported previously[7–9] that trimethylamine–(1,1,2-trimethylpropyl)borane (trimethylamine–thexylborane) (**2**) acts as an effective donor polarity reversal catalyst for reactions, including (11), in which t-butoxyl radicals abstract electron-deficient hydrogen from carbon. In the present paper we report further applications of the principle of PRC to hydrogen-abstraction reactions of t-butoxyl radicals, using the amine–alkylboranes (**2**)–(**6**) (Thx = Me_2CHCMe_2–) as donor catalysts.



(**2**)



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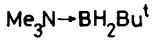

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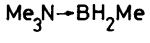

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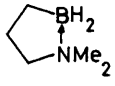


(**6**)

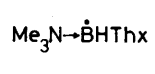
Results and Discussion

E.s.r. spectra were recorded during u.v. photolysis [equation (12)] of solutions containing DTBP (*ca.* 15% v/v) and the

$$Bu^tOOBu^t \xrightarrow{h\nu} 2Bu^tO^\bullet \quad (12)$$

substrate (*ca.* 1 mol dm^{-3}) in the absence and presence of catalyst, while the sample was positioned in the microwave cavity of the spectrometer.[9,12] Generally, the solvent used was cyclopropane and the catalyst concentration was usually *ca.* 0.1 mol dm^{-3}. Catalysts (**2**)–(**5**) are moisture sensitive and precautions must be taken to avoid their hydrolysis during sample preparation; the azaborolidine (**6**) is much more stable to water.[19,20] The catalyst may be added separately to the reagent mixture or (more conveniently) added as a stock solution in DTBP, since such solutions were shown by n.m.r. spectroscopy to be stable for several days if stored in a refrigerator in the absence of moisture.

E.s.r. spectra of the corresponding amine–alkylboryl radicals[9] (**7**)–(**11**) were observed during photolysis of cyclopropane solutions containing DTBP and the amine–alkylborane (0.5–1 mol dm^{-3}) in the absence of any reactive substrate. The e.s.r. parameters for (**7**), (**9**), and (**10**) have been reported previously.[9] The spectrum of the quinuclidine–thexylboryl radical (**8**) showed splitting from boron and from a single proton [$a(^{11}B)$ 57.3, $a(H_\alpha)$ 10.9 G, and *g* 2.0020 at 247 K]. Under the forcing instrumental conditions necessary for its observation, the spectrum of (**11**) appeared as a ^{11}B-quartet of 1:2:1 triplets [$a(^{11}B)$ 57.2, a(2 H) 20.7 G, and *g* 2.0019 at 236 K], although the lines were very broad (ΔB_{p-p} *ca.* 8 G). By comparison with the spectrum shown by the amine–methylboryl radical[9] (**10**) [$a(^{11}B)$ 61.6, $a(H_\alpha)$ 6.1, $a(3\ H_\beta)$ 14.8 G, and *g* 2.0020 at 199 K], we attribute the triplet splitting observed for (**11**) to coupling with the two β-ring protons, which are probably rendered equivalent on the e.s.r. timescale by inversion of the ring and at the pyramidal[9] radical centre. The α-proton splitting for (**11**) is unresolved within the envelope linewidth; the larger β-proton splitting for (**11**) compared with that for (**10**) reflects the smaller average dihedral angle between the β-C–H bonds and the axis of the semi-occupied hybrid orbital on boron in the former radical.



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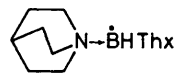

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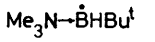
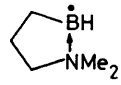


(**9**)

(**10**)



(**11**)

As reported previously,[7,9] a strong spectrum of the α-(ethoxycarbonyl)methyl radical (**12**) was observed during u.v. irradiation of a cyclopropane solution containing DTBP, ethyl acetate, and (**2**) (0.1 mol dm^{-3}) at 180–240 K; the amine–alkylboryl radical (**7**) was not detected. Similar results were obtained when (**2**) was replaced by (**3**)–(**6**), but in the absence of catalyst at 189 K the spectrum of (**12**) was very weak and spectra of (**13**) and of the cyclopropyl radical were also observed. In the presence of (**2**), the relatively slow single-step reaction (13) is replaced by the two-step catalytic cycle of

$$Bu^tO^\bullet + MeCO_2Et \longrightarrow {}^\bullet CH_2CO_2Et + Bu^tOH \quad (13)$$
(**12**)

reactions (14) and (15); hydrogen abstraction from the α-C–H group is brought about by the *nucleophilic* amine–alkylboryl radical (**7**) rather than by the *electrophilic* $Bu^tO^\bullet$.

$$Bu^tO^\bullet + Me_3N{\rightarrow}BH_2Thx \xrightarrow{k_{14}} Bu^tOH + Me_3N{\rightarrow}\dot{B}HThx \quad (14)$$

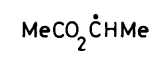
$$Me_3N{\rightarrow}\dot{B}HThx + MeCO_2Et \longrightarrow Me_3N{\rightarrow}BH_2Thx + {}^\bullet CH_2CO_2Et \quad (15)$$

A variety of other α-(alkoxycarbonyl)alkyl radicals were generated in a similar fashion by hydrogen-atom abstraction

Table 1. E.s.r. parameters for radicals produced by catalysed hydrogen abstraction from esters in the presence of $Me_3N{\rightarrow}BH_2Thx$ (**2**) in cyclopropane solvent.

Radical	*T*/K	*g*-Factor	Hyperfine splittings/G[a]
$H_2\dot{C}CO_2Me$	189	2.0034	21.56(1), 21.38(1), 1.40(3)
$H_2\dot{C}CO_2Et$ (**12**)	189	2.0034	21.50(1), 21.35(1), 1.54(2)
$H_2\dot{C}CO_2Pr^i$	189	2.0034	21.62(1), 21.42(1), 0.95(1)
$H_2\dot{C}CO_2Bu^t$	189	2.0034	21.38(2)[b]
$MeCH\dot{C}O_2Et$[c,d]	187[e]	2.0033	24.76(3), 20.56(1), 1.65(2)
	187	2.0034	25.02(3), 20.56(1), 1.40(2)
$Me_2\dot{C}CO_2Et$[d,f]	190	2.0033	21.63(6),[g] 1.39(2)
$H_2C{=}CHCH_2\dot{C}HCO_2Et$ (**14**)	192	2.0034	23.26(2), 20.59(1), 1.60(2), 0.54(2)
$MeO\dot{C}HCO_2Me$ (**15**)	221[e]	2.0040	17.65(1), 2.86(3), 1.56(3)
$MeO\dot{C}HCO_2Me$ (**16**)	221	2.0041	17.35(1), 2.82(3), 1.12(3)
$EtO_2CCH_2\dot{C}HCO_2Et$ (**18**)	189	2.0034	26.23(2), 21.02(1), 1.66(2)
$H_2\dot{C}CO_2CH_2CH{=}CH_2$ (**20**)	189	2.0034	21.51(1), 21.30(1), 1.45(2)
(**22**-β)	240	2.0034	21.40(2), 0.86(1)
(**22**-α)	241	2.0034	21.40(2), 0.96(1)
$H\dot{C}(CO_2Et)_2$ (**24**)	189	2.0039	20.42(1), 1.28(4), 14.4($^{13}C_\beta$)
$H\dot{C}(CO_2Bu^t)_2$ (**27**)	189	2.0039	20.40(1), 30.2($^{13}C_\alpha$), 14.2($^{13}C_\beta$)
$Me\dot{C}(CO_2Et)_2$ (**28**)	190	2.0038	23.95(3), 1.06(4)
$^{\bullet}C(CO_2Et)_3$ (**29**)	186	2.0038	0.80(6), 32.2($^{13}C_\alpha$),[h] 13.5($^{13}C_\beta$)
$^{\bullet}CHC(O)OCH_2CH_2$ (**30**)[i]	225	2.0034	41.35(2), 20.30(1), 1.02(2)
$^{\bullet}CH_2C(O)OC(O)Me$ (**32**)	188	2.0038	20.75(1), 20.44(1)
$NC\dot{C}HCO_2Et$[i]	217	2.0034	19.80(1), 1.24(2), 3.05(1 N)

[a] Numbers of equivalent protons, or other specified nuclei, shown in parentheses. [b] The difference in splittings between the two α-protons was unresolved. [c] Two rotamers which differ in conformation about the C_α–C(O) bond were detected, relative concentrations *ca.* 11.5:1. [d] Spectrum previously studied in great detail by W. Lung-min and H. Fischer, *Helv. Chim. Acta*, 1983, **66**, 138. [e] More abundant conformer. [f] Weak spectrum, a stronger spectrum was obtained with (**6**) as catalyst (see text). [g] The difference in splittings from the non-equivalent methyl groups was not resolved under the experimental conditions. [h] Value at 247 K. [i] Oxirane solvent.



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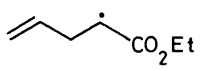

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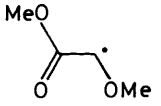

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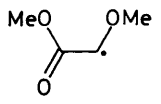

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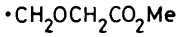

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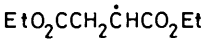


(**18**)

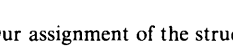
from esters catalysed by (**2**) and their e.s.r. parameters are given in Table 1. Spectra of good quality were usually obtained and this technique represents a useful general method for the production of specific α-(alkoxycarbonyl)alkyl radicals for e.s.r. study in solution. For example, the spectrum of the radical (**14**) (see Figure 1), obtained from ethyl pent-4-enoate, may be readily analysed in terms of $a(H_\alpha)$ 20.59, $a(2\ H_\beta)$ 23.26, $a(OCH_2)$ 1.60, and a(2 H) 0.54 G. These splitting constants are much more reasonable than those reported before[21] for this radical derived from another source and we believe that the previous analysis, which required that the β-protons be non-equivalent, is incorrect.

In the absence of catalyst, methyl methoxyacetate yields a composite spectrum arising from (**15**)–(**17**),[22,23] whereas in the presence of (**2**) (0.1 mol dm^{-3}) in cyclopropane at 190–240 K only the rotamers (**15**) and (**16**) of the α-carbonylalkyl radical are detected. Korth *et al.*[22] reported that the uncatalysed abstraction yields (**15**) and (**16**) in the concentration ratio 2.2:1 at 215 K in chlorobenzene.* We repeated their experiment and obtained a value of *ca.* 2.5 for [(**15**)]/[(**16**)] at 215 K. However, when (**2**) (0.1 mol dm^{-3}) was included in the sample the value of [(**15**)]/(**16**)] increased to *ca.* 5.0 under otherwise identical conditions. This result shows that hydrogen abstraction from methyl methoxyacetate by (**7**) yields a greater proportion of (**15**) than when abstraction is effected by $Bu^tO^{\bullet}$ and it shows that the captodatively substituted[24] radicals (**15**) and (**16**) do not equilibrate within their lifetimes (*ca.* 1 ms) at 215 K in chlorobenzene.

With some esters, spectra of secondary product radicals became evident after samples had been u.v. irradiated for relatively short periods of time. For example, a spectrum consisting of a doublet of triplets of smaller triplets was observed with ethyl acetate and we assign this to the radical (**18**), produced by hydrogen abstraction from diethyl succinate, itself formed by the dimerisation of (**12**). The same spectrum was obtained from authentic succinate (see Table 1) and the relatively rapid growth of the secondary-product spectrum implies that diethyl succinate is significantly more reactive towards (**7**) than ethyl acetate, as was confirmed in quantitative competition experiments (see later).

Uncatalysed hydrogen abstraction from allyl acetate in cyclopropane at 189 K afforded the allylic radical (**19**), although a complete analysis of the spectrum was not attempted and both *exo*- and *endo*-isomers are probably present. When the experiment was repeated in the presence of (**2**) (0.1 mol dm^{-3}), only the spectrum of the α-(allyloxycarbonyl)methyl radical (**20**) was detected. No evidence for cyclisation of (**20**) was found up to 278 K, in accord with the recent report by Beckwith and Glover.[25]

* Our assignment of the structure (**15**) to the more abundant rotamer follows that of Beckwith and Brumby.[23]



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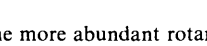

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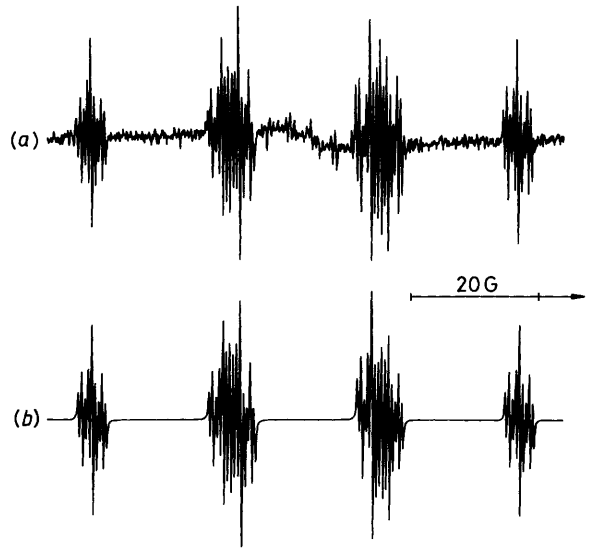


Figure 1. (*a*) E.s.r. spectrum of the radical (**14**) produced by catalysed hydrogen abstraction from ethyl pent-4-enoate in cyclopropane at 192 K. (*b*) Computer simulation of (*a*) using the coupling constants given in the text.

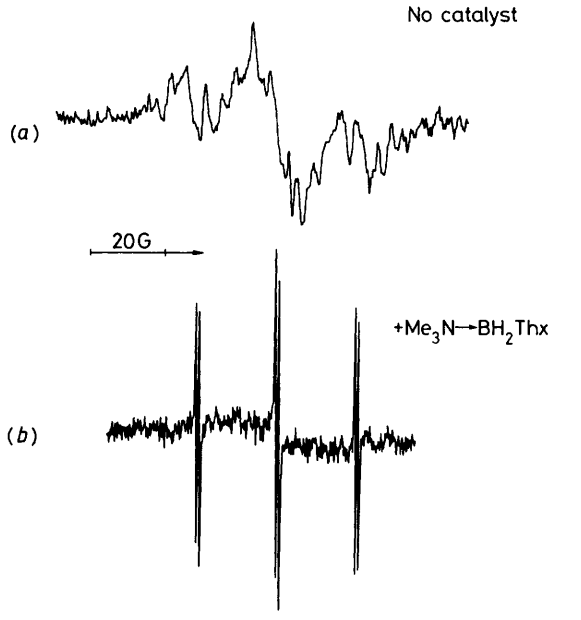
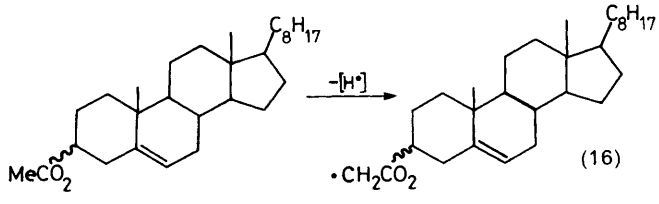
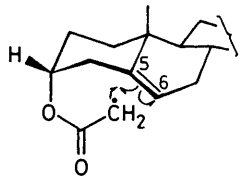


Figure 2. (*a*) E.s.r. spectra of the radicals produced by uncatalysed hydrogen abstraction from cholesteryl acetate (**21**-β) in cyclopropane at 240 K. (*b*) E.s.r. spectrum of the radical (**22**-β) generated by catalysed abstraction from (**21**-β) under the same conditions.



(**21**) (**22**)

The control of regioselectivity which can be exercised using PRC is strikingly illustrated by the reactions of cholesteryl acetate (**21**-β). Uncatalysed reaction of $Bu^tO^•$ with the 3β-isomer at 240 K in cyclopropane gave rise to the spectrum shown in Figure 2(*a*), which indicates the presence of several radicals resulting from unselective abstraction of hydrogen from the steroid moiety; no abstraction from the electron deficient acetylmethyl group [equation (16)] is evident. In contrast, when (**2**) (0.1 mol dm^{-3}) is also present, only the radical (**22**-β) is detected [see Figure 2(*b*)]. Although the radical centre in (**22**-β) is too far removed from the 5,6-double bond to permit cyclisation, analogous cyclisation of (**22**-α) derived from epicholesteryl acetate (**21**-α) might be possible, as indicated in structure (**23**). However, (**22**-α) was the only radical detected



(**23**)

during catalysed abstraction of hydrogen from epicholesteryl acetate up to 283 K. Inspection of molecular models indicates that the cyclisation depicted in (**23**) is probably disfavoured because of the stereoelectronic constraints on transition-state geometry[25] and the strain thereby induced; any twisting of the $CH_2^•$ moiety out of conjugation with the carbonyl group will contribute to the activation energy for cyclisation. Furthermore, the *syn*-conformation about the O–C(O) bond shown in (**23**) is likely[25] to be less stable than the *anti*-conformation, which could not cyclise.

In dialkyl malonates, the presence of two electron-withdrawing alkoxycarbonyl substituents suggests that the α-CH_2 group should by highly reactive towards hydrogen abstraction by nucleophilic amine–alkylboryl radicals. With diethyl malonate at 189 K in the absence of catalyst, a mixture of the radicals (**24**) and (**25**)[26] was detected, while in the presence of (**2**) (0.1 mol dm^{-3}) only the spectrum of (**24**) was observed. As with the acetates, the spectrum of a secondary-product radical was seen

$HC^•(CO_2Et)_2$ (**24**) $H_2C(CO_2Et)CO_2C^•HMe$ (**25**)

to 'grow-in' with time and this is tentatively assigned to (**26**) [*a*(4 H) 1.28 G at 189 K]. That $a(H_\beta)$ should be near to zero

$(EtO_2C)_2C^•CH(CO_2Et)_2$ (**26**) $HC^•(CO_2Bu^t)_2$ (**27**)

$MeC^•(CO_2Et)_2$ (**28**) $(EtO_2C)_3C^•$ (**29**)

and unresolved for (**26**) is not unreasonable since for steric reasons the β-C–H bond is likely to lie close to the nodal plane of the SOMO. The radical (**26**) would be formed by catalysed abstraction of hydrogen from the product of dimerisation of (**24**). Similarly, hydrogen abstraction catalysed by (**2**) from di-t-butyl malonate, diethyl methylmalonate, and triethyl methanetricarboxylate afforded clean e.s.r. spectra of (**27**)–(**29**), respectively. Signals were sufficiently intense to permit detection of ^{13}C-satellites without isotopic enrichment (see Table 1 and Figure 3). The values of $a(^{13}C_\alpha)$ and $a(^{13}C_\beta)$ for (**27**) (30.2 and 14.2 G, respectively, at 189 K) are similar to those reported previously[27] for $HC^•(CO_2^-)_2$ (31.44 and 11.92 G in water at *ca.* 288 K). The radical centres in (**27**) and (**29**) are evidently planar, as expected since this geometry will maximise conjugative interaction of the carbonyl groups with the unpaired electron.

When a saturated solution of γ-butyrolactone in cyclopropane containing DTBP (15% v/v) was u.v. irradiated at 260

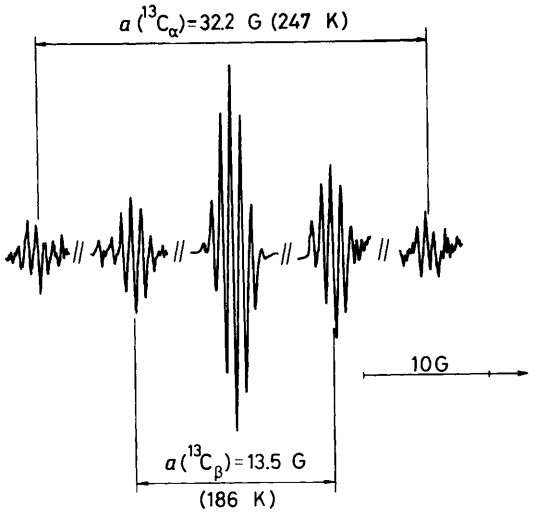


Figure 3. E.s.r. spectrum of $^{\bullet}C(CO_2Et)_3$ (**29**) produced by catalysed hydrogen abstraction from triethyl methanetricarboxylate in cyclopropane at 186 K. The ^{13}C-satellites were recorded at higher gain and the outer satellites were recorded at 247 K.

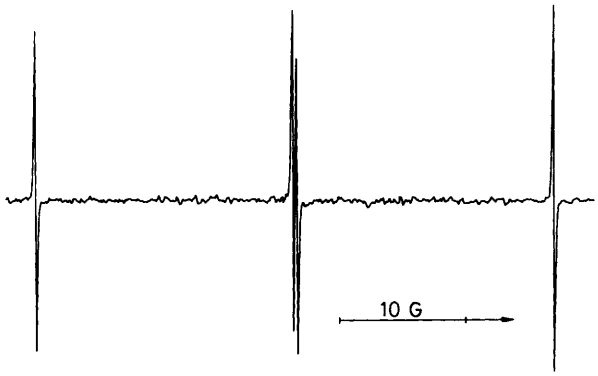
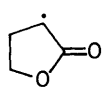
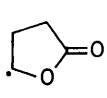


Figure 4. E.s.r. spectrum of the radical (**32**) produced by catalysed hydrogen abstraction from acetic anhydride in cyclopropane at 188 K.

K, a composite e.s.r. spectrum from the radicals (**30**) and (**31**) [$a(H_\alpha)$ 15.79, $a(2\ H_\beta)$ 31.22 G, and g 2.0028] was observed. In the presence of (**2**) (*ca.* 0.1 mol dm^{-3}), however, (**31**) was not detected and an intense spectrum of (**30**) was observed along



(**30**)



(**31**)

with a weak signal from an unidentified radical. Spectra could be obtained at lower temperatures and with high concentrations of the lactone by working in oxirane solvent.

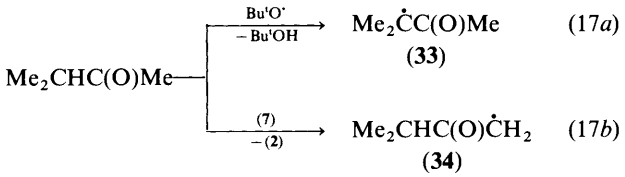
U.v. irradiation of a cyclopropane solution containing acetic anhydride (*ca.* 1 mol dm^{-3}), DTBP, and the amine–alkylborane (**2**) between 188 and 279 K afforded a strong spectrum of the radical (**32**) (see Figure 4), demonstrating the applicability of PRC to the abstraction of electron deficient α-hydrogen atoms from acid anhydrides. In the absence of catalyst at 189 K, the major spectrum observed was that of the cyclopropyl radical, but as the temperature was increased this was progressively replaced by the spectrum of (**32**). Although the activation

$^{\bullet}CH_2C(O)OC(O)Me$
(**32**)

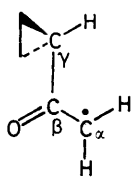
energy for hydrogen abstraction from acetic anhydride by $Bu^tO^{\bullet}$ is probably greater than for corresponding abstraction from cyclopropane, the difference is unlikely to be sufficiently large to account entirely for the temperature dependence and it is probable that the cyclopropyl radical abstracts hydrogen from the anhydride at the higher temperatures.

Hydrogen Abstraction from Ketones.—A suitably orientated carbonyl group in a ketone, like that in an ester, stabilises both a negative charge and an unpaired electron on an adjacent carbon atom. Thus, we would expect abstraction of hydrogen from an α-C–H group in a ketone by $Bu^tO^{\bullet}$ to be accelerated by donor catalysts such as the amine–alkylboranes (**2**)–(**6**). In order to minimise the effects of light absorption by the carbonyl chromophore, the DTBP:ketone concentration ratio was kept large; typically samples contained DTBP (40–50% v/v), the ketone (*ca.* 0.5 mol dm^{-3}), and the catalyst (**2**) (*ca.* 0.2 mol dm^{-3}) in cyclopropane. Without DTBP, u.v. irradiation of a sample containing 3-methylbutan-2-one and catalyst afforded only a weak ill-defined e.s.r. spectrum under the usual instrumental conditions.

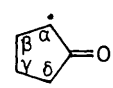
U.v. irradiation of a solution containing DTBP and 3-methylbutan-2-one, but no catalyst, at 190–220 K gave rise to the e.s.r. spectrum of the radical[28] (**33**) [$a(3\ H_\beta)$ 20.46, $a(3\ H'_\beta)$ 19.13, $a(3\ H_\gamma)$ 0.70 G, and g 2.0042 at 190 K]. In the presence of (**2**) (*ca.* 0.2 mol dm^{-3}), (**33**) was no longer detected and a strong spectrum of the radical (**34**) [$a(H_\alpha)$ 19.94, $a(H'_\alpha)$ 19.60,



$a(H_\gamma)$ 0.66, $a(6\ H_\delta)$ 0.33 G, and g 2.0044 at 190 K] was observed. While $Bu^tO^{\bullet}$ preferentially abstracts the more weakly bound and less electron deficient α-hydrogen from the ketone [equation (17*a*)], the amine–alkylboryl radical (**7**) abstracts a more strongly bound but more electron-deficient hydrogen from the MeC(O) group [equation (17*b*)]. Although polar effects are clearly important in determining the regioselectivities of $Bu^tO^{\bullet}$ and (**7**), the bulky amine–alkylboryl radical would also prefer to abstract from the MeC(O) group for steric reasons. Steric factors appear to be predominant, since when the



(**35**)



(**36**)

experiment was repeated with (**6**) as the catalyst, which yields the less bulky amine–alkylboryl radical (**11**), the radical (**33**) was detected rather than (**34**).

Catalysed abstraction from cyclopropyl methyl ketone afforded the e.s.r. spectrum of (**35**) [$a(H_\alpha)$ 19.96, $a(H'_\alpha)$ 19.62, a(4 H)* 0.36 G, and g 2.0045 at 189 K]. Cyclopentanone gave the

* Presumably the mean splitting from the two pairs of δ-protons. Under forcing instrumental conditions, some further fine structure was partially resolved; this appears not to be due only to coupling with H_γ. It is possible that a second conformation which differs from (**35**) by a 180° rotation about C_β–C_γ is also present.

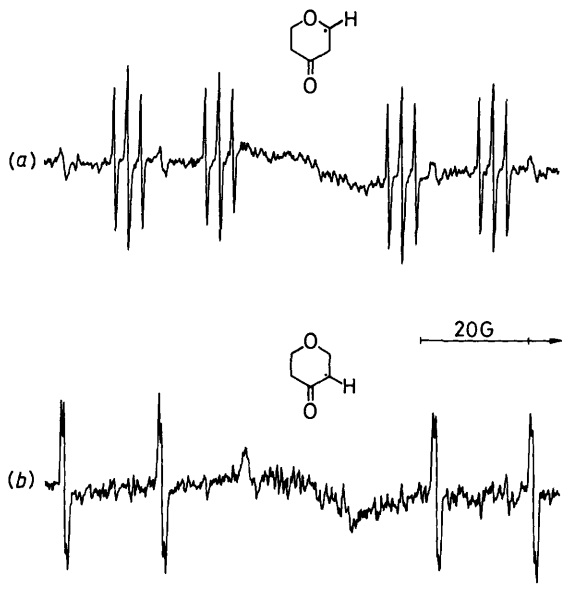
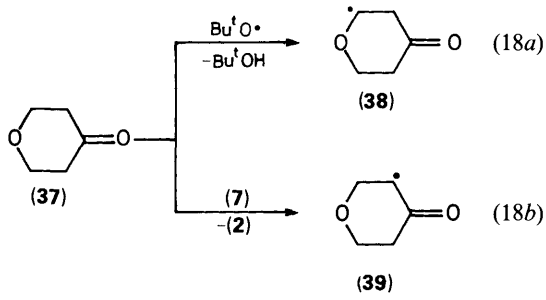


Figure 5. (*a*) E.s.r. spectrum of the radical (**38**) produced by uncatalysed hydrogen abstraction from (**37**) in DTBP at 268 K. (*b*) E.s.r. spectrum of the radical (**39**) generated by catalysed abstraction under the same conditions.



(18*a*)

(18*b*)

radical (**36**)[29] [$a(H_\alpha)$ 18.32, $a(2\ H_\beta)$ 36.45, $a(2\ H_\gamma)$ 0.39, $a(2\ H_\delta)$ 2.83 G, and g 2.0045 at 185 K] both in the absence and presence of (**2**), although without catalyst the spectrum was weaker. Evidently the unfavourable polar effects which retard hydrogen abstraction by Bu^{t}O$^\bullet$ from the $CH_2C(O)$ moiety in cyclopentanone are outweighed by the bond-weakening effect of the adjacent carbonyl group.

Catalytic control of regioselectivity is well illustrated by the reactions of tetrahydro-4*H*-pyran-4-one (**37**). As shown in Figure 5, u.v. irradiation of a 1 mol dm^{-3} solution of (**37**) in DTBP at 268 K yields mainly the oxygen-conjugated radical (**38**) [$a(H_\alpha)$ 16.75, $\bar{a}(2\ H_\beta)$ 25.15, $\bar{a}(2\ H)$ 2.48 G, and g 2.0033], while in the presence of (**2**) (0.1 mol dm^{-3}) the major product is the carbonyl-conjugated radical (**39**) [$a(H_\alpha)$ 18.00, $\bar{a}(2\ H_\beta)$ 34.25, $\bar{a}(2\ H)$ 0.50 G, and g 2.0045].*

Relative Reactivities.—We have determined the relative reactivities of a number of esters, cyclopropyl methyl ketone, and acetonitrile towards amine–alkylboryl radicals under conditions of PRC in cyclopropane at 189 K. The standard competition method[17] was used, making the assumption that the product radicals are removed by diffusion-controlled reactions which have equal rate coefficients. The experiments carried out with $Me_3N{\rightarrow}BH_2Thx$ (**2**) are listed in Table 2; each value of k_A/k_B represents the mean from two or three separate runs. Selected control experiments were carried out to confirm that the relative radical concentrations detected by e.s.r. spectroscopy reflect the relative rates of reaction of (**7**) and that no exchange between the intially produced radicals and the reagents takes place under the conditions employed. U.v. irradiation of a solution containing DTBP, ethyl propanoate (1 mol dm^{-3}), ethyl bromoacetate (1 mol dm^{-3}), and (**2**) (0.2 mol dm^{-3}) at 189 K afforded only the α-(ethoxycarbonyl)-methyl radical (**12**) produced[9] by reaction (19). This result

$$Me_3N{\rightarrow}\dot{B}HThx + BrCH_2CO_2Et \longrightarrow {}^\bullet CH_2CO_2Et + Me_3N{\rightarrow}BHBrThx \quad (19)$$
(**12**)

serves as a control for entry 1, since it shows that (**12**) does not abstract hydrogen from ethyl propanoate under the experimental conditions. A similar control for entry 7 was provided by u.v. irradiation of a sample containing DTBP, diethyl bromomalonate (2 mol dm^{-3}), triethyl methanetricarboxylate (0.5 mol dm^{-3}), and (**2**) (0.2 mol dm^{-3}), which afforded only the e.s.r. spectrum of $H\dot{C}(CO_2Et)_2$. Photolysis of dibutanoyl peroxide (1 mol dm^{-3}) in the presence of diethyl malonate (1 mol dm^{-3}) yielded only the spectrum of the propyl radical, showing that this species does not abstract hydrogen from the malonate at 189 K (control for entry 10).

Reactivities of the different substrates, relative to ethyl acetate, towards (**7**) are summarised in Table 3. The reactivities are evidently governed by enthalpic, polar, and steric factors. The more substituents (alkyl or alkoxycarbonyl) that are attached to the carbon atom from which hydrogen is removed, the more favourable is the abstraction thermodynamically, although it is more subject to steric retardation. The greater the number of alkoxycarbonyl groups attached to the developing radical centre, the more favoured by polar effects is the abstraction of hydrogen. The greater molar reactivity of diethyl succinate compared with ethyl propanoate is partly a statistical effect, but also probably reflects the greater electron-withdrawing power of a CH_2CO_2Et substituent as compared with a methyl group. The rate of abstraction from CH_3X increases in the order X = C(O)OEt < CN < C(O)R, an order which reflects both polar and enthalpic factors.

The relative reactivities of ethyl acetate, propanoate, and 2-methylpropanoate towards different amine–alkylboryl radicals under conditions of PRC were determined and the results are summarised in Table 4. The lower reactivity of the 2-methylpropanoate compared with the propanoate towards (**7**), which could be either polar or steric in origin, is clearly a steric effect, since towards the less bulky amine–alkylboryl radicals (**10**) and (**11**) the 2-methylpropanoate is the more reactive ester.

It is well-known that a trialkylsilyl group stabilises negative charge on an adjacent carbon atom,[30] although the carbon radical stabilising effect of an α-silyl substituent is thought to be small.[31] t-Butoxyl radicals react with tetraethylsilane to give a mixture of the radicals (**40**) and (**41**) (4:1 at 243 K in DTBP)[32] and it appeared possible that PRC using an amine–alkylborane might alter this regioselectivity in such a way as to make (**40**) the exclusive product. However, u.v. irradiation of a cyclopropane solution containing DTBP (15% v/v), tetraethylsilane

$$Et_4Si \xrightarrow[-Bu^tOH]{Bu^tO^\bullet} \underset{(40)}{Et_3Si\dot{C}HMe} + \underset{(41)}{Et_3SiCH_2\dot{C}H_2} \quad (20)$$

(1 mol dm^{-3}), and (**2**) (0.2 mol dm^{-3}) afforded only the e.s.r. spectrum of the amine–thexylboryl radical (**7**) and neither (**40**)

* Only the wing lines of the multiplets resulting from β-proton coupling are apparent in Figure 5 for both (**38**) and (**39**). This is because exchange of the non-equivalent β-protons is taking place at an 'intermediate' rate on the e.s.r. timescale, as a result of inversion of the six-membered ring, for both radicals.

Table 2. Competition experiments carried out under conditions of PRC using $Me_3N{\rightarrow}BH_2Thx$ (**2**) as catalyst in cyclopropane at 189 K.[a]

Entry	Competing pair of reagents A	B	[B]/[A]	(k_A/k_B)[b]
1	$MeCH_2CO_2Et$	$MeCO_2Et$	2.00	4.51[c]
2	$MeCH_2CO_2Et$	Me_2CHCO_2Et	5.00	10.25
3	$(CH_2CO_2Et)_2$	$MeCO_2Et$	10.00	18.15
4	$(CH_2CO_2Et)_2$	$MeCH_2CO_2Et$	4.00	4.00
5	$MeCH(CO_2Et)_2$	$(CH_2CO_2Et)_2$	2.00	9.32
6	$HC(CO_2Et)_3$	$MeCH(CO_2Et)_2$	10.00	60.50[d]
7	$HC(CO_2Et)_3$	$H_2C(CO_2Et)_2$	1.00	2.90
8	MeCN	$MeCH_2CO_2Et$	3.00	2.30
9	$c\text{-}C_3H_5C(O)CH_3$	$(CH_2CO_2Et)_2$	1.00	2.82
10	PrBr[e]	$H_2C(CO_2Et)_2$	4.00	15.14

[a] The concentration of (**2**) was 0.42 mol dm^{-3} unless noted otherwise. [b] Abstraction of hydrogen from an α-C–H group unless noted otherwise. [c] Variation of the catalyst concentration between 0.10 and 0.42 mol dm^{-3} did not alter (k_A/k_B). [d] Catalyst concentration 0.10 mol dm^{-3}. [e] The propyl radical was produced by non-catalytic halogen abstraction from propyl bromide (see ref. 9).

Table 3. Relative rates of α-hydrogen-atom abstraction by $Me_3N{\rightarrow}\dot{B}HThx$ (**7**) in cyclopropane at 189 K.

Compound	Relative reactivity[a]
Me_2CHCO_2Et	0.4
$MeCO_2Et$	(1)
$MeCH_2CO_2Et$	4.5
$(CH_2CO_2Et)_2$	18.2
$MeCH(CO_2Et)_2$	1.7×10^2
$H_2C(CO_2Et)_2$	3.5×10^3
$HC(CO_2Et)_3$	1.0×10^4
MeCN	10.4
$c\text{-}C_3H_5C(O)Me$[b]	51.2
PrBr[c]	5.3×10^4

[a] Per molecule basis. [b] Abstraction from the methyl group. [c] Abstraction of bromine.

Table 4. Relative rates of α-hydrogen-atom abstraction from esters by amine–alkylboryl radicals in cyclopropane.

Amine alkylboryl radical	T/K	Ester reactivity (per molecule) $MeCO_2Et$	$MeCH_2CO_2Et$	Me_2CHCO_2Et
(**7**)	157	(1)	5.4	—
	189	(1)	4.5	0.4
	241	(1)	3.3	—
(**8**)	189	(1)	4.0	—
(**9**)	189	(1)	4.4	—
(**10**)	189	(1)	6.7	7.3
(**11**)	189	(1)	8.3	9.0

nor (**41**) were detectable up to 290 K. Similar experiments with the azaborolidine (**6**) gave rise only to the spectrum of (**11**), even though this radical is less sterically demanding than (**7**). No abstraction of hydrogen by amine–alkylboryl radicals was detectable from tetramethylsilane (1 mol dm^{-3}) up to 280 K. The failure of (**7**) and (**11**) to abstract from the α-C–H groups of Me_4Si or Et_4Si is not too surprising. Evidently the smaller exothermicity, probably coupled with less favourable polar factors, is responsible for the slower rate of hydrogen transfer compared with that from the α-C–H groups of esters.

Catalyst Efficiency.—Efficient catalysis of hydrogen abstraction by amine–alkylboranes requires that reaction of $Bu^tO^{\bullet}$ with the catalyst to generate the corresponding amine–alkylboryl radical should be very rapid.

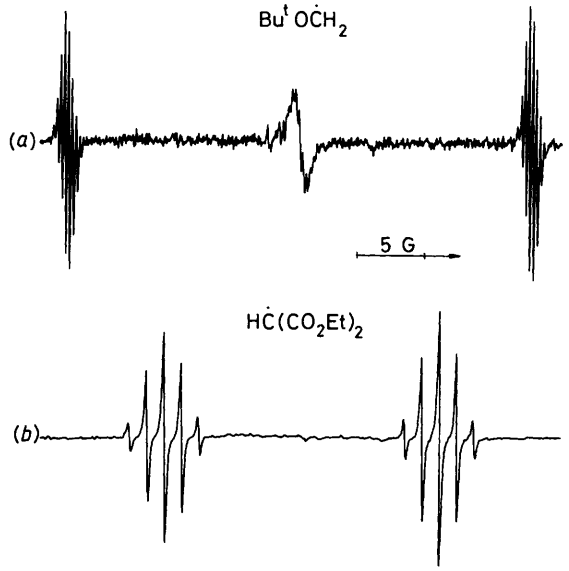


Figure 6. E.s.r. spectra of radicals obtained by hydrogen abstraction from an equimolar mixture of t-butyl methyl ether and diethyl malonate in cyclopropane at 189 K. (*a*) The radical $Bu^tO\dot{C}H_2$ produced in the absence of catalyst. (*b*) The radical (**24**) produced in the presence of (**2**) (0.07 mol dm^{-3}).

Cyclopropane solutions containing equimolar (0.64 mol dm^{-3}) quantities of t-butyl methyl ether and diethyl malonate, along with DTBP (15% v/v) and the catalyst (**2**) (0–0.1 mol dm^{-3}) were u.v. irradiated at 189 K. In the absence of catalyst only $Bu^tO\dot{C}H_2$ was detected, whilst with *ca.* 0.1 mol dm^{-3} catalyst only the spectrum of $H\dot{C}(CO_2Et)_2$ (**24**) was observed (see Figure 6). With catalyst concentrations in the range 6×10^{-4} to 2×10^{-2} mol dm^{-3}, both radicals could be detected and their relative concentrations were measured. If we make the assumption that reaction (21) represents the only fate of (**7**) and that the radicals $Bu^tO\dot{C}H_2$ and (**24**) are removed by self- and cross-reaction with equal (diffusion-controlled) rate coefficients, then equation (22) should hold. A plot of [(**24**)]/[$Bu^tO\dot{C}H_2$] *vs.* [(**2**)]/[Bu^tOMe] gave a straight line of slope

$$Me_3N{\rightarrow}\dot{B}HThx + H_2C(CO_2Et)_2 \longrightarrow Me_3N{\rightarrow}BH_2Thx + H\dot{C}(CO_2Et)_2 \quad (21)$$
(**24**)

$$[(\mathbf{24})]/[Bu^tO\dot{C}H_2] = (k_{14}/k_{10})[(\mathbf{2})]/[Bu^tOMe] \quad (22)$$

1.14×10^3, equal to the value of (k_{14}/k_{10}) at 189 K. From our previous work[18] k_{10} is known to be 4.15×10^4 dm^3 mol^{-1} s^{-1} at 189 K and thus k_{14} is 4.7×10^7 dm^3 mol^{-1} s^{-1} at this temperature. The very high rate of hydrogen transfer from a B–H group to the electrophilic t-butoxyl radical testifies to the importance of polar effects in this reaction. When approximate allowance is made for the different temperatures at which the measurements were made, the reactivity of $Me_3N{\rightarrow}BH_2Thx$ towards $Bu^tO^{\bullet}$ is similar to that of Bu_3GeH, since the rate coefficient for hydrogen abstraction from germanium is 8.0×10^7 dm^3 mol^{-1} s^{-1} at 300 K.[33]

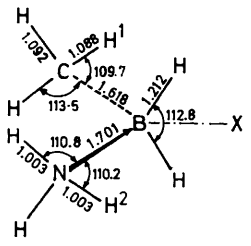
Molecular-orbital Calculations.—Since no experimental values of DH°(B–H) are available for amine–alkylborane complexes, we have carried out *ab initio* MO calculations for ammonia–methylborane (**42**) and the ammonia–methylboryl radical (**43**), using the GAUSSIAN 82 series of programs.[34] The spin-restricted (RHF) and spin-unrestricted Hartree–Fock (UHF) methods were used for closed-shell species and for

Table 5. Results of *ab initio* calculations using the 6-31G** basis set.

Molecule	Imposed symmetry	Total energy/hartree[a] U(R)HF	Total energy/hartree[a] MP3(full)	ZPVE/ kJ mol^{-1}	E_0/hartree[a]	μ_{calc}/D	$E_{i\,calc}$/eV
$H_3N{\rightarrow}\dot{B}H_2CH_3$ (**44**)	C_s	−121.672 579	−122.167 229	274.3	−122.073 201	5.23	10.73
$H_3N{\rightarrow}\dot{B}HCH_3$ (**45**)	C_1	−121.033 347	−121.498 211	243.8	−121.414 638	5.35	6.39
$H_3N{\rightarrow}\dot{B}H_2$[b]	C_s	−81.986 170	−82.290 719	162.9	−82.234 878	5.69	6.63
$CH_3\dot{C}H_2$[b]	C_s	−78.605 526	−78.914 623	165.2	−78.857 994	0.21	9.55
CH_3CH_3[b]	D_{3d}	−79.238 235	−79.583 016	208.0	−79.511 715	0	13.24
$CH_3CH_2CH_3$[b]	C_{2v}	−118.276 159	−118.780 683	288.4	−118.681 822	0.06	12.91

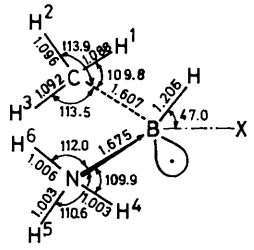
[a] 1 hartree = 2 625.5 kJ mol^{-1}; [b] Data from ref. 1.

radicals, respectively. Geometries were optimised using the standard 6-31G** basis set and electron correlation was included by single-point computations using a Møller–Plesset perturbation treatment taken to third order.[35] Structures were shown to correspond to local minima on the potential-energy surface by calculating the set of normal-mode vibrational frequencies and zero-point vibrational energies (ZPVEs) were derived. The equilibrium structures obtained for (**42**) and (**43**) are shown in (**44**) and (**45**), respectively.† The total energies are given in Table 5; the energy at 0 K (E_0) was obtained using



(**44**)

NBX = 114.0,
CBX = 139.5
$HNBH^2 = \pm 119.9$,
$HCBH^1 = \pm 118.7$



(**45**)

NBX = 113.7,
CBX = 137.4
$H^4NBX = -3.6$,
$H^6NBH^4 = +120.2$
$H^5NBH^4 = -119.4$,
$H^1CBX = +1.0$
$H^2CBH^1 = -118.9$
$H^3CBH^1 = +118.7$

equation (23), in which the factor of 0.9 is included to account for the fact that vibrational frequencies are usually overestimated at this level of theory.[35]

$$E_0 = E_{Total} + 0.9\,ZPVE \quad (23)$$

The values of ΔE_0 (which will be effectively equal to ΔH°_{298}) for the isodesmic reactions (24) and (25) are +12.7 and

$$Et^\bullet + H_3N{\rightarrow}BH_2Me \longrightarrow EtH + H_3N{\rightarrow}\dot{B}HMe \quad (24)$$

$$Et^\bullet + H_3N{\rightarrow}BH_2Me \longrightarrow PrH + H_3N{\rightarrow}\dot{B}H_2 \quad (25)$$

+38.1 kJ mol^{-1}, respectively. If we take DH°(Et–H) and DH°(Et–Me) to be 419 and 366 kJ mol^{-1}, respectively,[36] we estimate the strengths of the B–H and B–C bonds in ammonia–methylborane to be 432 and 404 kJ mol^{-1}, respectively. We have previously calculated DH°(B–H) in $H_3N{\rightarrow}BH_3$ ('inorganic ethane') to be 430 kJ mol^{-1} at the same level of theory, essentially equal to the value found for $H_3N{\rightarrow}BH_2Me$ which is an isoelectronic analogue of propane. A C–H bond in ethane is stronger by 16 kJ mol^{-1} than a secondary C–H bond in propane, because the isopropyl radical is more stabilised by hyperconjugation than the (primary) ethyl radical and because more strain present in the hydrocarbon is relieved upon homolytic cleavage of a secondary, as compared with a primary, C–H bond. However, $H_3N{\rightarrow}\dot{B}HMe$ is more strongly pyramidal at the radical centre than is MeĊHMe and thus less strain present in the parent will be relieved by homolysis of the B–H bond than by breaking a secondary C–H bond in propane. Hyperconjugative stabilisation will be less important for $H_3N{\rightarrow}\dot{B}HMe$ than for MeĊHMe, both because the former is more pyramidal and because the donor and acceptor orbitals involved in this interaction are less closely matched in energy for the former. The very low calculated ionisation potential of $H_3N{\rightarrow}\dot{B}HMe$ (6.39 eV) is in accord with the strongly nucleophilic character of the amine–alkylboryl radicals.

On the basis of these calculations, the strength of the B–H bond in an amine–alkylborane is intermediate between that of the O–H bond in Bu^{t}OH (440 kJ mol^{-1})[14] and the strengths of the α-C–H bonds in CH_3CN (394 kJ mol^{-1}),[15] $CH_3C(O)CH_3$ (385 kJ mol^{-1}),[37] and $CH_3C(O)OEt$ (*ca.* 395 kJ mol^{-1}),[38] making both steps of the catalytic cycles involved in PRC of hydrogen-atom abstraction by t-butoxyl radicals exothermic.

Experimental

E.s.r. spectra were recorded with a Varian E-109 instrument operating at *ca.* 9.1 GHz. Samples were sealed in evacuated Suprasil quartz tubes and irradiated with u.v. light (λ *ca.* 240–340 nm) while in the microwave cavity of the spectrometer. The techniques used have been described previously.[9]

Materials.—N.m.r. spectra were obtained with a Varian XL-200 instrument using tetramethylsilane as an internal standard (^1H) or $Et_2O{\rightarrow}BF_3$ external standard (^{11}B). Preparations and manipulations of all boron-containing compounds were carried out under dry nitrogen or argon; all solvents were dried before use.

Trimethylamine–thexylborane (**2**) was prepared as described previously.[9] As noted before,[9] some loss of amine occurred during distillation such that the product contained a small amount of thexylborane dimer. This was readily converted back into (**2**) by stirring the distillate with a small amount of trimethylamine at 0 °C followed by removal of the uncomplexed amine by pumping (0.1 Torr) at room temperature to give pure trimethylamine–thexylborane. Trimethylamine–t-butylborane (**4**),[39] trimethylamine–methylborane (**5**),[9] and 1,1-dimethyl-1,2-

† Bond lengths are given in Å, bond and dihedral angles in degrees. In (**44**) the H^1CBNH^2 fragment was constrained to be planar and the BH_2 group was forced to lie perpendicular to this plane; X is a dummy atom lying in both planes. In (**45**) the dummy atom X lies in the CBN plane which is perpendicular to the BHX plane; the barriers to torsional motion about the NB and CB bonds are very small.

azaborolidine (**6**)[20] were prepared using methods taken from the literature.

Quinuclidine–Thexylborane (**3**).—2,3-Dimethylbut-2-ene (9.26 g, 0.11 mol) was added dropwise with stirring to dimethyl sulphide–borane (10.0 cm^3 of 10 mol dm^{-3} solution in excess Me_2S) maintained at *ca.* −10 °C. When the addition was complete, the mixture was stirred for a further 3 h at 0 °C, before dimethyl sulphide was removed under reduced pressure and collected in a trap cooled to −78 °C to leave essentially pure thexylborane dimer. Diethyl ether (10 cm^3) was added to the borane and the solution was stirred and cooled to 0 °C during the dropwise addition of quinuclidine (11.12 g, 0.10 mol) in ether (30 cm^3). After the addition was complete, the solution was stirred for a further 20 min at room temperature before the ether was removed under reduced pressure to leave quinuclidine–thexylborane as a crystalline solid which was further purified by h.p.l.c. on silica gel using light petroleum (b.p. 60–70 °C)–ethyl acetate (10:1 v/v) as eluant. $\delta_H(C_6D_6)$ 0.91 (m, HCCH_2), 1.22 (s, CMe_2), 1.34 (d, *J* 6.8 Hz, CHMe_2), 1.78 (septet, *J* 6.8 Hz, CHMe$_2$), 2.69 (m, CH_2N). $\delta_B(C_6D_6)$ −0.20 (t, J_{BH} 93 Hz).

Cyclopropane (Argo International) and oxirane (Fluka) were used as received. Dibutanoyl peroxide was prepared by a published method.[40] Epicholesteryl acetate[41] (**21**-α) was prepared from epicholesterol[42] as described below.

Potassium superoxide (1.40 g, 19.7 mmol) was added to a solution of 18-crown-6 (3.70 g, 14.0 mmol) in dimethyl sulphoxide (100 cm^3) and cholesteryl toluene-*p*-sulphonate[43] (2.50 g, 4.6 mmol) in 1,2-dimethoxyethane (80 cm^3) was added dropwise during 20 min. After the addition was complete, the reaction mixture was stirred for a further 4 h at room temperature before addition of 10% aqueous HCl (100 cm^3). The mixture was extracted with diethyl ether (1 × 50 cm^3) and then with light petroleum (b.p. 40–60 °C) (3 × 50 cm^3). The combined organic phase was washed with water and dried ($MgSO_4$) before all volatiles were removed under reduced pressure to give a yellow oil. The product was purified by column chromatography (silica gel, dichloromethane eluant) to give epicholesterol which contained *ca.* 5% cholesterol as judged by ^{1}H n.m.r. spectroscopy. This mixture of epicholesterol and cholesterol (0.60 g, 1.6 mmol) was dissolved in a mixture of acetic anhydride (15 cm^3) and pyridine (20 cm^3) and left to stand at room temperature for 15 h. The reaction mixture was added to water (100 cm^3) and the product was extracted into ether (3 × 50 cm^3). The ether solution was washed with water (3 × 100 cm^3) and dried ($MgSO_4$) before removal of all volatiles under reduced pressure to leave crude acetate which was purified by column chromatography (silica gel, dichloromethane–pentane 6:1 v/v eluant). Final recrystallisation from methanol yielded pure epicholesteryl acetate, m.p. 84 °C (lit.,[41c] m.p. 83–85 °C).

All other compounds used in this work were obtained commercially and were purified by distillation or recrystallisation, as appropriate.

Acknowledgements

We thank Miss P. L. H. Mok for carrying out the experiments with 3-methylbutan-2-one.

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Received 13*th February* 1989; *Paper* 9/00682F