Carboxyketenes, methyleneketenes, vinylketenes, oxetanediones, ynols, and ylidic ketenes from Meldrum's acid derivatives†

Lisa George,[a] Ming Wah Wong[b] and Curt Wentrup*[a]

Received 16th February 2007, Accepted 9th March 2007
First published as an Advance Article on the web 26th March 2007
DOI: 10.1039/b702518a

It has been documented that 5-methylene-Meldrum's acid derivatives (**1**, **12**) and their enols (**2**, **13**) can undergo fragmentation to malonic anhydrides (**4**, **19**), carboxyketenes (**3**, **16**) and methyleneketene (**5**, **21**, **35**), as well as cyclization to pyrrole-3-one and thiophene-3-one derivatives **11a,b** (but not furan-3-ones **11c**) under the conditions of flash vacuum thermolysis (FVT). Here we report theoretical calculations at the B3LYP/6–311 + G(2d, p) and G3X(MP2) levels of theory, which allow a rationalization of these observations. The calculated activation barriers for these reactions are all of the order of 37–40 kcal mol^{-1}. Hydroxyacetylenes (alkynols) **7** are sometimes observed in FVT reactions of Meldrum's acid derivatives. Their formation is now explained as an FVT reaction of the carboxyketenes (*e.g.* **3** → **7** and **32** → **34**) with a calculated activation barrier of *ca.* 39 kcal mol^{-1}. The cyclization of alkylamino- and alkylthio-substituted methyleneketenes **8a,b** to pyrrolone and thiophenone derivatives **11a,b** is found to be energetically very feasible under FVT conditions, and even in some cases in solution, with activation barriers of 33–39 kcal mol^{-1}. This cyclization takes place *via* the fleeting ylidic ketene intermediates **9a,b**, **25**, and **37a,b**, which exist in very shallow energy minima. Alkoxy-substituted methyleneketenes **8c** do not cyclize in this manner due to the rather high, but in principle not impossible, activation barriers for the initial 1,4-H shifts to the ylidic ketenes **9c** (*ca.* 47 kcal mol^{-1}).

Introduction

Derivatives of Meldrum's acid (1,3-dioxane-4,6-dione) are excellent precursors for the production of a variety of ketenes, propadienones, iminopropadienones, and other reactive molecules by flash vacuum thermolysis (FVT).[1] It has been demonstrated that simple 5-alkylidene derivatives **1** of Meldrum's acid can interconvert with enol tautomers **2** in solution.[2a] In FVT reactions, the enol tautomers may be populated by evaporation of the solids or by tautomerization on the hot surface of the quartz thermolysis tube. A 6-electron cycloreversion reaction of the retro-Diels Alder type causes fragmentation of **2** to carboxyketenes **3** (Scheme 1).[2] Fragmentation of the keto forms **1** leads to methyleneketenes **5** directly. In one case (R-R′ = 1-methylpyrrolidin-2-ylidene) the anhydride 3-methyleneoxetane-2,4-dione **4** was isolable.[3] The fragile oxetane **4**, in turn, eliminates CO_2 to provide a second route to methyleneketenes **5**. This route (**3** → **4** → **5**) is the major reaction channel for vinyl(carboxy)ketenes.[2] However, for phenyl(carboxy)ketene this reaction is less likely, as the cyclization to **4** would destroy the benzene resonance. Therefore, phenyl(carboxy)ketene **3** decarboxylates to phenylketene **6** instead.[2e] There has been much discussion in the literature[2,4] about the direct rearrangement of methyleneketenes **5** to vinylketenes **6**, but since this constitutes a 1,3-H shift, it is expected to have a high activation barrier. There is strong experimental evidence that this reaction (**5** → **6**) does occur in alkylmethyleneletenes, but it requires forcing FVT conditions (*ca.* 800 °C).[2b]

Weak signals ascribed to vinylethynols **7** have also been observed experimentally by low temperature IR spectroscopy, and their role as precursors of vinylketenes **6** was discussed.[2b] However, the latter reaction (**7** → **6**) is again a 1,3-H shift, which will have a high activation barrier unless the reaction takes place as a surface-catalyzed reaction on the hot quartz surface. Carboxyketenes **3** constitute a more promising source of the ethynols **7** by means of a pseudopericyclic 1,5-H shift (Scheme 1).

Methyleneketenes **8** having an RX substituent (X = NR″ or S; Scheme 1) have been postulated to undergo an intriguing 1,4-H shift from the CH_2R' group (R′ = H or alkyl) to furnish transient ylidic ketenes **9**, which, however, have never been observed directly. The evidence for the existence of **9** is the isolation of their cyclization products **11** when X = R′N,[1c,2d,3,5] or S[1c,6] (but not[2d] when X = O). Here, we examine the reactions described in Scheme 1 computationally.

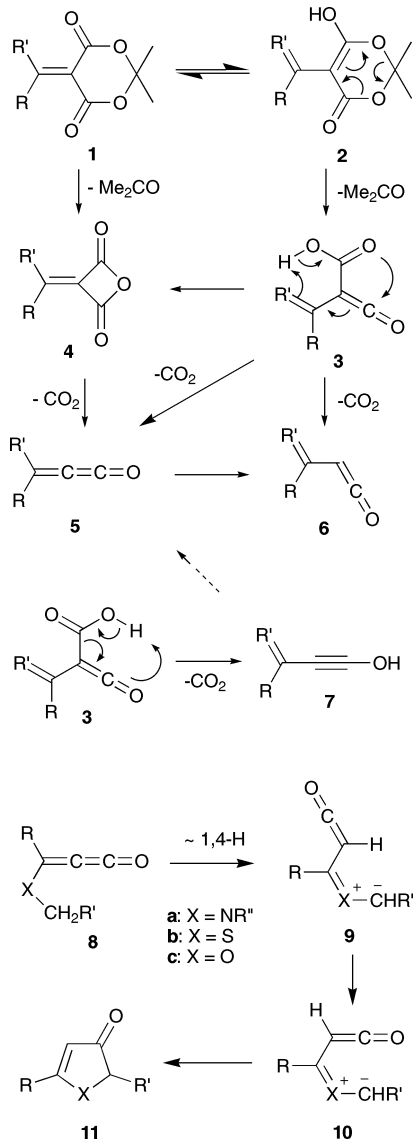
Results and discussion

Computational methods

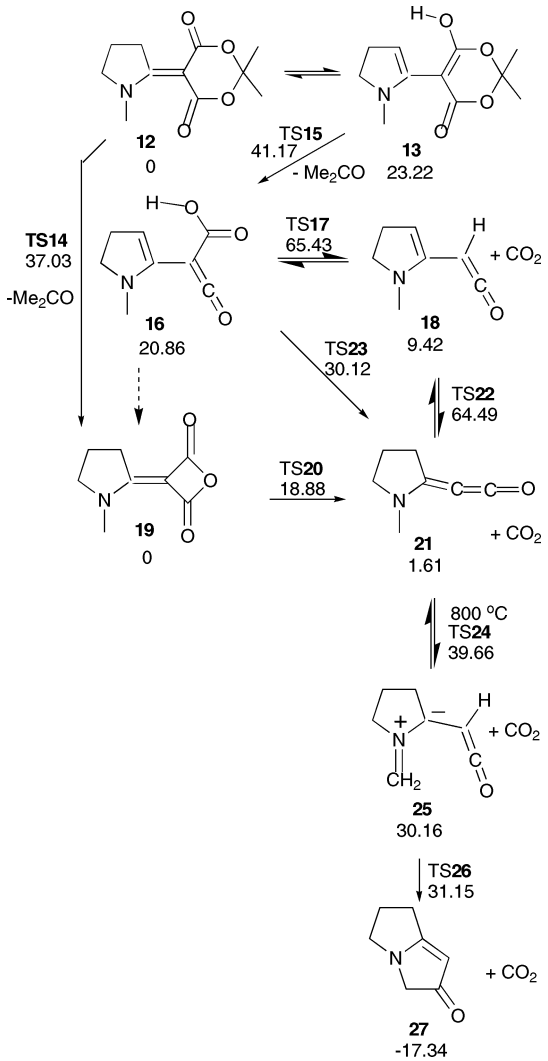
Calculations for the pyrrolidinylidene derivatives described in Scheme 2 were carried out the B3LYP/6–311 + G(2d,p) level of theory,[6] which has been shown to provide adequate agreement with experimental data in many instances.[7] Energies of ground and transition state structures are *ca.* 5–9 kcal mol^{-1} lower at this level than at the very popular B3LYP/6–31G* level (see table of relative energies of all calculated species in the ESI†). Some transition

[a]*Chemistry Building, School of Molecular and Microbial Sciences, The University of Queensland, Brisbane, Qld, 4072, Australia. E-mail: wentrup@uq.edu.au*
[b]*Department of Chemistry, National University of Singapore, 3 Science Drive, Singapore, 117543, Singapore. E-mail: chmwmw@nus.edu.sg*

† Electronic supplementary information (ESI) available: Computational data for all calculated species. IRC curves for TS **22**, TS **24** and TS **29**. See DOI: 10.1039/b702518a



Scheme 1



Scheme 2 Reactions of the pyrrolidine derivatives. Compound numbers in bold; relative energies of ground and transition state (TS) structures in kcal mol^{-1} at the B3LYP/6–311 + G(2d,p) level in Arabic numerals.

state energies may still be too high at the B3LYP/6–311 + G(2d,p) level. All energies were corrected for zero point vibrational energies (ZPVE), and all transition state (TS) structures were characterized by having one imaginary vibrational frequency. The identities of several key transition states were confirmed by intrinsic reaction coordinate (IRC) calculations. Examples are shown in Fig. S1–S3 in the ESI.†

The structures and energies of the species related to the formation and cyclization of the ylidic ketenes **9** (**37**) (X = NH, S, O; Schemes 1 and 3) were examined using the G3X(MP2) theory.[8] This composite method corresponds effectively to QCISD(T)/G3XL//B3LYP/6–31G(2df,p) energy calculations together with zero-point vibrational and isogyric corrections. The G3X(MP2) theory represents a modification of the G3(MP2) theory with three important changes: (1) B3LYP/6–31G(2df,p) geometry, (2) B3LYP/6–31G(2df,p) zero-point energy, and (3) addition of a *g* polarization function to the G3Large basis set for the second-row atoms at the Hartree–Fock level. All three features are particularly important for the proper description of the sulfur-containing species examined in this publication. For several investigated species, a charge density analysis was performed using the natural bond orbital (NBO) approach[9] based on the B3LYP/6–31G(2df,p) wavefunction. All calculations were performed using the GAUSSIAN 03 suite of programs.[6]

Reactions

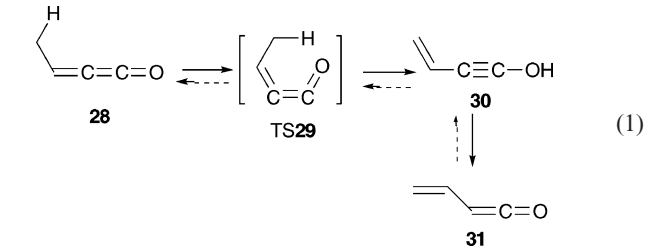
The reactions of the pyrrolidinylidene derivative[3] **12** of Meldrum's acid are summarized in Scheme 2 together with the calculated energies of ground and transition state structures at the B3LYP/6–311 + G(2d,p) level of theory. The enol tautomer **13** is considerably higher in energy (23 kcal mol^{-1}) than the keto form **12**, but it would be readily accessible in FVT reactions, and there is experimental evidence for the involvement of enols of alkylidene-Meldrum's acids in solution.[2a] Loss of acetone from the keto-form of Meldrum's acid **12** affords the isolable malonic anhydride (oxetanedione) **19** *via* an activation barrier TS **14** of 37 kcal mol^{-1}. **19** was characterized by IR and NMR spectroscopy.[3] Loss of acetone from the enol **13** leads to carboxyketene **16** *via* a transition

state TS **15**, which lies *ca.* 18 kcal mol^{-1} above **13** (41 kcal mol^{-1} above the keto-form **12**). The reaction **13** → **16** is slightly exothermic. Carboxyketene **16** has not actually been observed in this particular FVT reaction, but many examples of the formation of carboxyketenes of this type have been observed in analogous reactions.[2] Oxetane **19** undergoes easy loss of CO_2 to yield the methyleneketene **21**. The reaction takes place at room temperature, and both **21** and the CO_2 formed were observed by ^{13}C NMR spectroscopy.[3] In good agreement with this observation, the calculated activation barrier for this process is *ca.* 19 kcal mol^{-1} *via* TS **20** (drawings of the calculated transition structures are shown in the ESI†). There may be a second route to oxetane **19** from carboxyketene **16** by an attractive pseudopericyclic cyclization accompanied by a 1,5-H shift, but a transition state for this cyclization (**16** to **19**) was not located, since **16** decarboxylated directly to **21** with an activation energy of only *ca.* 12 kcal mol^{-1} *via* TS **23**. This low barrier explains the difficulty of observing **16** in this FVT reaction. Furthermore, carboxyketene **16** lies *ca.* 21 kcal mol^{-1} above the isolable oxetane **19**. Carboxyketene **16** could also have been thought to decarboxylate to vinylketene **18**, but this compound has a higher energy than both **19** and **21** and was not, in fact, observed experimentally.[3] The calculated barrier for this decarboxylative 1,3-shift **16** → TS **17** → **18** is *ca.* 65 kcal mol^{-1}. Vinylketenes have, however, been observed in other FVT reactions of alkylidene-Meldrum's acid derivatives under forcing conditions,[2,4] and in agreement with this, we find a high activation barrier (*ca.* 64 kcal mol^{-1}) for the conversion of methyleneketene **21** to the *higher energy* vinylketene **18**. The high barrier can be ascribed to the reaction being a 1,3-H shift, taking place *via* a 4-membered cyclic TS **22**.

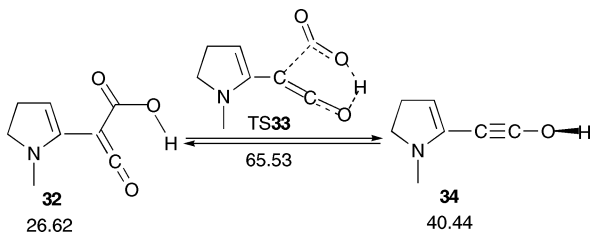
Up to this point, the two experimentally observed species, **19** and **21**, have the lowest relative energies, 0 and 1.6 kcal mol^{-1}, respectively. Higher temperature is needed for further reaction to occur. On FVT at 800 °C the otherwise remarkably stable methyleneketene **21** undergoes an intriguing rearrangement[3] to **27**, postulated to proceed by a 1,4-H shift to generate the transient ylidic ketene **25** *via* the TS **26**. Ylide **25** exists in a shallow minimum 29 kcal mol^{-1} above methyleneketene **21**, with only a 1 kcal mol^{-1} barrier to cyclization to the final FVT product **27**, which is the global minimum. This being the case, it is not surprising that all attempts to observe ylidic ketenes of type **25** have failed,[1b,5] and the 1 kcal mol^{-1} computed barrier is hardly of any significance at the high temperature of the reaction. The ylidic ketenes will be examined in more detail using G3X(MP2) calculations below.

Hydroxyacetylenes

There is strong infrared spectroscopic evidence for the formation of small amounts of hydroxyacetylenes **7** in some reactions of alkylidene-Meldrum's acids.[2b] The possible formation of ynols **30** from alkylmethyleneketenes **28** by a formally allowed 1,5-H shift is endothermic by *ca.* 21 kcal mol^{-1} and requires a highly strained transition structure TS **29** (eqn (1)) and an activation barrier of the order of 77 kcal mol^{-1} (the reactions in eqn (1) were examined at the G2(MP2) level, as a transition state could not be located using B3LYP calculations). The formally 'forbidden' 1,3-H shift from ynol **30** to vinylketene **31** (eqn (1)) also has a very high activation barrier of *ca.* 109 kcal mol^{-1}, although it is highly exothermic (by *ca.* 34 kcal mol^{-1}). Therefore, the formation[2b] of hydroxyacetylenes is not likely to take place *via* eqn (1). A much more appealing route to hydroxyacetylenes proceeds from the *s-E* conformers of carboxyketenes, *e.g.* **3** → **7** (Scheme 1) and **32** → **34** (eqn (2)). This reaction was examined at the B3LYP/6–311 + G(2d,p) level. The reaction *via* TS **33** is endothermic by 14 kcal mol^{-1} and has a barrier of 39 kcal mol^{-1} (see IRC curve in the ESI†). This is a feasible reaction under FVT conditions and explains the formation of small quantities of alkynols.[2] Once formed and isolated at low temperatures, the exothermic isomerization of alkynols to vinylketenes or methyleneketenes can take place by intermolecular H-transfer in the solid state or on the surface of the quartz thermolysis tube.



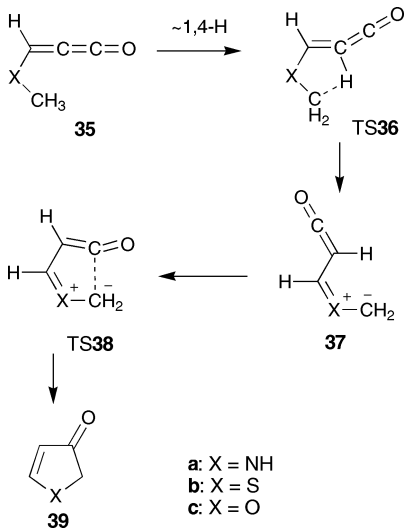
(1)



(2)

Ylidic ketenes (X = NH, S, O)

High-level G3X(MP2) calculations were used to examine the energy profiles for cyclization of the three types of methyleneketenes $CH_3XC(H)=C=C=O$ **35a–c** (Scheme 3). The calculated relative energies of the various equilibrium structures and transition states are summarized in Table 1. Very similar relative energies were obtained for the homologous series of *C*-methyl-methyleneketenes $CH_3XC(CH_3)=C=C=O$ and their isomers. As expected, the



Scheme 3 Cyclization of methyleneketenes $CH_3XC(H)=C=C=O$.

Table 1 Calculated relative energies (G3X(MP2); kcal mol^{-1}) of methyleneketenes $CH_3XC(H)=C=C=O$ **35a–c** and related isomeric species

Species	X = NH (**a**)	X = S (**b**)	X = O (**c**)
Methyleneketene **35**	0.0	0.0	0.0
1,4-H shift TS **36**	39.1	32.9	47.4
Ylidic ketene **37**	24.6	21.8	38.1
Ring closure TS **38**	25.5	22.8	38.8
Five-membered ring **39**	−26.5	−33.8	−30.2

cyclization of the methyleneketenes is strongly exothermic in all cases (Table 1). The formation of the ylidic ketene **37** is the rate-determining step in the overall cyclization reaction. The CH_3NH-substituted methyleneketene **35a** has a calculated barrier of 39 kcal mol^{-1} for the 1,4-H shift to the ylidic ketene **37a**. This value is virtually identical with that calculated for the pyrrolidine series in Scheme 2, *i.e.* **21** → **25**, at the B3LYP/6–311 + G(2d,p) level. In the alkylthiomethyleneketene series (X = S), the ylidic ketene **37b** is *ca.* 22 kcal mol^{-1} less stable than the methyleneketene **35b**, and the 1,4-H shift TS **36b** lies at a moderate 33 kcal mol^{-1} above **35b**. In the oxygen series, in contrast, the ylidic ketene intermediate **37c** is significantly higher in energy (*ca.* 38 kcal mol^{-1}), and the 1,4-H shift transition state TS **36c** is substantially higher (*ca.* 47 kcal mol^{-1}). The trend of the activation barriers (S < NH < O) follows the stabilities of the ylidic ketenes (Table 1), and the relative stabilities of these ylides is related inversely to the electronegativity of X. Nitrogen and sulfur, being less electronegative than oxygen, are apparently better able to stabilize the ylides, although other factors may also be of importance. This simple argument is supported by the calculated charge distributions in the ylides, based on the NBO analysis. The calculated NBO charges of the X atoms are +0.72, +0.03 and −0.37 for X = S, NH and O, respectively. There are two possible conformations of the ylidic ketenes: s-*trans* and s-*cis*. The s-*cis* form is slightly more favourable, by ∼1 kcal mol^{-1} in all 3 cases. The ring closing reactions of the ylidic ketene intermediates to the five-membered rings **39** *via* transition state TS **38** is predicted to be extremely facile. In all cases, the barrier height is only about 1 kcal mol^{-1}. Not surprisingly, the geometry of TS **38** resembles the structure of the ylidic ketene **37** (see Fig. 1). Given this very low activation barrier for ring closure, it is unlikely that the ylides will be observable. Thus, in agreement with experimental observations,[1b,3,5] the rearrangement to ylidic ketenes **37** and consequently cyclization to pyrrolones and thiophenones **39** is feasible for the *N*- and *S*-substituted methyleneketenes, but more difficult, although in principle not impossible, for the *O*-substituted analogs. It is just that the alkoxymethyleneketenes **35c** are thermodynamically quite stable, and hence isolable, and they have high activation barriers towards further reaction.

Conclusion

In conclusion, the formation of the observable FVT products, malonic anhydride **19** and methyleneketene **21**, is readily explained by means of fragmentation reactions of the Meldrum's acid derivative **12** and its enol **13** with activation energies of *ca.* 37 and 41 kcal mol^{-1}, respectively. Carboxyketenes such as **16** have

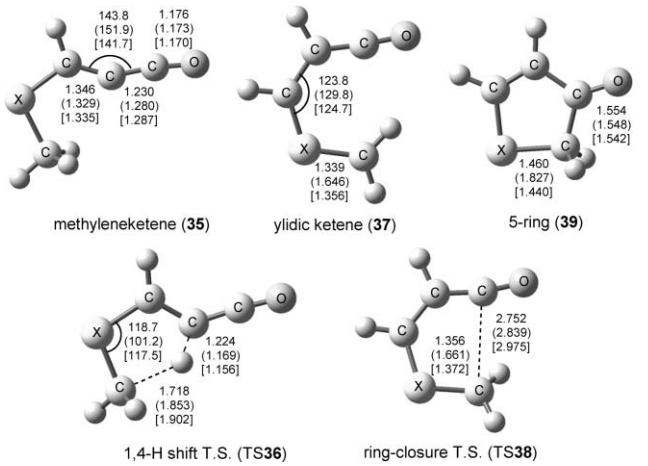


Fig. 1 Calculated geometries (B3LYP/6–31G(2df,p)) of the isomers and transition states of methyleneketenes $CH_3XC(H)=C=C=O$ **35a**, **35b** (in parentheses) and **35c** [in brackets] (G3X(MP2)). Selected bond lengths in Å and angles in degrees.

been observed in several other FVT reactions of Meldrum's acid derivatives.[2] The formation of malonic anhydrides, such as **19**, as well as methyleneketenes, such as **21**, requires the possibility of accommodating the exocyclic C=C double bond. This is a much less likely process in phenyl-Meldrum's acid and not possible in the unsubstituted Meldrum's acid; in these compounds, therefore, the carboxyketenes analogous to **16** decarboxylate directly to vinylketenes of the type **18**.[2e]

The formation of hydroxyacetylenes (alkynols)[2b] **7** (and likewise **30** and **34**) in FVT reactions of Meldrum's acid derivatives is now explained as an FVT reaction of the carboxyketenes **3** → **7** (Scheme 1) and **32** → **34** (eqn (2)). This reaction has a low enough activation barrier, *ca.* 39 kcal mol^{-1}, to be feasible under FVT conditions, competitive with the other observed reactions, and much easier than the formation of vinylketenes **18**.

The cyclization of alkylamino- and alkylthio-substituted methyleneketenes **8a,b**, **21**, and **35a,b** to pyrrolone and thiophenone derivatives **11a,b**, **27**, and **39a,b** (Schemes 1–3), which has been observed experimentally in several methyleneketenes,[3,5] is energetically very feasible under FVT conditions, and the activation barriers are low enough (*ca.* 33 kcal mol^{-1}) that the reaction could even take place in solution in some cases when X = S. It is a stepwise process taking place *via* the ylidic ketene intermediates **9a,b**, **25**, and **37a,b**, which exist in very shallow energy minima, and the formation of these ylides is the rate-determining step. The reluctance of alkoxy-substituted methyleneketenes **8c** and **35c** to cyclize in this manner is due to the relative stability of these compounds and the rather high, but in principle not impossible, activation barriers for the initial 1,4-H shifts to the ylidic ketenes **9c** and **37c**.

Acknowledgements

This work was supported by the Australian Research Council and by the Centre for Computational Molecular Science at the University of Queensland.

References

1 (*a*) G. Kollenz, S. Ebner, Acylketenes, in *Science of Synthesis*, Thieme, Stuttgart, Germany, 2006, vol. 23/9, p. 271; (*b*) A. El-Aal, M. Gaber and H. McNab, *Synthesis*, 2001, 2059; (*c*) G. I. Yranzo, J. Elguero, R. Flammang and C. Wentrup, *Eur. J. Org. Chem.*, 2001, 2209; (*d*) C. Wentrup, W. Heilmayer and G. Kollenz, *Synthesis*, 1994, 1220.

2 (*a*) C. Wentrup, G. Gross, H.-M. Berstermann and P. Lorencak, *J. Org. Chem.*, 1985, **50**, 2877; (*b*) C. Wentrup and P. Lorencak, *J. Am. Chem. Soc.*, 1988, **110**, 1880; (*c*) C. Wentrup, R. Blanch, H. Briehl and G. Gross, *J. Am. Chem. Soc.*, 1988, **110**, 1874; (*d*) H. Bibas, C. O. Kappe, M. W. Wong and C. Wentrup, *J. Chem. Soc., Perkin Trans. 2*, 1998, 493; (*e*) L. George, R. N. Veedu, H. Sheibani, A. A. Taherpour, R. Flammang and C. Wentrup, *J. Org. Chem.*, 2007, **72**, 1399.

3 P. Lorencak, J. C. Pommelet, J. Chuche and C. Wentrup, *J. Chem. Soc., Chem. Commun.*, 1986, 369.

4 S. Mohmand, T. Hirabayashi and H Bock, *Chem. Ber.*, 1981, **114**, 2609.

5 (*a*) C. L. Hickson, E. M. Keith, J. C. Martin, H. McNab, L. C. Monahan and M. D. Walkinshaw, *J. Chem. Soc., Perkin Trans. 1*, 1986, 1465; (*b*) H. McNab and L. C. Monahan, *J. Chem. Soc., Perkin Trans. 1*, 1988, 863; (*c*) H. McNab and L. C. Monahan, *J. Chem. Soc., Perkin Trans. 1*, 1988, 869; (*d*) J. C. Pommelet, H. Dhimane, J. Chuche, J.-P. Celerier, M. Haddad and G. Lhommet, *J. Org. Chem.*, 1988, **53**, 5680; (*e*) H. McNab and M. Morrow, *ARKIVOC*, 2002, **VIII**, 125.

6 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez and J. A. Pople, *Gaussian 03*, Gaussian, Inc., Pittsburgh, PA, 2003.

7 T. Bally and W. T. Borden, *Reviews in Computational Chemistry*, ed. K. B. Lipkowitz and D. B. Boyd, Wiley, New York, 1999, pp. 1–97.

8 L. A. Curtiss, P. C. Redfern, K. Raghavachari and J. A. Pople, *J. Chem. Phys.*, 2001, **114**, 108.

9 A. E. Reed, L. A. Curtiss and F. Weinhold, *Chem. Rev.*, 1988, **88**, 899.