An *ab initio* study of β-fragmentation reactions in some alkoxyacyl (alkoxycarbonyl) and related radicals †

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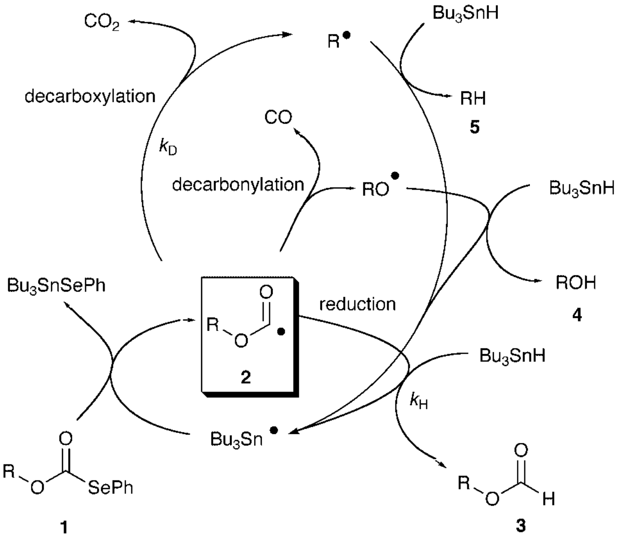
Ab initio molecular orbital calculations using the 6-311G**, cc-pVDZ and aug-cc-pVDZ basis sets, with (MP2, QCISD, CCSD(T)) and without (HF) the inclusion of electron correlation indicate that decarboxylation reactions of alkoxyacyl (alkoxycarbonyl) radicals are significantly exothermic. Transition states (**16**) for these decarboxylation reactions are calculated to have C_{TS}–O_{TS} separations in the range: 1.813–1.892 Å; these distances appear to be affected somewhat by steric compression. At the CCSD(T)/6-311G**//MP2/6-311G** level of theory, energy barriers of 75.9, 72.8, 67.0 and 60.3 kJ mol^{-1} are calculated for the decarboxylation reactions involving the methoxyacyl, ethoxyacyl, isopropoxyacyl and *tert*-butoxyacyl radicals (**2**) respectively, while the reverse reactions are calculated to require energies in excess of 130.9 kJ mol^{-1}. By comparison, the decarbonylation reaction of the acetyl radical (**8**) is predicted to be significantly endothermic; methyl radicals are calculated to prefer to add to carbon monoxide with an energy barrier of only 24.0 kJ mol^{-1} at the CCSD(T)/aug-cc-pVDZ//MP2/aug-cc-pVDZ level of theory, in good agreement with available experimental data.

Similar calculations for reactions involving (methoxy)thioacyl, (methylthio)acyl and (methylthio)thioacyl radicals (**12**–**14**, R = Me) suggest that only (alkoxy)thioacyl radicals (**12**) provide synthetically useful β-fragmentation reactions, the remaining systems (**13**, **14**) are unlikely to be useful as alkyl radical precursors in synthesis; the reverse reactions are calculated to be competitive with the β-fragmentation process in these cases.

Introduction

(Phenylseleno)formates (**1**) have emerged as synthetically useful precursors of alkoxyacyl (alkoxycarbonyl) radicals (**2**).[1,2] Substrates **1** can become involved in stannane-mediated radical chain processes (Scheme 1) and may lead to formate esters (**3**) through direct reduction of the oxyacyl radical (**2**), to alcohols (**4**) through decarbonylation of **2** followed by hydrogen abstraction from the stannane, or to rearranged or unrearranged nor-alkanes (**5**) through decarboxylation of **2** and subsequent reduction.[1] Pfenninger and co-workers demonstrated that the reaction outcome could be controlled to some extent through variation of reaction conditions and choice of substrate; in this manner both formate ester and nor-alkane could be achieved in a wide cross-section of steroidal systems.[1] On the other hand, Bachi and Bosch were able to trap the oxyacyl radical through intramolecular homolytic addition to afford several types of lactones.[2]



Scheme 1

Recently, we have been interested in exploiting the synthetic potential of alkoxyacyl radicals in the absence of chain-carrying reagents such as tributyltin hydride in order to effect intramolecular homolytic substitution at selenium. We reported that (aryltelluro)formates (**6**) are excellent precursors of **2**.[3,4] Upon photolysis, telluroformates (**6**) undergo facile carbon–tellurium bond cleavage to afford oxyacyl radicals which can be trapped by inter- and intramolecular homolytic substitution chemistry (Scheme 2),[3,4] while at elevated temperatures these radicals undergo decarboxylation to provide synthetically useful alkyl radicals.[3] Despite being thermally labile, (aryltelluro)formates (**6**) have half-lives in the order of days at 160°, a property which detracts from their synthetic utility.[3]

The efficient design of synthetic strategies based on free-radical chain chemistry requires a thorough understanding of the kinetics of each of the individual steps involved in the overall chain.[5,6] Until recently, rate data have not generally been available for the key reactions depicted in Scheme 1. Specifically, kinetic data for the decarboxylation of radicals **2** have been limited to those provided by Fischer and co-workers[7] for the *tert*-butoxyacyl radical (**2**, R = *tert*-Bu) and to data for some systems bearing stabilized substituents provided by Beckwith and Bowry.[8] These studies provided decarboxylation rate constants (k_D) which ranged from 3.6×10^6 s^{-1} (80°) for (**2**, R = *tert*-Bu)[7] to 5×10^9 s^{-1} (80°) for **7**,[8] together with activation energies ($\Delta E^{\ddagger}$) of 49.0 and 21.8 kJ mol^{-1} for (**2**, R = *tert*-Bu) and **7** respectively.

Newcomb provided recently the first laser-flash photolysis

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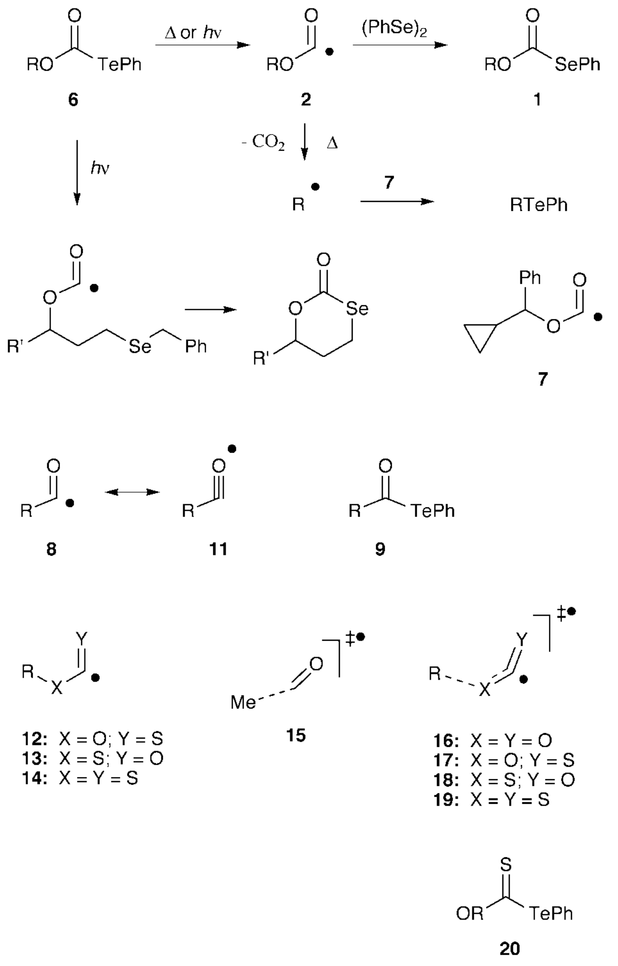
† HF/6-311G**, MP2/6-311G**, MP2/cc-pVDZ and MP2/aug-cc-pVDZ Gaussian Archive entries for the optimized structures in this study and higher-level calculated single-point energies are available as supplementary data. For direct electronic access see http://www.rsc.org/suppdata/p2/1999/2041, otherwise available from BLDSC (SUPPL. NO 57623, pp. 40) or the RSC Library. See Instructions for Authors available *via* the RSC web page (http:www.rsc.org/authors).



Scheme 2

(LFP) kinetic data for the decarboxylation of some benzyl and cyclopropyl substituted oxyacyl radicals and was largely able to corroborate the earlier work of Beckwith.[9] This work also provided the first estimates for the kinetic parameters associated with the abstraction of hydrogen atom from tributyltin hydride by oxyacyl radicals, namely values of log (A/M^{-1} s^{-1}) and $\Delta E^‡$ of 9 and 20.1 kJ mol^{-1} respectively.[9]

Despite these important contributions to our understanding of the chemistry of radicals **2**, there still remains little quantitative kinetic data for the decarboxylation of simple primary and secondary alkyl substituted oxyacyl radicals (**2**, R = 1°-, 2°-alkyl). Indeed the original work of Pfenninger still provides the only useful information pertaining to the radicals in question and the product distribution data provided by these workers have been extrapolated to provide estimates for the required decarboxylation rate constants.[1,9] Unfortunately, extrapolating the data of Pfenninger into rate constant data is fraught with inherent problems. Firstly, it is very likely that the (phenylseleno)formates used in this early study were contaminated by trace amounts of diphenyl diselenide. Newcomb addresses this issue and notes that "it seems apparent from the reported product ratios in that study that PhSeH was produced in photochemically initiated reactions, and it is possible that PhSeH interfered in thermally initiated reactions".[9] Crich has established that diphenyl diselenide reacts rapidly with Bu_3SnH to afford PhSeH which delivers hydrogen atom some three orders of magnitude more rapidly to carbon-centred radicals than does Bu_3SnH.[10,11]

Close inspection of the data provided by Pfenninger also reveals significant discrepancies between the data provided for different, but closely related, secondary systems.[1] In addition, extrapolation of the data for the primary system provides an unrealistic value of 17 for log(A/s^{-1}); studies to date provide values of log(A/s^{-1}) for decarboxylation reactions of **2** which fall between 12 and 14.[7–9]

Nevertheless, these data are the only available for primary- and secondary-alkyl substituted oxyacyl radicals, and while their work was not intended to provide kinetic data, very approximate values of k_D of 200 and 500 s^{-1} (20°) can be extrapolated for primary and secondary systems respectively.[1,9]

During the course of our synthetic work it has become apparent that there is a substantial difference in the stabilities of oxyacyl (**2**) and acyl (**8**) radicals. We not only found that (phenyltelluro)formates (**6**) are less likely to decompose upon standing than the closely related (phenyltelluro)esters (**9**),[12] but recent studies in our laboratories have demonstrated that radicals **2** are poorer leaving groups than **8** in homolytic substitution chemistry involving selenium.[13] Both of these observations suggest that radicals **8** are likely to be more stable than **2** and that this contrariety may well lead to different rates of hydrogen abstraction from chain-carrying species such as Bu_3SnH.

As an adjunct to our synthetic studies, we felt it necessary to provide further insight into the relative stabilities and reactivities of radicals **2**; we turned to *ab initio* molecular orbital theory to provide this understanding. Specific points which we wished to address included an indication of the relative stabilities of acyl and oxyacyl radicals, the relative reactivities of primary, secondary and tertiary oxyacyl radicals toward decarboxylation, and whether modification of the radical itself might lead to more synthetically useful properties.

Methods

All *ab initio* molecular orbital calculations were carried out using the GAUSSIAN94[14] program. Geometry optimisations were performed using standard gradient techniques at the SCF and MP2 levels of theory using RHF and UHF methods for closed and open shell systems, respectively with the basis sets indicated in the Tables.[15] Further single-point QCISD and CCSD(T) calculations were performed on the MP2 optimised structures wherever possible. When correlated methods were used calculations were performed using the frozen core approximation. Vibrational frequencies were calculated on each optimized structure in this study, except for the MP2/aug-cc-pVDZ structures of **2**, **16** (R = *tert*-Bu). Energy barriers ($\Delta E^‡$) calculated in this study are not corrected for basis set superposition error. Where appropriate, zero-point vibrational energy (ZPE) corrections have been applied. Except for UHF/6-311G** calculations on transition states **16**–**19** and MP2 calculations on structure **19** where values of $\langle s^2 \rangle$ were calculated to be 0.90–0.94, indicating low-levels of higher-order spin contamination, values of $\langle s^2 \rangle$ never exceeded 0.88 before annihilation of quartet contamination.

All calculations were performed on Sun SparcStation 10/516, Cray J916e, DEC Alphaserver 8400, Alphastation 400/233, Personal Workstation 433au or 600au computers.

Results and discussion

On the stability of acyl and oxyacyl radicals

We began our study by examining the difference in the relative energies for the formation of the methoxyacyl radical **2** (R = Me) and acetyl radical **8** (R = Me). To that end, the energies of **2** (R = Me), **8** (R = Me) and the parent structures, methyl formate (**10a**) and acetaldehyde (**10b**) were determined at the levels of theory listed in Table 1. A full listing of the optimized structures and energies determined in this study is provided in the Supplementary Material.†

The data in Table 1 clearly demonstrate that at all levels of theory, the methoxyacyl radical is calculated to be less stable relative to the parent formate than the analogous acyl radical; at the highest level of theory (CCSD(T)/aug-cc-pVDZ//MP2/cc-pVDZ) this difference is calculated to be 44.1 kJ mol^{-1}.

Table 1 Calculated differences (ΔE) in relative energies[a] for the formation of the methoxyacyl radical **2** (R = Me) and the acetyl radical **8** (R = Me) [(E(**2**) − E(**10a**)) − (E(**8**) − E(**10b**))] and calculated C=O vibrational frequencies[b]

Method	ΔE^a	ν(C=O)^{b,c} **2**	ν(C=O)^{b,c} **8**
HF/6-311G**	41.9	2047 (1991)	2131 (2014)
MP2/6-311G**	45.1	1862 (1810)	1947 (1793)
B3LYP/6-311G**	30.8	1847 (1814)	1931 (1822)
MP2/cc-pVDZ	44.1	1856 (1817)	1940 (1832)
MP2/aug-cc-pVDZ	46.6	1799 (1745)	1890 (1741)
MP2/cc-pVTZ//MP2/aug-cc-pVDZ	46.1	—	—
MP2/aug-cc-pVTZ//MP2/aug-cc-pVDZ	47.1	—	—
QCISD/6-311G**//MP2/6-311G**	42.7	—	—
CCSD(T)/6-311G**//MP2/6-311G**	38.0	—	—
QCISD/cc-pVDZ//MP2/cc-pVDZ	42.6	—	—
CCSD(T)/cc-pVDZ//MP2/cc-pVDZ	42.7	—	—
QCISD(T)/aug-cc-pVDZ//MP2/aug-cc-pVDZ	44.3	—	—
CCSD(T)/aug-cc-pVDZ//MP2aug-cc-pVDZ	44.1	—	—

[a] Energies in kJ mol^{-1}. [b] Frequencies in cm^{-1}. Frequencies are unscaled. [c] Values in parentheses refer to the calculated C=O stretching frequencies of the parent compounds (**10a**, **10b**).

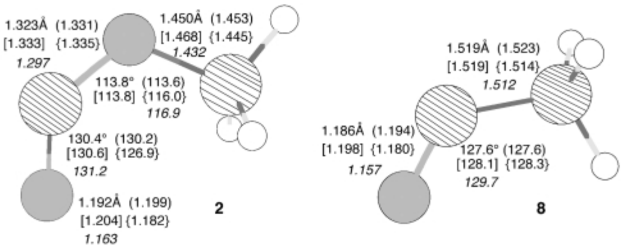


Fig. 1 MP2/6-311G** calculated structures of radicals (**2**, **8**, R = Me). (MP2/cc-pVDZ data in parentheses). [MP2/aug-cc-pVDZ data in square brackets]. {B3LYP/6-311G** data in curly brackets}. *UHF/6-311G** data in italics.*

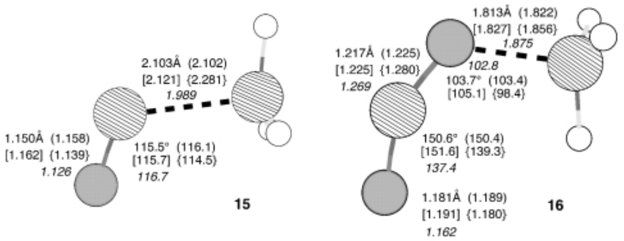
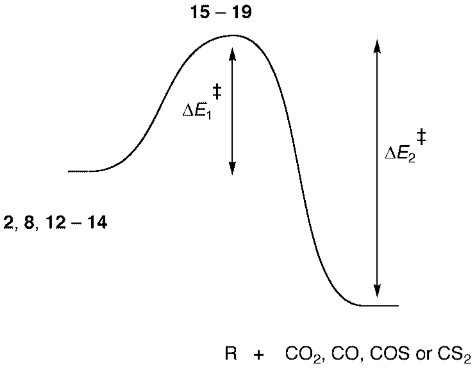


Fig. 2 MP2/6-311G** calculated structures in transition states **15**, **16**. (MP2/cc-pVDZ data in parentheses). [MP2/aug-cc-pVDZ data in square brackets]. {B3LYP/6-311G** data in curly brackets}. *UHF/6-311G** data in italics.*

These results clearly confirm our suspicions about the origin of the observed instability of (phenyltelluro)esters relative to the corresponding (phenyltelluro)formate and the relative leaving group abilities of oxyacyl radicals when compared to acyl radicals as previously noted. It is interesting to speculate on the electronic origin of this difference. Lusztyk and co-workers have suggested that acyl radicals **8** are stabilized by substantial resonance contributions from contributors **11** on account of the significant triple-bond character observed in the infrared spectra of radicals **8** generated during laser-flash experiments.[16] We suggest that this stabilization mechanism is not as accessible to radicals **2**. Inspection of the MP2/aug-cc-pVDZ optimized structures of **2** (R = Me) and **8** (R = Me) (Fig. 1) and calculated vibrational frequencies (Table 1) provide support for this suggestion. Noticeably, while the (carbonyl) carbon–oxygen separation in **2** (R = Me) is calculated to be only marginally shorter than the similar distance in **8** (R = Me) (1.198 *vs.* 1.204 Å), the calculated C=O vibrational frequencies suggest a significant difference in the nature of the bonding in each structure. The agreement between the calculated and experimental frequencies for **8** (R = Me), **10a** and **10b** at the highest optimized level of theory is satisfying.‡ The MP2/aug-cc-pVDZ values of 1890, 1741 and 1745 cm^{-1} for **8** (R = Me), **10a** and **10b** respectively compare favourably with available experimental data (1864, 1761 and 1755 cm^{-1}).[16,17] These results provide confidence in our calculated frequency data for **2** (R = Me); the value of 1799 cm^{-1} (MP2/aug-cc-pVDZ) strongly suggesting significantly reduced triple-bond character in radicals **2** when compared with **8**.

Fragmentations of methoxyacyl and acetyl radicals (2, 8, R = Me)

We next turned our attention to pathways for the generation of alkyl radicals from acyl and oxyacyl radicals (**2**, **8**). Extensive searching of the $C_2H_3O_2$ and C_2H_3O potential energy surfaces located transition states (**15**, **16**, R = Me) for the decarbonylation and decarboxylation reactions of the acetyl and methoxyacyl radicals (**8**, **2**, R = Me) respectively at all levels of theory employed in this study. The optimized geometries of **15**, **16** (R = Me) are displayed in Fig. 2, while the energy barriers ($\Delta E_1^{\ddagger}$, $\Delta E_2^{\ddagger}$) for the forward and reverse reactions in question (Scheme 3) are listed in Table 2. A full listing of all optimized geometries and energies (Gaussian Archive entries) of the structures in this study are provided in the Supplementary Information.†



Scheme 3

Inspection of Fig. 1 reveals that the transition state (**16**) for the decarboxylation of **2** is calculated to have shorter transition state distances than that (**15**) for the corresponding decarbonylation of **8** at all levels of theory. At the highest level of theory (MP2/aug-cc-pVDZ), the C_{TS}–O_{TS} distances are calculated to be 1.827 and 2.121 Å for **16** (R = Me) and **15** respectively.

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‡ All frequencies reported are unscaled.

Table 2 Calculated energy barriers[a] for the forward ($\Delta E_1^\ddagger$) and reverse ($\Delta E_2^\ddagger$) decarboxylation and decarbonylation reactions of methoxyacyl and acetyl radicals (**2**, **8**, R = Me) respectively, and imaginary frequencies (ν)[b] of transition structures **15**, **16**

Radical		$\Delta E_1^\ddagger$	$\Delta E_1^\ddagger$ + ZPE[c]	$\Delta E_2^\ddagger$	$\Delta E_2^\ddagger$ + ZPE[c]	ν
2	UHF/6-311G**	230.8	218.9	345.6	358.9	923i
	MP2/6-311G**	98.1	86.5	198.6	208.7	1715i
	MP2/cc-pVDZ	96.6	86.8	195.6	207.9	1695i
	MP2/aug-cc-pVDZ	92.4	81.5	179.0	192.7	1677i
	MP2/cc-pVTZ//MP2/aug-cc-pVDZ	97.9	—	186.7	—	—
	MP2/aug-cc-pVTZ//MP2/aug-cc-pVDZ	94.8	—	177.8	—	—
	QCISD/6-311G**//MP2/6-311G**	80.9	—	168.4	—	—
	CCSD(T)/6-311G**//MP2/6-311G**	75.9	—	161.3	—	—
	QCISD/cc-pVDZ//MP2/cc-pVDZ	80.8	—	165.0	—	—
	CCSD(T)/cc-pVDZ//MP2/cc-pVDZ	73.9	—	158.8	—	—
	QCISD/aug-cc-pVDZ//MP2/aug-cc-pVDZ	77.9	—	150.2	—	—
	CCSD(T)/aug-cc-pVDZ//MP2aug-cc-pVDZ	70.4	—	142.1	—	—
	B3LYP/6-311G**	160.3	150.3	239.7	249.7	984i
8	UHF/6-311G**	58.0	49.0	71.3	82.7	589i
	MP2/6-311G**	83.6	73.1	38.1	48.2	527i
	MP2/cc-pVDZ	84.5	71.8	37.8	48.3	531i
	MP2/aug-cc-pVDZ	89.4	76.8	31.9	41.5	512i
	MP2/cc-pVTZ//MP2/aug-cc-pVDZ	90.9	—	31.9	—	—
	MP2/aug-cc-pVTZ//MP2/aug-cc-pVDZ	93.6	—	28.3	—	—
	QCISD/6-311G**//MP2/6-311G**	69.4	—	35.6	—	—
	CCSD(T)/6-311G**//MP2/6-311G**	68.7	—	30.7	—	—
	QCISD/cc-pVDZ//MP2/cc-pVDZ	69.6	—	35.4	—	—
	CCSD(T)/cc-pVDZ//MP2/cc-pVDZ	68.7	—	30.8	—	—
	QCISD/aug-cc-pVDZ//MP2/aug-cc-pVDZ	74.2	—	29.7	—	—
	CCSD(T)/aug-cc-pVDZ//MP2aug-cc-pVDZ	72.7	—	24.0	—	—
	B3LYP/6-311G**	75.6	66.7	12.6	18.2	277i

[a] Energies in kJ mol^{-1}. [b] Frequencies in cm^{-1}. [c] Zero-point vibrational energy correction.

Table 2 lists interesting trends in calculated activation energies ($\Delta E_1^\ddagger$, $\Delta E_2^\ddagger$, Scheme 3) as the basis set and degree of electron correlation are improved. It is clear that the data for both reactions converge slowly toward values which we assume are close to experimental numbers. The energy barrier ($\Delta E_1^\ddagger$) for the decarboxylation of methoxyacyl (**2**, R = Me) is calculated to be 230.8 kJ mol^{-1} at the HF/6-311G** level of theory. Inclusion of electron correlation at the MP2 level has the dramatic effect of lowering this energy to 98.1 kJ mol^{-1}, while further improvement provides values of 92.4 (MP2/aug-cc-pVDZ), 80.9 (QCISD/6-311G**//MP2/6-311G**) and 73.9 kJ mol^{-1} (CCSD(T)/cc-pVDZ//MP2/cc-pVDZ). At the highest level of theory in this study (CCSD(T)/aug-cc-pVDZ//MP2/aug-cc-pVDZ), $\Delta E_1^\ddagger$ is predicted to be only 70.4 kJ mol^{-1}, some 160.4 kJ mol^{-1} lower than the HF/6-311G** determined value. Similar trends are observed for the energy barrier ($\Delta E_2^\ddagger$) for the reverse reaction; values of between 345.6 (HF/6-311G**) and 142.1 kJ mol^{-1} (CCSD(T)/aug-cc-pVDZ//MP2/aug-cc-pVDZ) are calculated for the homolytic addition of methyl radical to carbon dioxide. At all levels of theory in this study, the decarboxylation of **2** (R = Me) is predicted to be significantly exothermic; at the highest level of theory this exothermicity is calculated to be 71.7 kJ mol^{-1}. It should be noted that the B3LYP (density functional) method performs relatively poorly for the systems in question and we urge caution in its use for these and related systems.

If we turn our attention to the decarbonylation of **8** (R = Me), the data in Table 2 reveal that at all levels of theory except HF/6-311G**, this reaction is calculated to be endothermic. Once again the inclusion of electron correlation is crucial to obtaining reliable data. Values for $\Delta E_1^\ddagger$ are predicted to range from 58.8 kJ mol^{-1} (HF/6-311G**) to 72.7 kJ mol^{-1} at the highest level of theory, while the barrier for the reverse reaction is calculated to be only 24.0 kJ mol^{-1} at the highest level. It is interesting to note that the B3LYP data appear to, once again, be out of step with the remaining data in Table 2.

The low energy barrier calculated for the addition of methyl radical to carbon monoxide is pleasing and sits well with the knowledge that several workers have employed radical carbonylation chemistry during the synthesis of interesting synthetic targets.[18,19] While little kinetic data exist for the reaction of methyl radical with carbon monoxide, the value of 2 × 10^6 M^{-1} s^{-1} (25°)[20] for the rate constant for this homolytic addition in water can be extrapolated to an energy barrier ($\Delta E_1^\ddagger$) of 18–21 kJ mol^{-1},[§] assuming a value of log(A/M^{-1} s^{-1}) of 9.5–10.[21] In addition, Ryu and co-workers have determined an energy barrier ($\Delta E_1^\ddagger$) of 25.1 kJ mol^{-1} for the homolytic addition of a primary alkyl radical to carbon monoxide.[21] These experimentally determined energy barriers compare very favourably with that calculated at the CCSD(T)/aug-cc-pVDZ//MP2/aug-cc-pVDZ level of theory, namely 24.0 kJ mol^{-1}. The good level of agreement between the calculated and available experimental data provides confidence in our ability to reproduce the mechanistic details of the radical decarboxylation and decarbonylation reactions of interest in this study.

Decarboxylation reactions of primary, secondary and tertiary alkoxyacyl radicals (2)

We next turned our attention to the analogous decarboxylation reactions involving ethoxyacyl, isopropoxyacyl and *tert*-butoxyacyl radicals (**2**, R = Et, iso-Pr, *tert*-Bu). Due to resource limitations, calculations were performed with the 6-311G** basis set with electron correlation included up to CCSD(T); we expected these calculations to provide, at the very least, good qualitative data for the reactions of interest. The data provided in Table 2 indicate that calculations performed at the CCSD(T)/6-311G**//MP2/6-311G** level of theory provide energy barriers for the decarboxylation and decarbonylation reactions of interest which lie within a few kJ mol^{-1} from those calculated at the highest level of theory (CCSD(T)/aug-cc-pVDZ//MP2/aug-cc-pVDZ) at a considerable saving in cost.[¶]

[§] The value of $\Delta E_1^\ddagger$ in water is very likely to be lower than the analogous barrier in non-polar solvents such as benzene. See reference 19.

[¶] For example, a CCSD(T)/6-311G** single point calculation on radical **2** (R = Me) requires 190 minutes of CPU time on a CRAY J916e supercomputer, while the analogous CCSD(T)/aug-cc-pVDZ calculation requires 631 minutes on the same computer.

Table 3 Calculated energy barriers[a] for the forward ($\Delta E_1^‡$) and reverse ($\Delta E_2^‡$) decarboxylation reactions of ethoxyacyl, isopropoxyacyl and *tert*-butoxyacyl radicals (**2**, R = Et, iso-Pr, *tert*-Bu), and imaginary frequencies (ν)[b] of transition structures **16**

		$\Delta E_1^‡$	$\Delta E_1^‡$ + ZPE[c]	$\Delta E_2^‡$	$\Delta E_2^‡$ + ZPE[c]	ν
R = Et	UHF/6-311G**	105.3	91.9	216.9	222.9	1267i
	MP2/6-311G**	95.0	84.9	185.7	192.4	1676i
	QCISD/6-311G**[d]	80.2	—	158.9	—	—
	CCSD(T)/6-311G**[e]	72.8	—	150.6	—	—
	B3LYP6-311G**	113.5	101.9	191.7	197.1	1182i
R = iso-Pr	UHF/6-311G**	101.7	88.4	215.2	219.6	1346i
	MP2/6-311G**	87.5	76.8	174.1	179.5	1624i
	QCISD/6-31G**[d]	74.1	—	152.0	—	—
	CCSD(T)/6-311G**[e]	67.0	—	141.9	—	—
	B3LYP6-311G**	36.5	27.1	122.4	127.9	629i
R = *tert*-Bu	UHF/6-311G**	93.9	81.6	208.7	210.5	1403i
	MP2/6-311G**	79.5	—	160.3	199.4	—
	QCISD/6-311G**[d]	67.3	—	142.0	—	—
	CCSD(T)/6-311G**[e]	60.3	—	130.9	—	—
	B3LYP6-311G**	27.8	19.3	117.8	122.3	562i

[a] Energies in kJ mol^{-1}. [b] Frequencies in cm^{-1}. [c] Zero-point vibrational energy correction. [d] QCISD/6-311G**//MP2/6-311G**. [e] CCSD(T)/6-311G**//MP2/6-311G**.

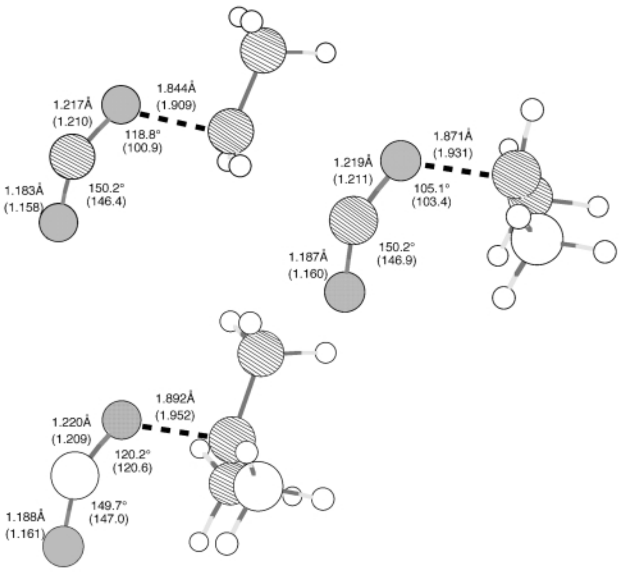

Fig. 3 MP2/6-311G** calculated structures of transition states (**16**, R = Et, iso-Pr, *tert*-Bu). (UHF/6-311G** data in parentheses).

Transition states (**16**, R = Et, iso-Pr, *tert*-Bu) were located at the HF/6-311G** and MP2/6-311G** levels of theory for each of the reactions in question; these structures are displayed in Fig. 3. Inspection of Fig. 2 and 3 reveals that the C_{TS}–O_{TS} separations in transition states **16** are calculated at the MP2/6-311G** level of theory to systematically increase in the range: 1.81–1.89 Å. The systematic increases in this distance as the radical leaving group stability is improved are unlikely to reflect the degree of "earliness/lateness" in the transition states **16**, but rather reflect a similar degree of bond lengthening (1.450–1.484 Å: MP2/6-311G**) calculated for the ground state radicals **2**. In both cases (**2**, **16**) the origin of these trends is most likely due to steric compression. This suggestion is supported by the observation that in each case, the transition state distance is calculated to be consistently about 25% longer than the corresponding separation in **2**.

The data in Table 3 reveal, once again, the importance of electron correlation in these calculations and highlight the divergence between B3LYP and other correlated calculations. It is interesting to compare the calculated energy barriers ($\Delta E_1^‡$, $\Delta E_2^‡$) for reactions involving different radical leaving groups. Not surprisingly, the reactions in question are all calculated to be significantly exothermic, with values of $\Delta E_1^‡$ ranging from 60.3 kJ mol^{-1} (R = *tert*-Bu, CCSD(T)/6-311G**//MP2/6-311G**) to 105.3 kJ mol^{-1} (R = Et, HF/6-311G**), and $\Delta E_2^‡$ calculated to be greater than 130.9 kJ mol^{-1} at all levels of theory (except B3LYP).

The data presented in Table 3 can be used to provide a prediction of the relative reactivities of primary, secondary and tertiary alkyl substituted oxyacyl radicals toward decarboxylation. At the highest level of theory (CCSD(T)/6-311G**//MP2/6-311G**), energy barriers ($\Delta E_1^‡$) of 72.8, 67.0 and 60.3 kJ mol^{-1} for the ethyl, isopropyl and *tert*-butyl substituted radicals **2** respectively translate into relative rates at 25° of approximately 1 : 28 : 442, assuming similar values of $\log(A/\mathrm{s}^{-1})$ for each reaction in question. These calculated data are to be compared with the data of Pfenninger which have been extrapolated to provide relative rates of 1 : 2.5 : 550 at the same temperature.[1,9] While the calculations presented in this paper provide a good level of convergence between theory and experiment for the primary and tertiary substituted systems, the divergence between data available for the secondary system requires further comment. Given the difficulties in extrapolating the data of Pfenninger alluded to by us and Newcomb[9] (*vide supra*), we suggest that secondary alkoxyacyl radicals (**2**, R = 2°-alkyl) are significantly more reactive to decarboxylation than suggested by Newcomb.[9] Further experimental data will be required in order to verify this prediction.

Designing better precursors: fragmentations in radicals related to 2

Given the significant energy barriers ($\Delta E_1^‡$) calculated for the decarboxylation reactions of alkoxyacyl radicals **2** presented above, we were interested in whether or not slight structural modifications of the fragmenting moiety would lead to reaction profiles more conducive to synthetic application. We therefore examined the β-fragmentation reactions of the (methoxy)-thioacyl, (methylthio)acyl and (methylthio)thioacyl radicals (**12**–**14**, R = Me) in which one or both oxygen atoms originally in **2** have been replaced by sulfur. Transition states (**17**–**19**, R = Me) for the reactions in question were located at all levels of theory (as listed in Table 4) and are displayed in Fig. 4 while the calculated energy barriers ($\Delta E_1^‡$, $\Delta E_2^‡$) for the forward and reverse reactions (Scheme 3) are listed in Table 4. A complete listing of the calculated geometries and energies for all structures in this study can be found in the Supplementary Material.†

Inspection of Fig. 4 reveals that the geometry of transition state (**17**, R = Me) for the loss of COS from (methoxy)thioacyl (**12**, R = Me) is very similar to that (**16**, R = Me) for the

Table 4 Calculated energy barriers[a] for the forward ($\Delta E_1^\ddagger$) and reverse ($\Delta E_2^\ddagger$) β-fragmentation reactions of (methoxy)thioacyl, (methylthio)acyl and (methylthio)thioacyl radicals (**12**–**14**), and imaginary frequencies (ν)[b] of transition structures **17**–**19**

Radical		$\Delta E_1^\ddagger$	$\Delta E_1^\ddagger$ + ZPE[c]	$\Delta E_2^\ddagger$	$\Delta E_2^\ddagger$ + ZPE[c]	ν
12	UHF/6-311G**	88.7	74.2	195.5	207.3	1155i
	MP2/6-311G**	77.3	64.6	180.7	191.9	1453i
	MP2/cc-pVDZ	76.0	63.8	181.4	193.0	1418i
	MP2/aug-cc-pVDZ	73.7	55.3	166.4	177.3	1455i
	QCISD/6-311G**//MP2/6-311G**	65.2	—	146.4	—	—
	CCSD(T)/6-311G**//MP2/6-311G**	58.3	—	140.7	—	—
	QCISD/cc-pVDZ//MP2/cc-pVDZ	63.0	—	147.4	—	—
	CCSD(T)/cc-pVDZ//MP2/cc-pVDZ	56.1	—	141.9	—	—
	QCISD/aug-cc-pVDZ//MP2/aug-cc-pVDZ	62.2	—	133.9	—	—
	CCSD(T)/aug-cc-pVDZ//MP2aug-cc-pVDZ	54.9	—	126.7	—	—
13	UHF/6-311G**	85.9	77.2	110.8	121.7	604i
	MP2/6-311G**	79.0	72.3	87.1	96.9	635i
	MP2/cc-pVDZ	75.8	69.0	89.9	100.0	630i
	MP2/aug-cc-pVDZ	75.7	69.0	79.6	88.5	622i
	QCISD/6-311G**//MP2/6-311G**	76.3	—	67.9	—	—
	CCSD(T)/6-311G**//MP2/6-311G**	69.7	—	63.6	—	—
	QCISD/cc-pVDZ//MP2/cc-pVDZ	70.0	—	70.1	—	—
	CCSD(T)/cc-pVDZ//MP2/cc-pVDZ	63.7	—	67.1	—	—
	QCISD/aug-cc-pVDZ//MP2/aug-cc-pVDZ	71.9	—	59.5	—	—
	CCSD(T)/aug-cc-pVDZ//MP2aug-cc-pVDZ	66.0	—	55.2	—	—
14	UHF/6-311G**	65.2	54.5	65.5	77.0	435i
	MP2/6-311G**	68.9	59.3	65.9	75.8	550i
	MP2/cc-pVDZ	66.8	58.0	69.5	80.1	552i
	MP2/aug-cc-pVDZ	70.4	61.4	62.2	71.5	551i
	QCISD/6-311G**//MP2/6-311G**	61.1	—	38.0	—	—
	CCSD(T)/6-311G**//MP2/6-311G**	55.2	—	35.8	—	—
	QCISD/cc-pVDZ//MP2/cc-pVDZ	58.0	—	40.8	—	—
	CCSD(T)/cc-pVDZ//MP2/cc-pVDZ	52.0	—	39.9	—	—
	QCISD/aug-cc-pVDZ//MP2/aug-cc-pVDZ	61.7	—	31.9	—	—
	CCSD(T)/aug-cc-pVDZ//MP2aug-cc-pVDZ	56.0	—	29.8	—	—

[a] Energies in kJ mol^{-1}. [b] Frequencies in cm^{-1}. [c] Zero-point vibrational energy correction.

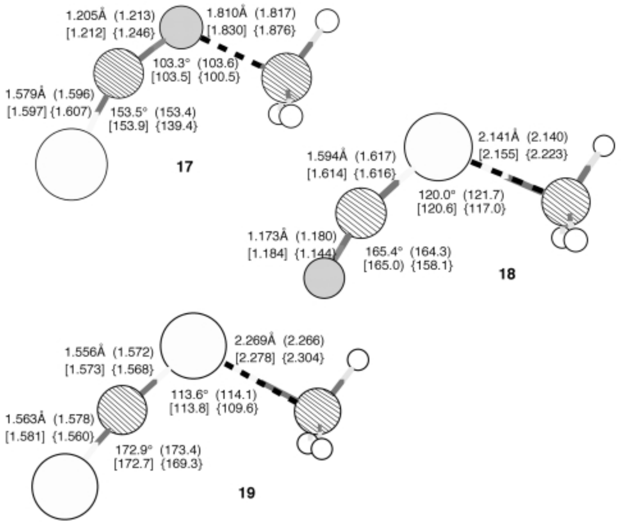

Fig. 4 MP2/6-311G** calculated structures of transition states **17**–**19**. (MP2/cc-pVDZ data in parentheses). [MP2/aug-cc-pVDZ data in square brackets]. {UHF/6-311G** data in curly brackets}.

decarboxylation of **2** (R = Me).|| Transition state distances (C_{TS}–O_{TS}) in **17** range from 1.810 Å (MP2/6-311G**) to 1.830 Å (MP2/aug-cc-pVDZ) while the corresponding distance in **12** is calculated to lie in the range: 1.813–1.856 Å at the same correlated levels of theory. In addition the C_{TS}–O_{TS}–C angle is calculated to be approximately 151–153° in both systems, suggesting similar levels of bond breaking/formation in both transition states. These similarities are somewhat reflected in the energy profiles for both reactions. Inspection of Table 4 reveals that the energy barriers for the forward reaction ($\Delta E_1^\ddagger$) for radical (**12**, R = Me) at correlated levels of theory range from 54.9 kJ mol^{-1} (CCSD(T)/aug-cc-pVDZ) to 77.3 kJ mol^{-1} (MP2/6-311G**). These values are to be compared with the barrier for the similar reaction of (**2**, R = Me) which is calculated to be approximately 15–20 kJ mol^{-1} higher than that calculated for **12**. At all levels of theory, both reactions are predicted to be significantly exothermic. These calculated differences in $\Delta E_1^\ddagger$ suggest that (alkoxy)thioacyl radicals **12** are likely to fragment with the loss of COS some two to three orders of magnitude more rapidly than their alkoxyacyl counterparts **2**, given similar log(A/s^{-1}) for each reaction. This prediction has significant synthetic potential.

If replacement of the carbonyl oxygen by sulfur in appropriate radical precursors is predicted to provide more synthetically useful radicals, the same cannot be said for the replacement of the other oxygen or both oxygens by sulfur. Inspection of the data provided in Fig. 4 and Table 4 reveals that β-fragmentation reactions of (methylthio)acyl and (methylthio)thioacyl radicals (**13**, **14**, R = Me) with the loss of COS and CS_2 respectively proceed *via* significantly "later" transition states than those associated with the similar reactions of **2** and **12** (R = Me). Transition state distances (C_{TS}–S_{TS}) in structures **18** and **19** (R = Me) are calculated to be 2.155 and 2.278 Å respectively at the highest level of theory. More significantly, the S_{TS}–C_{TS}–O or S_{TS}–C_{TS}–S angle is calculated to be approximately 165° (**18**) and 173° (**19**) at each correlated level of theory, strongly suggesting more complete formation of COS and CS_2 in the transition states (**18**, **19**, R = Me) than in the other transition states in this study.

These transition state geometries translate into significantly less exothermic character, with very similar values of $\Delta E_1^\ddagger$ and $\Delta E_2^\ddagger$ for the reaction of **18**, and endothermic reactions at all correlated levels of theory for **19**. Once again, the degree of

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|| Close inspection of Fig. 2 and 4 reveals opposite orientations of the methyl group. We have explored the energy barrier for the rotation of the methyl group in **16** (R = Me) and find it to be insignificant at all levels of theory. The methyl group in **16** (R = Me) is effectively in free rotation during the course of decarboxylation.

electron correlation has a profound effect on the reactions in question. Indeed, inspection of the data for the reaction involving **13** (R = Me) reveals that as the degree of correlation is increased, the reaction is predicted to cross from exothermic to one which is clearly endothermic. For example, values for $\Delta E_1^‡$ and $\Delta E_2^‡$ are calculated to be 79.0 and 87.1 kJ mol^{-1} respectively at the MP2/6-311G** level of theory, while the analogous numbers at the CCSD(T)/aug-cc-pVDZ//MP2/aug-cc-pVDZ level are calculated to be 66.0 and 55.2 kJ mol^{-1} respectively. In any case, the similarity between the two energy barriers in question would be expected to lead to an equilibrium between the (methylthio)acyl radical (**13**, R = Me) and the methyl radical and COS, a situation which would not be suitable in any synthetic application.

Inspection of the analogous data for the (methylthio)thioacyl radical (**14**, R = Me) presented in Table 4 reveals that as the level of theory is improved, the β-fragmentation reaction of interest becomes more endothermic; at the highest level of theory in this study, the barriers for the forward and reverse reactions ($\Delta E_1^‡$, $\Delta E_2^‡$, Scheme 3) are calculated to be 56.0 and 29.8 kJ mol^{-1} respectively. The data strongly suggest that the methyl radical prefers to react with carbon disulfide to form the (methylthio)thioacyl radical (**14**, R = Me). This outcome is not unexpected as it is well established that radicals add effectively to the sulfur terminus of thiocarbonyl containing radical precursors such as dithio- and thionoformates.[22]

Conclusion

The potential energy surfaces for the β-fragmentation of methoxyacyl, ethoxyacyl, isopropoxyacyl and *tert*-butoxyacyl radicals **2** have been examined by high-level *ab initio* molecular orbital calculations. The results obtained depend strongly on the level of correlation included in the calculation and, to a lesser extent, the quality of the basis set employed. At the highest level of theory (CCSD(T)/aug-cc-pVDZ//MP2/aug-cc-pVDZ), energy barriers ($\Delta E_1^‡$, $\Delta E_2^‡$) for the forward and reverse reactions involving the methoxyacyl radical are calculated to be 70.4 and 142.1 kJ mol^{-1} respectively, indicating a strongly exothermic reaction. When the data for the primary, secondary and tertiary alkyl substituted radicals **2** are compared at the same level of theory (CCSD(T)/6-311G**//MP2/6-311G**), relative reaction rates of 1 : 28 : 442 are calculated from energy barriers of 72.8, 67.0 and 60.3 kJ mol^{-1} respectively . These data lead us to suggest that the relative reactivity of secondary alkoxyacyl radicals extrapolated from the work of Pfenninger needs to be more closely examined.

To aid in the design of new radical precursors, the analogous β-fragmentation reactions of (methoxy)thioacyl, (methylthio)acyl and (methylthio)thioacyl (**17**–**19**) were also examined. We conclude that (alkoxy)thioacyl radicals (**17**) may provide superior properties as alkyl radical precursors than alkoxyacyl radicals (**2**), but that radicals **18** and **19** are unlikely to be synthetically useful. As a consequence of these calculations, we are currently exploring the use of (phenyltelluro)thionoformates[12] (**20**) as radical precursors.

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