Synthesis of α-Cyano Carbonyl Compounds by Flash Vacuum Thermolysis of (Alkylamino)methylene Derivatives of Meldrum's Acid. Evidence for Facile 1,3-Shifts of Alkylamino and Alkylthio Groups in Imidoylketene Intermediates

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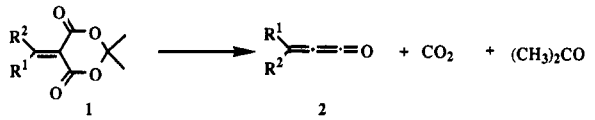
The syntheses and flash vacuum thermolyses of 5-[(alkylamino)methylene]-2,2-dimethyl-1,3-dioxane-4,6-diones (Meldrum's acid derivatives) **13a–i** are described. Thermolysis of **13a** as well as of ethyl 3-(*tert*-butylamino)acrylate (**22**) gives a tautomeric mixture of cyanoacetaldehyde (**14**) and 3-hydroxypropenenitrile (**15**). Thermolysis of **13b** gives iminoacrolein **26** and not cyanoacetone (**29**). Thermolysis of **13c,d** gives *S*-methyl cyanothioacetate (**30**), and **13f–h** give cyanoacetamides **31** in high yields. 2-Cyanopent-4-enoic acid derivatives **32** are obtained from Meldrum's acids **13e,i**. The results are discussed in terms of facile 1,3-shifts of methylthio and alkylamino groups in imidoylketenes, interconverting imidoylketenes and acylketene imines.

Introduction

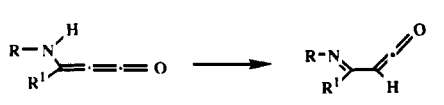
The generation of methyleneketenes (**2**) by thermal decomposition of Meldrum's acid derivatives (**1**) (5-alkylidene-2,2-dimethyl-1,3-dioxane-4,6-diones) has been the subject of several recent studies.[2] It is particularly noteworthy that alkyl- and arylmethyleneketenes are highly reactive species which can only be preserved at low temperatures, typically dimerizing above ca. −100 °C. In contrast, heteroatom-substituted methyleneketenes (**2**, R^1 and/or R^2 = OR, NR_2, or SR) can be extraordinarily stable, in some cases permitting direct spectroscopic observation at room temperature.[3,4]



1 **2**

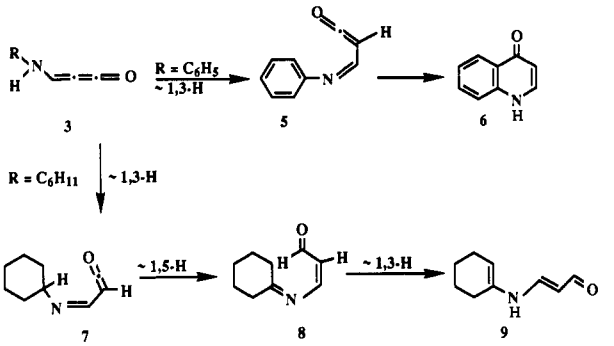
Intramolecular reactions of a number of methyleneketenes have been reported.[2-6] The increased kinetic stability of heteroatom-substituted methyleneketenes also makes them amenable to intermolecular cycloaddition chemistry.[7]

Methyleneketenes **3** carrying a primary[8] or secondary[9] amino substituent are not kinetically stable but exist in tautomeric equilibrium with imidoylketenes **4** in the gas phase.



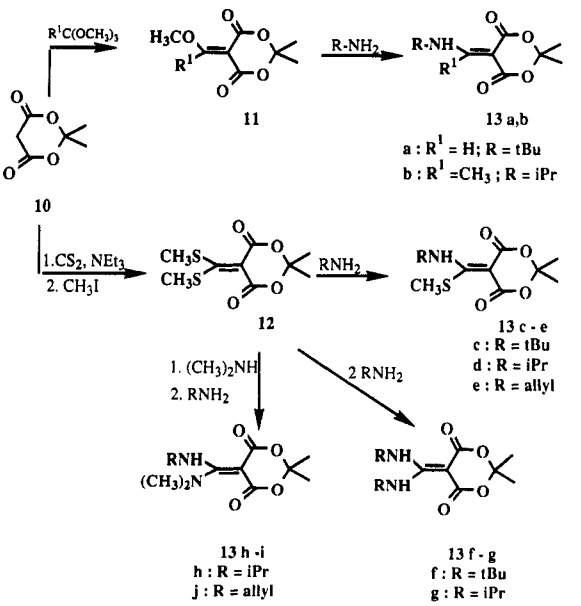
3 **4**

Scheme I



3 **5** **6** **7** **8** **9**

Scheme II



10 **11** **13 a,b** **12** **13 c - e** **13 h -i** **13 f - g**

(1) (a) Thèse de Doctorat, 1990. (b) Université de Reims. (c) Netsch, K.-P. Ph.D. Thesis, University of Marburg, 1985. (d) Lorenčak, P. Ph.D. Thesis, University of Marburg, 1985. Present address: BASF AG, Ludwigshafen, Germany. (e) University of Queensland.

(2) (a) Brown, R. F. C.; Eastwood, F. W.; Harrington, K. J. *Aust. J. Chem.* **1974**, *27*, 2373. (b) Brown, R. F. C.; Eastwood, F. W. In *The Chemistry of Ketenes, Allenes and Related Compounds*; Patai, S., Ed.; Wiley-Interscience: Chichester, England, 1980; p 757 ff. (c) McNab, H. *Chem. Soc. Rev.* **1978**, *7*, 345. McNab, H.; Monahan, L. C. *J. Chem. Soc., Perkin Trans. 1* **1988**, 863, 869, and references therein. (d) Wentrup, C.; Gross, G.; Berstermann, H.-M.; Lorenčak, P. *J. Org. Chem.* **1985**, *50*, 2877. (e) Wentrup, C.; Lorenčak, P. *J. Am. Chem. Soc.* **1988**, *110*, 1880 and references therein.

(3) Lorenčak, P.; Pommelet, J. C.; Chuche, J.; Wentrup, C. *J. Chem. Soc., Chem. Commun.* **1986**, 369.

(4) Ben Cheikh, A.; Dhimane, H.; Pommelet, J. C.; Chuche, J. *Tetrahedron Lett.* **1988**, *29*, 5919.

(5) (a) Pommelet, J. C.; Dhimane, H.; Chuche, J.; Célérier, J. P.; Haddad, M.; Lhommet, G. *J. Org. Chem.* **1989**, *53*, 5680. (b) Célérier, J. P.; Haddad, M.; Saliou, C.; Lhommet, G.; Dhimane, H.; Pommelet, J. C.; Chuche, J. *Tetrahedron* **1989**, *45*, 6161.

(6) Grandjean, D.; Dhimane, H.; Pommelet, J. C.; Chuche, J. *Bull. Soc. Chim. Fr.* **1989**, 657.

(7) Ben Cheikh, A.; Pommelet, J. C.; Chuche, J. *J. Chem. Soc., Chem. Commun.* **1990**, 615.

(8) Wentrup, C.; Briehl, H.; Lorenčak, P.; Vogelbacher, U. J.; Winter, H.-W.; Maquestiau, A.; Flammang, R. *J. Am. Chem. Soc.* **1988**, *110*, 1337.

(9) Briehl, H.; Lukosch, A.; Wentrup, C. *J. Org. Chem.* **1984**, *49*, 2772.

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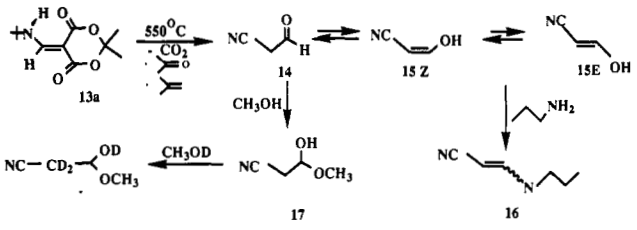
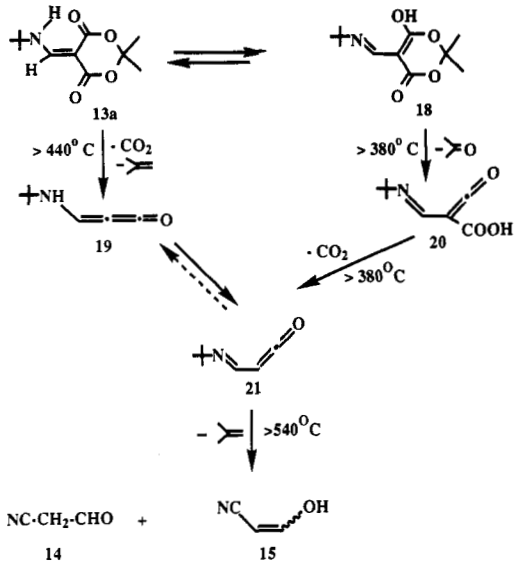
Scheme III



Scheme IV



In the aromatic series, the imidoylketenes **5** undergo efficient electrocyclization to give quinolones **6** (Scheme I).[9,10a] In the aliphatic series, derivatives of alkyl- and cycloalkylamines carrying an α-hydrogen atom have been shown by deuteration and low-temperature IR spectroscopy to undergo successive 1,3-, 1,5-, and 1,3-hydrogen shifts, as illustrated in Scheme I for the cyclohexyl case (**3** → **7** → **8** → **9**). The final products are enaminoacroleins of the type **9**.[9,10] Similar results have been obtained with imidoylketenes generated from ethyl β-aminoacrylates.[11]

We now describe the generation of a new series of imidoylketenes from Meldrum's acid derivatives, with strong evidence for the occurrence of a facile 1,3-shift interconverting imidoylketenes and acylketene imines (see eq 4).

Results and Discussion

1. Synthesis of Meldrum's Acid Derivatives. The monoaminomethylenedioxanediones **13a–b** were obtained by treatment of Meldrum's acid (**10**) with methyl orthoformate or orthoacetate, followed by displacement of the methoxy group in **11** by the appropriate amine[9,12] (Scheme II). The remaining derivatives **13c–i** were synthesized from bis(methylthio)methylene-Meldrum's acid **12**.[13] Treatment of **12** with 1 equiv of a primary amine gave the amino(methylthio)methylene derivatives **13c–e**. Treatment with 2 equiv of the primary amine gave the diaminomethylene-Meldrum's acids **13f–g**, and reaction with 1 equiv of dimethylamine followed by the primary amine (isopropyl- or allylamine) gave access to the mixed derivatives **13h–i** (Scheme II). Yields were generally in the range 60–90%.

2. Flash Vacuum Thermolysis of 13a. All the derivatives **13a–i** were thermolyzed at temperatures between 550 and 650 °C (10^{-4}–10^{-5} Torr). The pyrolyzates were collected on a cold finger cooled with liquid N_2 and previously coated with chloroform or methylene chloride and, after the completion of the experiments, warmed to room temperature and examined spectroscopically.

The derivatives of *tert*-butylamine **13a,c,f** and isopropylamine **13d,g** all behaved in the same manner, undergoing loss of CO_2 and acetone, as well as an alkene. Thus, **13a** (R = H) gave cyanoacetaldehyde (**14**), which, depending on the solvent, exists in tautomeric equilibrium with (*Z*/*E*)-3-hydroxypropenenitrile (**15**) (in CD_2Cl_2, **14**/**15** = 99:1; in $(CD_3)_2CO$, **14**/**15** = 1:4). The structures of **14** and **15** were determined by ^1H NMR (see the Experimental Section) and IR spectroscopy (**14**, 1735 cm^{-1}; **15**, 1680 cm^{-1} (typical of $\nu_{C=C}$ in enols[14])). Furthermore, the mixture of **14** and **15** was converted with propylamine into *N*-propylacrylonitrile (**16**),[15] and with methanol to the hemiacetal **17**.[16] The latter undergoes exchange of three hydrogen atoms with CH_3OD (Scheme III).

In order to obtain more detailed information on the intermediates involved, the products of thermolysis of **13a** were examined by IR spectroscopy at 77 K using an apparatus previously described.[9,17] At the lowest pyrolysis temperatures (380–440 °C) two ketenes were observed and interpreted as the carboxy(imidoyl)ketene **20** (2150 (m), 2500–3200 (m) cm^{-1}; stable to −75 °C on warm up) and the imidoylketene **21** (2120 (s) cm^{-1}; stable to −120 °C). At a pyrolysis temperature of 440 °C a third ketene started appearing (2080 (m) cm^{-1}; stable to −105 °C). The position of the ketene absorption below 2100 cm^{-1} identifies this species as a methyleneketene,[2e,9] assigned as compound **19** (Scheme IV).

In analogy with previous work[2d,e,8,9] the carboxyketene **20** is formed by elimination of acetone from the enol tautomer **18** of the starting material. Decarboxylation of **20** can give either **21** or **19**, but **19** can also be formed directly from **13a** by concerted elimination of acetone and CO_2. In the aminomethylene-Meldrum's acid series we often see imidoylketenes (here **21**) appearing *before* the methyleneketenes (here **19**),[8,18] whereas in the alkylidene-Meldrum's acid series the sequence carboxy(vinyl)ketene–methyleneketene–vinylketene has been established.[2e] In the higher temperature regime **19** is interconverting with **21**.

The signal due to the imidoylketene **21** was strong at pyrolysis temperatures up to ca. 500 °C and started decreasing at 540 °C. At the same time, the medium-strength signal due to **19** also decreased. At 800 °C both **21** and **19** had completely disappeared. Synchronous with the disappearance of **19** and **21** above 540 °C, new signals due to the end products **14** (2250 (m) cm^{-1}, stable at room temperature) and **15** (2200 (s) cm^{-1}) appeared, and these were the only products (apart from acetone) remaining in the end spectrum at room temperature from the 800 °C pyrolysis. Compounds **14** and **15** were identified by com-

(10) (a) Gordon, H. J.; Martin, J. C.; McNab, H. *J. Chem. Soc., Chem. Commun.* **1983**, 957. (b) Gordon, H. J.; Martin, J. C.; McNab, H. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2129.

(11) Maujean, A.; Marcy, G.; Chuche, J. *Tetrahedron Lett.* **1980**, *21*, 519.

(12) Bihlmayer, G. A.; Derflinger, G.; Derkosch, J.; Polansky, O. E. *Monatsh. Chem.* **1967**, *98*, 564.

(13) Huang, X.; Chen, B.-C. *Synthesis* **1986**, 967; **1987**, 481.

(14) Ripoll, J. L. *Nouv. J. Chim.* **1979**, *3*, 195.

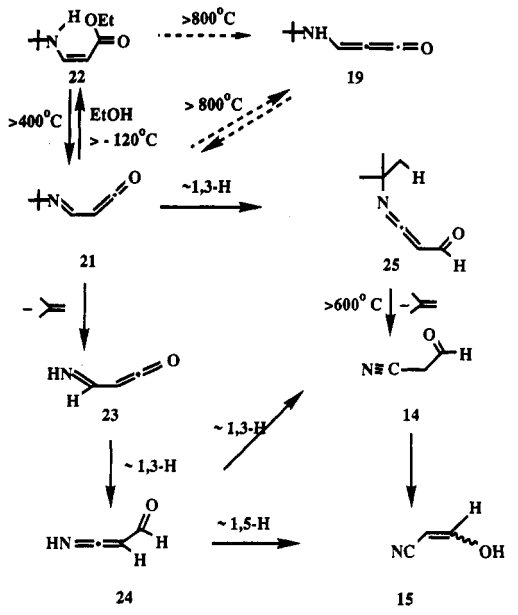
(15) Cf.: Hart, H. *Chem. Rev.* **1979**, *79*, 515.

(16) Cyanoacetaldehyde is considered a possible prebiotic molecule, and its reactivity in aqueous solution has been well studied: Raulin, F.; Toupance, G. *Bull. Soc. Chim. Fr.* **1975**, 188; **1976**, 667. Ferris, J. P.; Goldstein, G.; Beaulien, D. J. *J. Am. Chem. Soc.* **1970**, *92*, 6598.

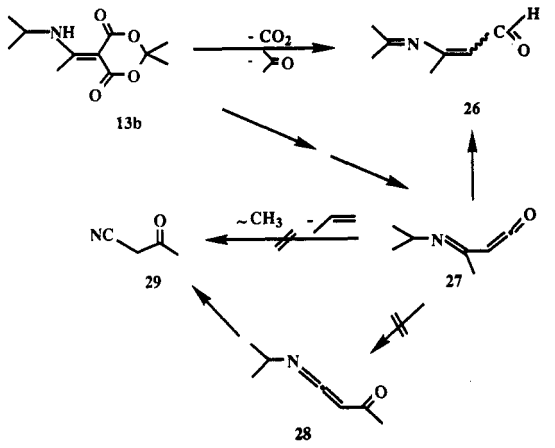
(17) Wentrup, C.; Blanch, R.; Briehl, H.; Gross, G. *J. Am. Chem. Soc.* **1988**, *110*, 1874.

(18) Lorenčak, P. Ph.D. Thesis, University of Marburg, 1985.

Scheme V



Scheme VI



parison with the material isolated from the preparative experiments described above.

For further elaboration of the reaction mechanism, an independent precursor of imidoylketene **21** was sought. β-Enamino esters have previously been shown to be useful precursors of imidoylketenes in several cases.[19-23] Accordingly, ethyl 3-(*N*-*tert*-butylamino)propenoate (**22**) was pyrolyzed at 400–850 °C with IR spectroscopy of the products at 77 K. Indeed, at pyrolysis temperatures of 400–600 °C only a single, strong absorption for ketene **21** was observed (2120 (s) cm^{-1}; stable to −120 °C). Compound **21** again reacted with the ethanol on warm up, so that the end spectrum at room temperature was virtually identical with that of the starting material **22** (Scheme V).

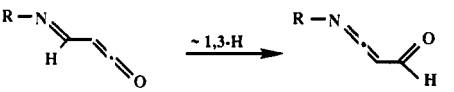
No evidence for the methyleneketene **19** was found below 800 °C, but at 800–850 °C a very weak band at 2080 cm^{-1} indicated that a small amount of **19** might be formed, possibly due to tautomerization of the imidoylketene **21**.

The main signal at 2120 cm^{-1} decreased rapidly in intensity above ca. 700 °C and had completely disappeared at 800 °C concomitant with the appearance of the end products **14** and **15**, which were again identified by comparison with the products of the preparative pyrolyses (vide supra).

Between 750 °C and 850 °C a further band appeared at 2030 cm^{-1} which was weak at 750 °C, medium at 800 °C, and very weak at 850 °C. This behavior indicates that it could be an intermediate between the imidoylketene **21** and the end products **14** and **15**. The position of the band is typical of ketene imines, and either **24** or **25** is a possible candidate.

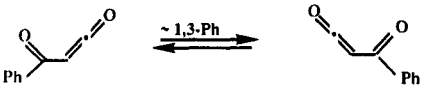
These results are summarized in Scheme V. There are two possible pathways from imidoylketene **21**, which differ only by the timing of isobutene elimination: (i) a 1,3-hydrogen shift in **21** to give a ketene imine **25**, followed by isobutene loss, or (ii) isobutene loss (**21** → **23**) followed by the 1,3-hydrogen shift (**23** → **24**). The timing of these events is unimportant for the present purposes, but it may be noted that **25** presents a more favorable 6-membered transition state for isobutene elimination in a reaction analogous to a retro-ene reaction. The elimination of isobutene from *N*-*tert*-butyl ketene imines is known to have activation enthalpies around 30 kcal/mol and negative entropies of activation.[24] Furthermore, in our previous work with imidoylketene **23**[8] we have never seen the formation of a ketene imine at 2030 cm^{-1}. Therefore, the most likely sequence of events in Scheme V is **21** → **25** → **14** + **15**.

At any rate, a 1,3-hydrogen shift converting an imidoylketene to a ketene imine is required (eq 1).



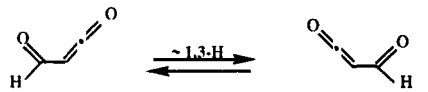
(1)

This reaction is analogous to the ketoketene–ketoketene rearrangement previously reported by us.[25]



(2)

The latter reaction (eq 2) is known[25] to possess a relatively high activation energy, taking place above 500 °C under flash vacuum pyrolysis conditions, and being complete at 700–800 °C. Recent ab initio calculations on the formylketene system (eq 3) indicate an activation barrier of ca. 39.5 kcal/mol.[26]



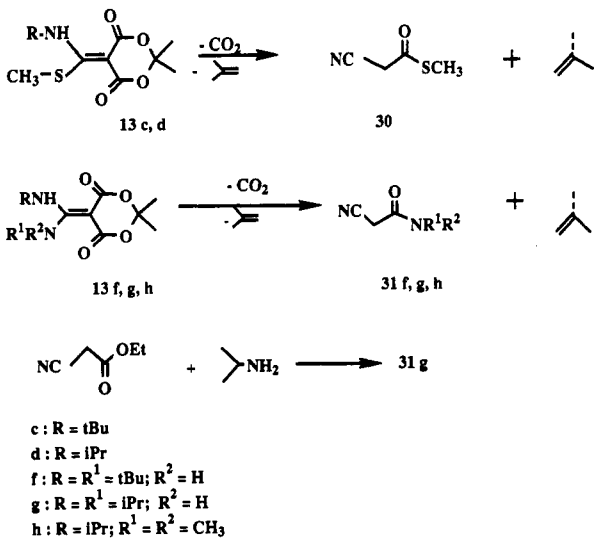
(3)

As will be shown below, this activation barrier can be dramatically reduced for other migrating groups.

3. Flash Vacuum Thermolysis of 13b. If the mode of decomposition of **13a** was complex, that of **13b** was straightforward, following the pattern established earlier. The iminoacrolein **26** was the only product obtained from the 600 °C reaction, and no trace of cyanoacetone (**29**) was detectable. Thus, the normal 1,3- and 1,5-hydrogen shifts

(19) Pale-Grosdemange, C.; Chuche, J. *Tetrahedron* **1989**, *45*, 3397.
(20) Pale-Grosdemange, C.; Chuche, J. *Bull. Soc. Chim. Fr.* **1989**, 344 and references therein.
(21) Coqueret, X.; Bourelle-Wargnier, F.; Chuche, J.; Toupet, L. *Bull. Soc. Chim. Fr.* **1987**, 365 and references therein.
(22) Arya, F.; Bouquant, J.; Chuche, J. *Tetrahedron Lett.* **1986**, *27*, 1913.
(23) Maujean, A.; Pale-Grosdemange, C.; Marcy, G.; Chuche, J. *J. Chem. Soc., Chem. Commun.* **1984**, 1135.
(24) Ciganek, E. *Tetrahedron Lett.* **1969**, 5179.
(25) Wentrup, C.; Netsch, K.-P. *Angew. Chem.* **1984**, *96*, 792; *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 802. Wentrup, C.; Winter, H.-W.; Gross, G.; Netsch, K.-P.; Kollenz, G.; Ott, W.; Biedermann, A. G. *Angew. Chem.* **1984**, *96*, 791; *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 800.
(26) Nguyen, M. T.; Ha, T.-K.; More O'Ferrall, R. A. *J. Org. Chem.* **1990**, *55*, 3251.

Scheme VII

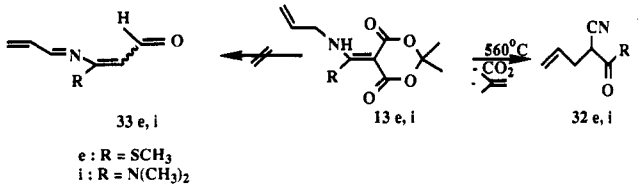


are occurring (Scheme VI; cf. Scheme I), and a methyl group migration interconverting imidoylketene **27** and ketoketene imine **28** is not discernible. As will be shown below, had **28** been formed at 600 °C, it would readily have eliminated propene, giving **29**.

4. Flash Vacuum Thermolysis of 13c–i. Compounds **13c,d,f–h** underwent clean fragmentation to acetone, CO_2, and isobutene or propene, giving cyanothioacetate **30** and cyanoacetamides **31**, respectively, in yields of 60–70% (Scheme VII). These products were purified by column chromatography and identified spectroscopically. In addition, **31g** was independently synthesized by treatment of ethyl cyanoacetate with isopropylamine.

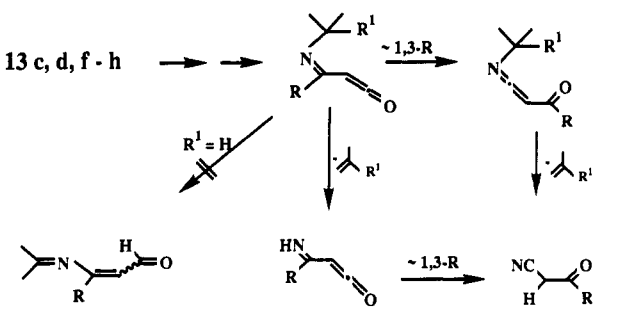
There was *no formation of imino- or enaminoacroleins* in this series, in sharp contrast to the reactions described in Schemes I and VI. Whereas the *tert*-butylamino compounds **13c** and **13f** are prevented from the formation of iminoacroleins by the lack of an α-hydrogen atom, the isopropylamino compounds **13d** and **13g–h** could in principle have reacted to iminoacroleins but failed to do so. The formation of the observed products requires 1,3-migrations of the SCH_3 and NR_2 substituents in intermediate ketenes analogous to the 1,3-H shifts in Scheme V. Again there are two possibilities, depending on the timing of alkene elimination, but in any event a 1,3-shift of the group R has to take place, as illustrated in Scheme VIII.

The last two compounds, **13e** and **13i**, reacted at 560 °C to give products in which both the allyl group and the methylthio (in **13e**) or dimethylamino group (in **13i**) have undergone migration. The yields of the resulting compounds **32e,i** were 61 and 74%, respectively. Again, there was *no* formation of iminoacroleins (**33**).

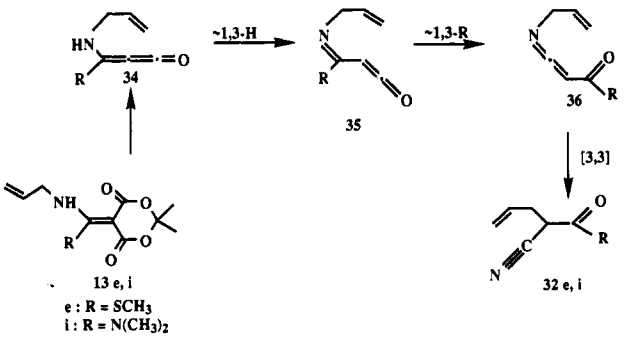


A mechanism for the formation of compounds **32** is proposed in Scheme IX. In analogy with the previous examples, the first two intermediates are expected to be the methyleneketene **34** and the imidoylketene **35**. In order to allow an allyl group migration in **35**, the substituent R must first undergo a 1,3-shift to the ketene imine **36**. A [3,3] sigmatropic shift of the allyl group[27]

Scheme VIII

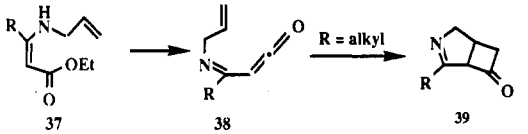


Scheme IX

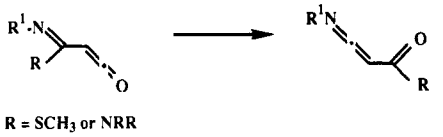


directly converts **36** to the product **32**.[28]

It should be noted that *N*-allylimidoylketenes **38** generated from β-enamino esters **37** and substituted by *alkyl* groups undergo intramolecular [2 + 2] cycloaddition reactions giving **39** in the gas phase.[22] No such reaction was observed for compounds **13e,i**.



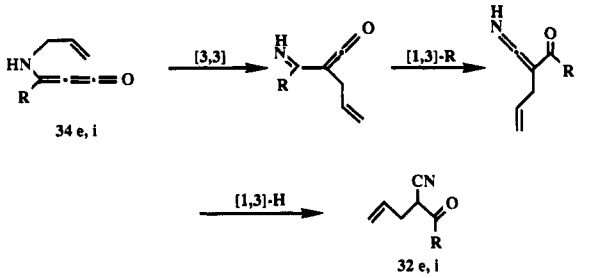
The inescapable conclusion from these studies is that the imidoylketene-to-ketoketene imine rearrangement (eq 4) is dramatically facilitated when the migrating group is an electron-rich methylthio or alkylamino group. In



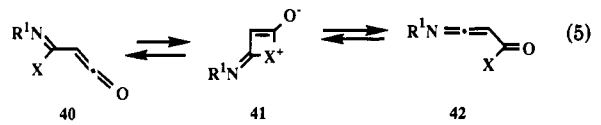
(4)

(27) For [3,3] sigmatropic rearrangements in 3-azahexa-1,5-dienes, see: Rhoads, S. I.; Raulins, N. R. The Claisen and Cope Rearrangements. *Org. React.* **1975**, *22*, 1–252. Heimgartner, H.; Hansen, H.-J. In *Iminium Salts in Organic Chemistry*; Böhme, H., Viehe, H. G., Eds.; Wiley-Interscience: New York, 1979; Part 2, p 655 ff. Chu, M.; Wu, P. L.; Givre, S.; Fowler, F. W. *Tetrahedron Lett.* **1986**, *27*, 461.

(28) It is possible in principle to revert the sequence of [3,3] and [1,3] shifts by letting the former take place in the methyleneketenes **34**, but in any event an efficient 1,3-R shift has to take place:



Scheme VIII either the propene elimination or the 1,3-R shift competes successfully with the nonobserved 1,5-H shift to an iminoacrolein. A methyl group, in contrast, is not able to enter into competition with the 1,5-H shift (Scheme VI). In Scheme IX the 1,3-R shift is required to precede the [3,3] allyl migration, and it also successfully competes with intramolecular [2 + 2] cycloaddition of the type exhibited by **38**. A lowering of the activation energy for 1,3-X migration can be readily understood if an intermediate of the type **41** is involved (eq 5).



(5)

40 **41** **42**

X = SCH_3 or NRR

By implication, this effect should also apply to the ketoketene–ketoketene rearrangement (eq 2) as well as to other cumulated systems. While the present study was largely exploratory and preparative in intent, further research aimed at a direct observation of the interconverting ketenes and ketene imines **40** and **42** using low-temperature IR spectroscopy is now being planned. The results will be reported in due course.

Experimental Section

Apparatus. Preparative thermolyses were carried out in a horizontal quartz tube (600 mm × 30 mm i.d.) heated by an electrical Solo oven. Products were collected on a cold finger cooled in liquid N_2 and directly connected to a diffusion pump, giving an operating pressure of 10^{-4}–10^{-5} Torr. An entrance port placed between the exit of the oven and the cold finger permits the coating of the cold finger with a solvent (CH_2Cl_2, $CHCl_3$, methanol, and deuterated solvents) before the experiment. After the end of the expeiment the cold finger was warmed to room temperature and the solvent with products was collected in an NMR tube and/or subjected to flash chromatography on silica gel.

The apparatus for low-temperature IR spectroscopy was as previously described[9,17] (100 mm × 8 mm i.d. quartz tube). Because of the vastly different geometries of the preparative and analytical reactors, temperatures of the two cannot be directly compared. In general, the analytical reactor required a higher temperature for a reaction to go to completion.

5-[Bis(methylthio)methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione (12). To a solution of Meldrum's acid (10 g, 0.07 mol) in DMSO (30 mL) was successively added triethylamine (14.16 g, 0.14 mol) and carbon disulfide (5.30 g; 0.07 mol). After the mixture was stirred for 1 h at room temperature under Ar, methyl iodide (19.87 g; 0.14 mol) was added dropwise. After the mixture was stirred for 14 h, ice was added, and the yellow precipitate was collected and recrystallized from methanol, giving 9.5 g (55%): mp 119–121 °C (lit.[13] mp 119–121 °C); IR ($CDCl_3$) 3000, 1728, 1680, 1410, 1310, 1280, 1040, 955 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.75 (s, 6 H), 2.65 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 21.3 (q), 26.6 (q), 102.9 (s), 103.0 (s), 159.7 (s), 192.3 (s); MS *m/z* 248 (17), 191 (15), 190 (17), 172 (35), 146 (29), 118 (29), 100 (27), 99 (98), 85 (21).

Anal. Calcd for $C_9H_{12}O_4S_2$: C, 43.53; H, 4.87. Found: C, 43.55; H, 4.80.

2,2-Dimethyl-5-[(*tert*-butylamino)methylene]-1,3-dioxane-4,6-dione (13a). A mixture of Meldrum's acid (7.2 g, 50 mmol) and ethyl orthoformate (60 mL, 6 equiv) was heated at 90 °C for 2 h. After being cooled to room temperature and the addition 4 equiv of *tert*-butylamine (14.6 g), the mixture was stirred at 40 °C for 10 h and then at room temperature for 2 h. The product was filtered and recrystallized from methanol: 10.2 g (90%); mp 148 °C; IR ($CHCl_3$) 3000, 2970, 1710, 1660, 1610, 1430, 1380, 1370, 1330, 1270, 1190, 1010, 935 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.40 (s, 9 H), 1.70 (s, 6 H), 8.20 (d, *J* = 12 Hz, 1 H), 9.70 (d, 1 H); ^{13}C NMR ($CDCl_3$) δ 26.4 (q), 29.2 (q), 54.7 (s), 83.5 (s), 104.1 (s), 155.0 (d), 163.8 (s), 165.3 (s); MS *m/z* 227 (23), 170 (20), 154 (34), 125 (38), 114 (39), 110 (45), 70 (37), 69 (37), 57 (100).

2,2-Dimethyl-5-[2-(isopropylamino)ethylidene]-1,3-dioxane-4,6-dione (13b). Isopropylamine (2.35 g, 0.04 mol) was added to 2,2-dimethyl-5-(2-methoxyethylidene)-1,3-dioxane-4,6-dione (**11b**, 2 g, 0.01 mol) in CH_3CN (20 mL). The mixture was stirred at room temperature for 12 h. The solvent was evaporated, and the product was recrystallized from cyclohexane: 1.9 g (84%); mp 80 °C; IR ($CHCl_3$) 3400, 2990, 1690, 1640, 1580, 1455, 1370, 1320, 1290, 1245, 1050, 1020, 985, 920, 830 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.35 (d, *J* = 7.5 Hz, 6 H), 1.7 (s, 6 H), 2.65 (s, 3 H), 4.00 (sept, 1 H), 11.38 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 17.5 (q), 27.7 (q), 26.1 (s), 45.7 (d), 83.8 (s), 102.0 (s), 163.0 (s), 168.0 (s), 172.0 (s); MS *m/z* 228 (6), 227 (41), 170 (58), 169 (26), 154 (18), 125 (62), 110 (11), 97 (17), 96 (100), 82 (30), 67 (21).

Anal. Calcd for $C_{11}H_{17}NO_4$: C, 58.17; H, 7.54; N, 6.10. Found: C, 58.14; H, 7.64; N, 6.26.

2,2-Dimethyl-5-[(methylthio)(*tert*-butylamino)methylene]-1,3-dioxane-4,6-dione (13c). *tert*-Butylamine (0.59 g, 8.06 mmol) was added to a solution of **12** (2 g, 8.06 mmol) in ethanol (30 mL). The mixture was stirred at room temperature for 24 h and concentrated, and the product was recrystallized from ethanol: 1.33 g (60%); mp 110 °C; IR ($CHCl_3$) 2990, 2910, 1695, 1650, 1570, 1390, 1370, 1310, 1285, 1265, 1190, 1160, 1020, 965, 900 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.50 (s, 9 H), 1.65 (s, 6 H), 2.5 (s, 3 H), 11.15 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 18.4 (q), 25.9 (q), 29.3 (q), 56.5 (s), 83.1 (s), 102.2 (s), 163.7 (s), 177.6 (s); MS *m/z* 273 (19), 226 (10), 216 (7), 215 (9), 200 (7), 168 (26), 59 (23), 57 (100).

Anal. Calcd for $C_{12}H_{19}NO_4S$: C, 52.72; H, 7.01; N, 5.12. Found: C, 52.64; H, 6.90; N, 5.03.

2,2-Dimethyl-5-[(isopropylamino)(methylthio)methylene]-1,3-dioxane-4,6-dione (13d). The same procedure as described for **13c** was applied, giving a 77% yield of **13d**, recrystallized from ethanol: mp 135 °C; IR ($CHCl_3$) 2980, 2920, 1690, 1640, 1560, 1385, 1320, 1310, 1280, 1260, 1165 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.3 (d, *J* = 6.5 Hz, 6 H), 1.7 (s, 6 H), 2.55 (s, 3 H), 4.30 (sept, 1 H), 10.9 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 18.1 (q) 22.3 (q), 26.0 (q), 82.0 (s), 102.4 (s), 163.8 (s), 176.9 (s); MS *m/z* 259 (16), 202 (8), 201 (11), 157 (13), 154 (60), 142 (12), 114 (12), 112 (100), 110 (30), 68 (89), 59 (19), 58 (19).

Anal. Calcd for $C_{11}H_{17}NO_4S$: C, 50.95; H, 6.61; N, 5.40. Found: C, 50.77; H, 6.51; N, 5.46.

5-[(Allylamino)(methylthio)methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione (13e). The same procedure as described for **13c** was applied, using 1.2 equiv of allylamine. The product was recrystallized from ethanol, giving **13e** (91%): mp 114 °C; IR ($CHCl_3$) 3000, 1700, 1640, 1550, 1395, 1380, 1320, 1285, 1180, 1150, 930, 850 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.70 (s, 6 H), 2.6 (s, 3 H), 4.30 (m, 2 H), 5.35 (m, 2 H), 5.90 (m, 1 H); ^{13}C NMR ($CDCl_3$) 18.2 (q), 25.9 (q), 47.8 (t), 83.3 (s), 102.4 (s), 118.3 (t), 131.0 (d), 163.5 (s), 178.7 (s); MS *m/z* 258 (4), 257 (26), 200 (12), 199 (24), 184 (14), 152 (100).

Anal. Calcd for $C_{11}H_{15}NSO_4$: C, 52.34; H, 5.88; N, 5.44. Found: C, 51.50; H, 5.99; N, 5.54.

5-[Bis(*tert*-butylamino)methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione (13f). Two equivalents of *tert*-butylamine (1.18 g; 16.1 mmol) were added to a solution of **12** (2 g, 8.06 mmol) in ethanol (30 mL). The mixture was stirred at room temperature for 48 h, concentrated in vacuo, and the product was recrystallized from petroleum ether–tetrahydrofuran (70:30): 2.0 g (85%); mp 151 °C; IR ($CHCl_3$) 3000, 1685, 1630, 1435, 1400, 1390, 1380, 1240, 1175, 1100 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.50 (s, 18 H), 1.70 (s, 6 H), 6.61 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 26.7 (q), 30.0 (q), 55.4 (s), 101.9 (s), 162.5 (s), 164.7 (s); MS *m/z* 298 (14), 241 (14), 225 (23), 207 (14), 169 (23), 168 (25), 141 (17), 140 (30), 125 (38), 112 (13), 97 (14), 85 (26), 84 (51), 68 (21), 58 (100); high-resolution MS calcd for $C_{15}H_{26}N_2O_4$ 298.1893, found 298.1909.

5-[Bis(isopropylamino)methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione (13g) was prepared as described for **13f**, using isopropylamine. Recrystallization from ethanol gave 0.97 g (90%; from 1.0 g of **12**): mp 79 °C; IR ($CHCl_3$) 2990, 1640, 1530, 1450, 1400, 1380, 1360, 1330, 1260, 1170, 1140 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.33 (d, *J* = 6.5 Hz, 12 H), 1.65 (s, 6 H), 3.83 (sept, 1 H), 9.95 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 23.5 (q), 26.2 (q), 46.6 (d), 74.4 (s), 101.9 (s), 161.6 (s), 166.9 (s); MS *m/z* 271 (12), 270 (79), 213 (59), 212 (38), 197 (39), 194 (68), 193 (35), 179 (77), 168 (26), 153 (37), 140 (19), 128 (53), 127 (39), 112 (48), 110 (85), 98 (68), 97 (38), 84 (38), 83 (70), 68 (10), 58 (100).

Anal. Calcd for $C_{10}H_{22}N_2O_4$: C, 57.75; H, 8.20; N, 10.36. Found: C, 57.77; H, 8.15; N, 10.37.

2,2-Dimethyl-5-[(dimethylamino)(isopropylamino)-methylene]-1,3-dioxane-4,6-dione (13 h). Dimethylamine (0.40 g, 8.87 mmol) in ethanol solution was added to **12** (2 g, 8.06 mmol) in 30 mL of ethanol, and the solution was stirred for 12 h at room temperature. Isopropylamine (0.59 g, 9.67 mmol) was then added, and stirring was continued for 24 h. After removal of the solvent in vacuo, recrystallization of the residue from tetrahydrofuran gave 1.24 g (60%): mp 171 °C; IR ($CHCl_3$) 3000, 1630, 1580, 1470, 1390, 1370, 1250, 1070, 930 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (d, J = 6.5 Hz, 6 H), 1.65 (s, 6 H), 3.15 (s, 6 H), 3.90 (sept, 1 H), 7.0 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 23.1 (q), 26.3 (q), 40.3 (q), 48.7 (d); 102.1 (s), 163.3 (s), 163.9 (s); MS m/z 256 (21), 199 (27), 198 (26), 180 (91), 179 (26), 165 (56), 139 (25), 112 (49), 111 (21), 110 (22), 96 (34), 83 (26), 69 (78), 68 (63), 58 (100).

5-[(Allylamino)(dimethylamino)methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione (13i) was prepared using the method described for **13h**, but replacing isopropylamine by allylamine (0.55 g, 9.67 mmol). Recrystallization from cyclohexane–ethanol (80:20) gave **13i** (1.175 g, 54%): mp 145 °C; IR ($CHCl_3$) 3000, 1685, 1635, 1590, 1480, 1430, 1400, 1380, 1355, 1260, 1060, 920 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.6 (s, 6 H), 3.15 (s, 6 H), 3.75 (m, 2 H), 5.2 (m, 2 H), 5.75 (m, 1 H), 7.3 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 26.3 (q), 48.1 (t), 102.5 (s), 117.8 (t), 132.8 (d), 163.4 (s), 164.5 (s); MS m/z 255 (4), 254 (28), 239 (46), 211 (71), 209 (49), 197 (48), 178 (21), 153 (59), 152 (100), 125 (72), 124 (64), 110 (100), 109 (76), 80 (42), 69 (74).

Anal. Calcd for $C_{12}H_{18}N_2O_4$: C, 56.68; H, 7.13; N, 11.02. Found: C, 56.36; H, 7.23; N, 10.93.

Thermolysis of 13a and 22. A mixture of cyanoacetaldehyde (**14**) and 3-hydroxypropenenitrile (**15**) was obtained by thermolysis of **13a** at 550 °C, or of **22** at >660 °C. **15** existed as a Z/E mixture (ca. 1:1). The ratio of **14** and **15** was solvent dependent as determined by ^1H NMR: in CD_2Cl_2, 99:1; in $(CD_3)_2CO$, 1:4.

Cyanoacetaldehyde (14): IR (neat) 2250, 1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.60 (d, J = 0.5 Hz, 1 H), 9.45 (t, J = 0.5 Hz, 1 H).

3-Hydroxypropenenitrile (15): IR (neat) 2220, 1680 cm^{-1}; ^1H NMR ($CDCl_3$), E isomer, δ 4.45 (d, J = 12.6 Hz, 1 H), 7.57 (d, J = 12.6 Hz, 1 H); Z isomer, δ 4.31 (d, J = 6.3 Hz, 1 H), 7.02 (d, J = 6.3 Hz, 1 H).

3-Hydroxy-3-methoxypropanenitrile (17) was obtained by the action of excess methanol on the thermolysate from **13a**: ^1H NMR ($CDCl_3$) δ 2.71 (d, J = 5 Hz, 2 H), 3.45 (s, 3 H), 4.87 (t, J = 5 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 26.6 (t), 54.9 (q), 94.7 (d), 118.0 (s).

3-(*N*-Propylamino)propenenitrile (16) was obtained by treatment of the pyrolyzate from **13a** with an excess of propylamine: ^1H NMR (($CDCl_3$) δ 0.95 (t, 3 H), 1.56 (m, 2 H), 2.98 (m, 2 H), 3.90 (d, J = 13.8 Hz, 1 H), 6.97 (dd, J_1 = 13.8 Hz, J_2 = 7 Hz, 1 H).

Thermolysis of 13b (700 mg, 3.08 mmol) at 600 °C gave a liquid product which was purified by vacuum distillation to give 120 mg (31%) of **26**: IR ($CHCl_3$) 3000, 1675, 1640, 1600, 1560, 1430, 1370, 1300, 1160, 1070, 1020, 900, 850 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.00 (s, 6 H), 2.25 (s, 3 H), 5.60 (d, J = 8.0 Hz, 1 H), 9.85 (d, 1 H); ^{13}C NMR ($CDCl_3$) δ 16.8 (q), 19.8 (q), 23.6 (q), 112.7 (d), 113.7 (s), 143.6 (s), 190.4 (d); MS m/z 125 (64), 110 (53), 109 (45), 96 (100), 84 (68), 82 (60), 80 (68).

Thermolysis of 13c and 13d at 600 °C gave in both cases ***S*-methyl cyanothioacetate (30)**, isolated by flash chromatography on silica gel, eluting with ethyl acetate–petroleum ether (30:70). **13c** (350 mg, 1.27 mmol) gave 85 mg (58%) of **30**; **13d** (1.44 g; 5.5 mmol) gave 463 mg (72%) of **30**: IR ($CHCl_3$) 3030, 2260, 1700, 1610, 1200, 1030, 430 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.41 (s, 3 H), 3.72 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 12.25 (q), 32.1 (t), 112.8 (s), 187.5 (s); MS m/z 116 (2), 115 (50), 75 (98), 68 (100).

Anal. Calcd for C_4H_5NOS: C, 41.72; H, 4.38; N, 12.16. Found: C, 41.89, H, 4.51; N, 12.14.

Thremolysis of 13e was carried out at 500 °C. The product from 512 mg (1.98 mmol) of **13e** was chromatographed on silica gel, eluting with methylene chloride–petroleum ether (50:50), to give 185 mg (60%) of ***S*-methyl 2-cyanopent-4-enethioate (32e)**: IR ($CHCl_3$) 3000, 2930, 2230, 1685, 1430, 1310, 1220, 1070, 980, 925 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.42 (s, 3 H), 2.70 (m, 2 H), 3.70 (dd, J = 6.5 and 7.5 Hz, 1 H), 5.3 (m, 2 H), 5.8 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 12.2 (q), 34.6 (t), 44.7 (d), 115.9 (s), 12.01 (t), 131.0 (d), 191.4 (s); MS m/z 156 (8), 155 (33), 127 (13), 108 (15), 88 (40), 80 (100), 75 (100), 53 (87).

Anal. Calcd for C_7H_9NOS: C, 54.16; H, 5.84; N, 9.02. Found: C, 54.26; H, 5.86; N, 9.05.

Thermolysis of 13f (435 mg, 1.45 mmol) at 600 °C and flash chromatography (ethyl acetate–petroleum ether (60:40)) of the product gave 118 mg (58%) of ***N*-*tert*-butylcyanoacetamide (31f)**: mp 97 °C; IR ($CHCl_3$) 3420, 3340, 2240, 1680, 1510, 1450, 1390, 1365 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.35 (s, 9 H), 3.35 (s, 2 H), 6.10 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 26.9 (t), 28.6 (q), 52.7 (s), 115.2 (s), 160.2 (s); MS m/z 140 (7), 126 (3), 125 (42), 85 (12), 58 (100), 57 (19), 56 (26).

Anal. Calcd for $C_7H_{12}N_2O$: C, 59.97; H, 8.63; N, 19.88. Found: C, 59.98; H, 8.66; N, 19.99.

Thermolysis of 13g (1 g, 3.68 mmol) at 600 °C and chromatography of the product (ethyl acetate–petroleum ether (60:40)) gave 306 mg (66%) of ***N*-isopropylcyanoacetamide (31g)**: mp 62 °C; IR ($CHCl_3$) 3420, 3200, 3000, 2260, 1695, 1510, 1450 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.12 (d, J = 6.4 Hz, 6 H), 3.35 (s, 2 H), 3.98 (sept, 1 H), 6.6 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 22.3 (q), 26.2 (t), 42.7 (d), 115.2 (s), 160.8 (s); MS m/z 126 (21), 112 (7), 111 (100), 68 (17), 58 (17).

Anal. Calcd for $C_6H_{10}N_2O$: C, 57.12; H, 7.99; N, 22.21. Found: C, 57.33; H, 8.00; N, 22.12.

31g was also obtained by refluxing ethyl cyanoacetate with excess isopropylamine, concentrating, and recrystallizing from ethyl acetate.

Thermolysis of 13h (670 mg; 2.60 mmol) at 600 °C and chromatography of the product (ethyl acetate–petroleum ether (80:20)) gave 175 mg (60%) of ***N*,*N*-dimethylcyanoacetamide (31h)**: mp 62 °C; IR ($CHCl_3$) 3000, 2245, 1660, 1400, 1210, 1130 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.00 (s, 3 H), 3.06 (s, 3 H), 3.50 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 25.0 (t), 36.0 (q), 37.7 (q), 113.9 (s), 161.5 (s); MS m/z 112 (70), 72 (100), 70 (11), 68 (10).

Anal. Calcd for $C_5H_8N_2O$: C, 53.55; H, 7.19; N, 24.98. Found: C, 53.52; H, 7.25; N, 24.99.

Thermolysis of 13i (476 mg, 1.86 mmol) at 550 °C and chromatography of the product (ethyl acetate–petroleum ether (60:40)) gave 215 mg (75%) of ***N*,*N*-dimethyl-2-cyanopent-4-enecarboxamide (32i)**: IR ($CHCl_3$) 3010, 2240, 1670, 1395, 1210, 925 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.67 (t, J = 7 Hz, 2 H), 3.02 (s, 3 H), 3.14 (s, 3 H), 3.69 (t, J = 7 Hz, 1 H), 5.2 (m, 2 H), 5.85 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 33.6 (t), 34.7 (d), 36.3 (q), 37.5 (q), 116.7 (s), 119.2 (t), 132.4 (d), 163.8 (s); MS m/z 153 (15), 152 (15), 151 (8), 112 (14), 80 (11), 72 (100).

Anal. Calcd for $C_8H_{12}N_2O$: C, 63.13; H, 7.95; N, 18.41. Found: C, 63.16; H, 7.97; N, 18.53.

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