Thermolysis of 2-acyloxy-Δ^3-1,3,4-oxadiazolines. Evidence for a preferred sense of cycloreversion to carbonyl ylides and for fast 1,4-sigmatropic ylide rearrangement

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This paper is dedicated to Professor Ronald J. Gillespie on the occasion of his 65th birthday

MICHAEL W. MAJCHRZAK and JOHN WARKENTIN. Can. J. Chem. **67**, 1753 (1989).

Thermolysis of 2-acyloxy-2,5,5-trialkyl-Δ^3-1,3,4-oxadiazolines in benzene solution at 80°C furnishes acyloxy-substituted enol ethers (hemiacylals) in high yield. Mixtures of *cis*:*trans* isomers of such oxadiazolines afford mixtures of isomeric hemiacylals in nearly the same ratio. Those and other results are rationalized in terms of cycloreversion of the oxadiazolines to carbonyl ylides that are not equilibrated during their lifetimes and undergo primarily 1,4-sigmatropic H-migration. Some fragmentation of the ylides to anhydrides and carbenes was also observed. A consistent mechanistic account includes concerted suprafacial ($4\pi + 2\pi$) cycloreversion in the sense that places a large ylide substituent at C-1 or at C-3, preferentially *exo*. A smaller preference for the cycloreversion that places the acetoxy group at C-1 in the *endo* position, when the steric effect of the alkyl group at C-1 is small, can be inferred. The possibility that the overall 1,4-H shift is the result of sequential 1,7-antarafacial and 1,4-suprafacial shifts, in some cases, is considered.

Key words: carbonyl ylide; 1,4-sigmatropic rearrangement; cycloreversion, thermal, of oxadiazolines; ylide, carbonyl; oxadiazoline, thermolysis of.

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La thermolyse des 2-acyloxy-2,5,5-alkyl-Δ^3-1,3,4-oxadiazolines, en solution dans le benzène à 80°C, fournit des éthers énoliques substitués par des groupements acyloxy (hémiacylals) avec un excellent rendement. Les mélanges *cis*:*trans* de telles oxadiazolines fournissent des mélanges d'hémiacylals isomères qui sont dans le même rapport. On rationalise ces résultats ainsi que d'autres en fonction d'une cycloréversion des oxadiazolines en ylures de carbonyles qui ne s'équilibrent pas durant leur existence et qui subissent principalement des migrations sigmatropiques-1,4 d'hydrogène. On a aussi observé quelques fragmentations des ylures en anhydrides et en carbènes. Un mécanisme cohérent comporte une cycloréversion ($4\pi + 2\pi$) suprafaciale concertée dans le sens qui permet de placer un substituant ylure volumineux en positions C-1 ou C-3, d'une façon préférentielle *exo*. On peut supposer qu'il existe aussi une préférence plus faible pour la cycloréversion qui place le groupement acétoxy en position *endo* en C-1, où l'effet stérique du groupement alkyle en C-1 est faible. On considère qu'il est possible, dans quelques cas, que le déplacement global 1,4 d'hydrogène puisse être le résultat des déplacements successifs antérafacial-1,7 et suprafacial-1,4.

Mots clés : carbonyle ylure; transposition sigmatropique-1,4; cycloréversion, thermique, d'oxadiazolines; ylure, carbonyle; oxadiazoline, thermolyse de.

[Traduit par la revue]

Introduction

1,4-Sigmatropic H-migrations (1) in ylides, including azomethine ylides (2–4) and carbonyl ylides (5–7), are well known. Many details of those rearrangements, however, are poorly understood. First, there is the question of whether ylide equilibration, by rotation about one or both carbon–heteroatom bonds, is faster or slower than sigmatropic rearrangement. Second, the preferred geometry (*E* or *Z*) about the newly formed double bond of the product of H-migration is not known. Third, the sense of sigmatropic rearrangement (toward C-1 or C-3) in unsymmetric systems is not established for a variety of cases. Finally, there is little information in the literature concerning substitution patterns that cause suppression of the sigmatropic rearrangement in favour of alternative unimolecular processes such as fragmentations to carbonyl compounds and carbenes.

These questions are illustrated in Scheme 1 for a simple carbonyl ylide to which they would apply.

We now report the synthesis and thermolysis of a series of 2-acetoxy-2,5,5-trialkyl-Δ^3-1,3,4-oxadiazolines (**2** and **5**). Systematic changes of the alkyl substituents and a study of *cis*/*trans* mixtures provided information concerning some of the questions posed above.

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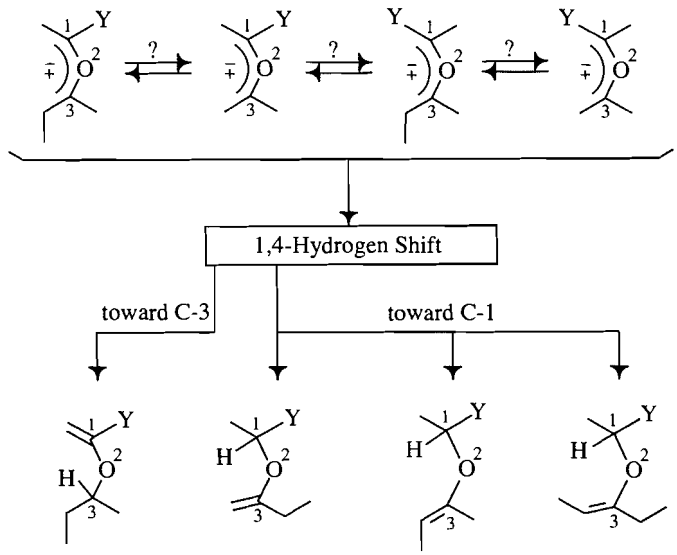


SCHEME 1

Methods and results

Oxadiazolines **2** were prepared by oxidation of acyl hydrazones (**1**) of ketones with lead tetraacetate (LTA) in methylene chloride (1), eq. [1]. That method afforded *cis*:*trans* mixtures

TABLE 1. Substrate ratios and product yields[a–d]

Substrate	R^1	R^2	R^3	Isomer ratio *trans*:*cis*	Products (yields)
2*b*	Me	Et	Me	2.2:1.0	**7**(62), **8**(28)
2*b*				1.0:1.9	**7**(35), **8**(55)
2*c*	Et	Et	Me		**20**(88)
2*d*	Me	*i*-Pr	Me	3.0:1.0	**10**(69), **12**(17)
2*d*				1.0:2.6	**10**(37), **12**(45)
2*e*	*i*-Pr	*i*-Pr	Me		**17**(11), **16**(60)
2*f*	Me	*t*-Bu	Me	14.5:1.0	**24**(~95)
2*g*	Me	Et	*i*-Pr	2.5:1.0	**18**(57), **19**(28)
2*h*	Me	*i*-Pr	*i*-Pr	2.4:1.0	**26**(60), **12**(30)
5	See eq. [4]				**28**(91)

[a]All isomer ratios were estimated by integration of the ^{1}H nmr spectra.
[b]Yields were estimated by analysis of the nmr spectra of the crude pyrolysates after identification of the major components, and are not subject to losses incurred during separations.
[c]Errors in the isomer ratios were estimated to be no more than 5%. Errors in product yields were estimated to range from about 5% to 20% of the values quoted, depending on their actual magnitude.
[d]Additional products, usually minor, are mentioned in the Experimental.

of **2***b*, **2***d*, and **2***f* in which the *trans* isomer predominated (Table 1). Oxadiazolines **2***b* and **2***d* were also obtained from 2-oxooxadiazolines **3**, by the alkylation/acylation sequence of eq. [2]. Compounds **3** were prepared by the oxidative cyclization/hydrolysis sequence of eq. [3], from semicarbazones **4**. The procedure of eq. [2] afforded *cis*/*trans* mixtures of **2** in which the *cis* isomer predominated. These two synthetic approaches permitted the assignment of the *trans* structure to the major product of the synthesis according to eq. [1] and of the *cis* structure to the major product of the synthesis according to eq. [2]. Finally the oxadiazoline **5** was prepared from **2***c* by the deacylation/reacylation sequence illustrated with eq. [4].

[1] $R^1R^2C{=}NNHCOR^3 \xrightarrow{LTA}$ **2**

1

2

2*a*: $R^1 = R^2 = R^3 = CH_3$
2*b*: $R^1 = R^3 = CH_3$, $R^2 = CH_2CH_3$
2*c*: $R^1 = R^2 = CH_2CH_3$, $R^3 = CH_3$
2*d*: $R^1 = R^3 = CH_3$, $R^2 = CH(CH_3)_2$
2*e*: $R^1 = R^2 = CH(CH_3)_2$, $R^3 = CH_3$
2*f*: $R^1 = R^3 = CH_3$, $R^2 = C(CH_3)_3$
2*g*: $R^1 = CH_3$, $R^2 = CH_2CH_3$, $R^3 = CH(CH_3)_2$
2*h*: $R^1 = CH_3$, $R^2 = R^3 = CH(CH_3)_2$

[2] **3** $\xrightarrow[(2)\ CH_3COCl]{(1)\ CH_3Li}$ **2**

3

b: $R^1 = CH_3$, $R^2 = CH_2CH_3$; *d*: $R^1 = CH_3$, $R^2 = CH(CH_3)_2$

[3] $R^1R^2C{=}NNHCONH_2$ **4** $\xrightarrow[(2)\ H_3O^+]{(1)\ LTA,\ CH_2Cl_2}$ **3**

[4] **2***c* $\xrightarrow[(2)\ Me_2CHCOCl]{(1)\ MeLi(-30\ to\ 0\,°C)}$ **5**

5

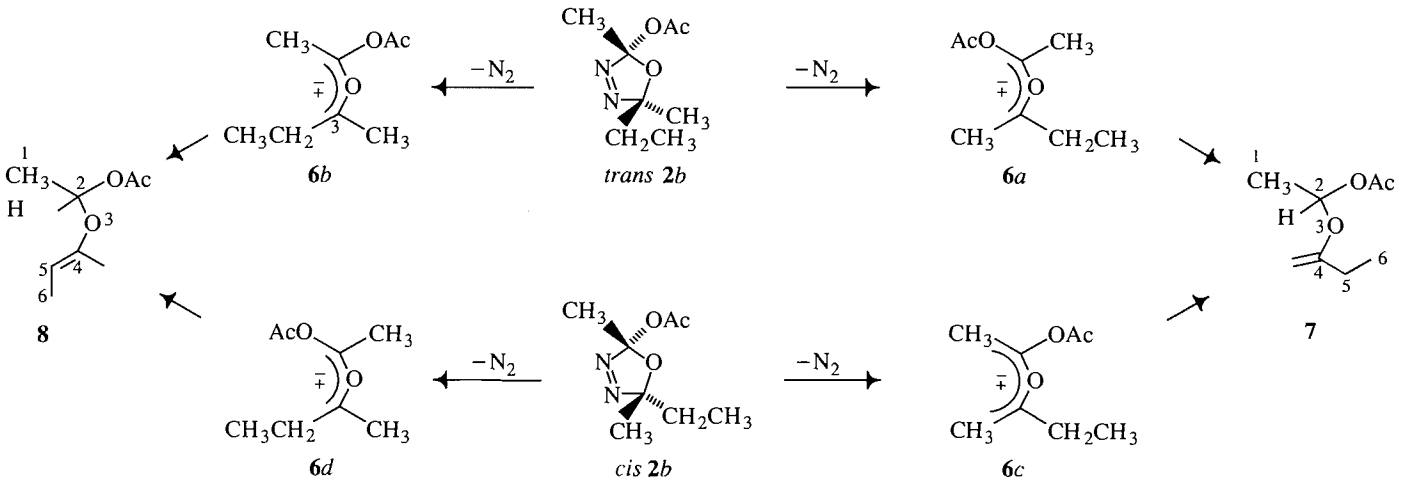
Separation of the geometric isomers of the oxadiazolines by hplc was not successful and they are too unstable to survive glpc conditions. Selective deacylation of one of the isomers by treatment of the mixture **2***b* (*trans*:*cis* = 2.3:1) with half an equivalent of methyllithium at −78°C was not promising. The *trans*:*cis* ratio in recovered **2***b* was only slightly different from that in the starting material. It was therefore necessary to use the different mixtures of isomers of **2***b* and of **2***d*, from the two synthetic approaches (eqs. [1], [2]), to infer the selectivities of the cycloreversion step and of the subsequent 1,4-sigmatropic hydrogen atom shifts, illustrated for the case of **2***b* with Scheme 2.

A striking result is the fact that a mixture (*trans*:*cis* = 2.3:1) of the isomers **2***b* afforded a product mixture in which the ratio **7**:**8** was 2.2:1. Similarly, when the isomer ratio for **2***b* was *trans*:*cis* = 1:1.9, the product ratio was **7**:**8** = 1:1.6, suggesting a substantial overall memory effect. An immediate conclusion from those results is that the geometric isomers (**6***a*–*d*) of the carbonyl ylide intermediate are not equilibrated by rotation about the bonds to the central oxygen atom during their lifetimes. Equilibration would require a product ratio independent of the ratio of isomers in the starting material.

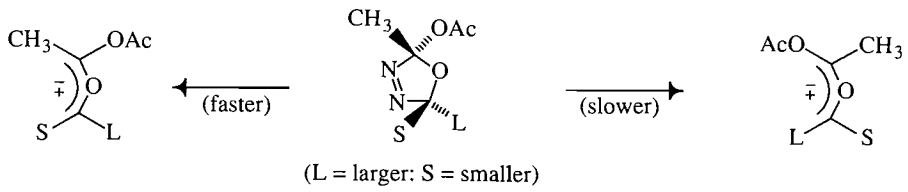
The fact that carbonyl ylides **6***a*–**6***d* are not equilibrated during their lifetimes means that it is possible, in principle, to discover which ones are formed preferentially by the cycloreversions of *trans*- and *cis*-**2***b*. Because stereochemical information is lost in the 1,4-hydrogen atom shifts that convert the transient ylides to stable products, it was necessary to use an indirect probe. The probe chosen relies on the assumption that the cycloreversion transition states are sufficiently productlike to reflect steric effects on product stability. That is, a transition state leading to an ylide with the larger substituents *endo* will, other factors being equal, be of higher energy than a transition state leading to an isomeric ylide with the larger substituents *exo*, Scheme 3.

The assumption that large groups cannot be accommodated well in the *endo* position of a planar carbonyl ylide received strong support from the results of thermolysis of **2***d* (Scheme 4). A sample of **2***d* (*trans*:*cis* = 3:1) gave **10** and **12** in 4:1 ratio. Isomer **11** was not formed. Similarly, a sample of **2***d* (*trans*:*cis* = 1:2.6) gave **10** and **12** in 1.2:1 ratio and, again, **11** could not be detected. In both cases the combined yields of **10** and **12** accounted for more than 90% of the original isopropyl groups. Although there was a preference for formation of **12** in each case, the carbonyl ylides from **2***d* are clearly only partially equilibrated during their lifetimes and the sense of equilibration is most likely to be **9***b* → **9***c* and **9***d* → **9***a* (Scheme 4). Fragmentation presumably competes quite effectively with those rotational equilibrations, to afford **12** and 1-acetoxyethylidene (**13**), which rearranges to biacetyl **14**.

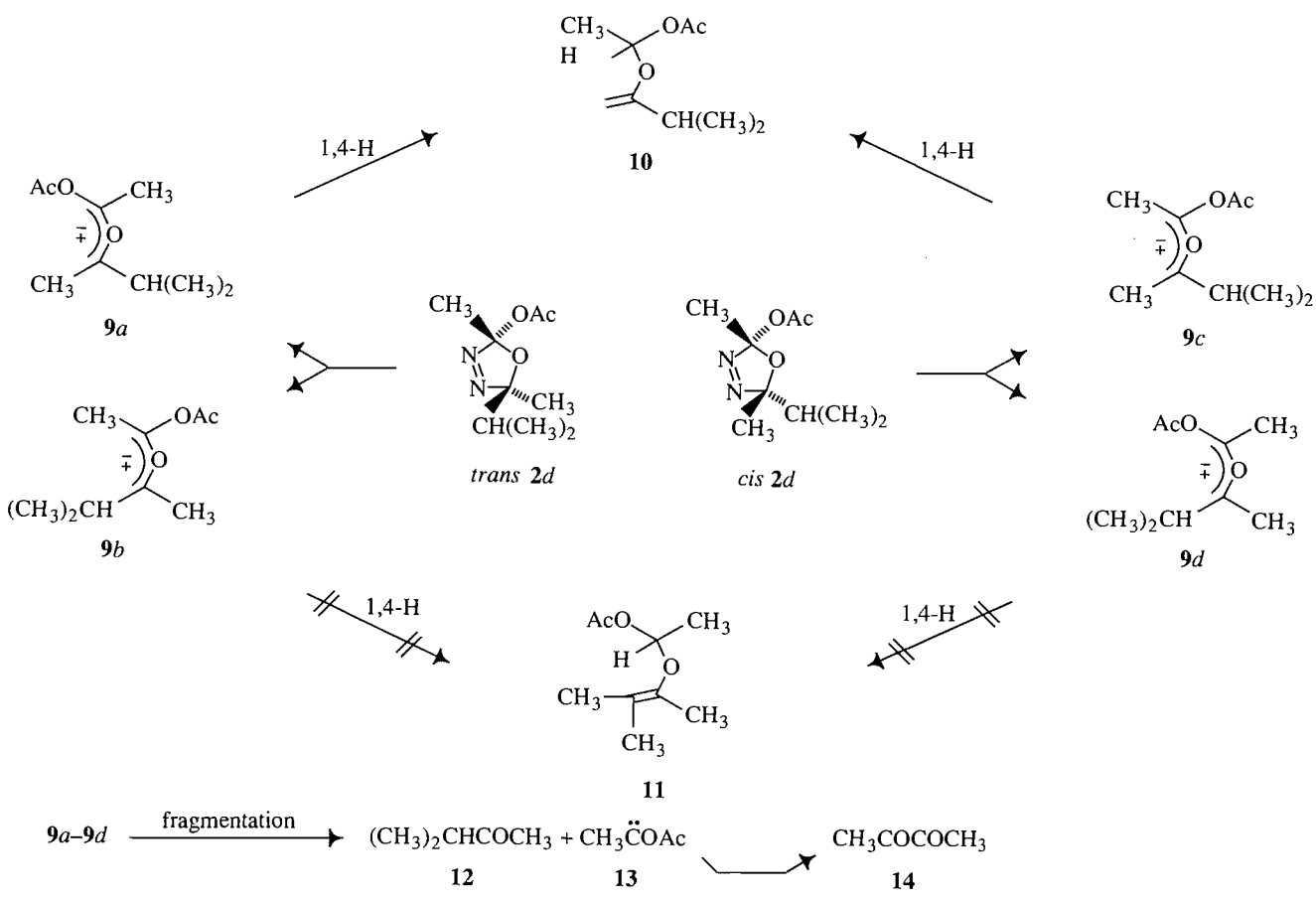
Further support for the presumed crowding experienced by *endo* isopropyl substituents of carbonyl ylides came from the



SCHEME 2



SCHEME 3



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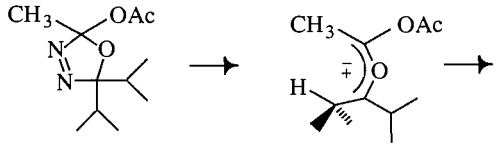
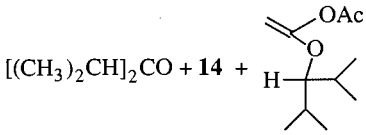
[5] 

2e 15



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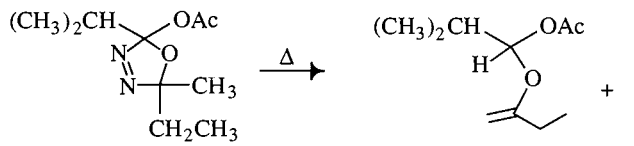
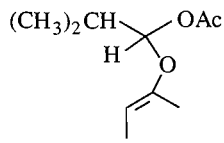
finding that **2e** afforded none of the product of 1,4-sigmatropic rearrangement in the normal sense but only products from fragmentation (**14** and **16**) and, in approximately 10% yield, the product (**17**) of 1,4-sigmatropic rearrangement from the methyl group at C-1 (eq. [5]). Presumably the ylide **15** cannot readily adopt the conformation (8) required for sigmatropic migration of methine hydrogen and is constrained instead to a conformation in which the methine hydrogen of the *endo* isopropyl group lies in the ylide plane, or to nonplanar conformations of the ylide. The alternative migration, toward C-3, which is not competitive in other 1-acetoxy or 1-alkoxy carbonyl ylides, therefore becomes observable.

The evidence that *endo* isopropyl conformations of carbonyl ylides are probably unstable, presumably because they cannot adopt the 0°,0° geometry that is the ground state (9), was used to prepare a carbonyl ylide with an *endo* acetoxy substituent. Oxadiazoline **2g** (*trans*:*cis* = 2.5:1) gave **18** and **19** in the ratio 2.0:1 in good yield (85%) on thermolysis, eq. [6]. Again

[6] 

2g 18



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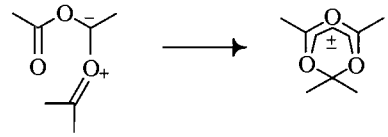
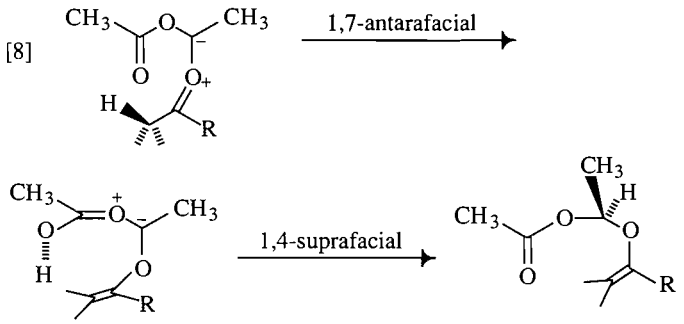
only partial equilibration of ylides occurred and the overall 1,4-hydrogen atom transfer took place efficiently from the "acetoxy *endo*" conformation, the "isopropyl *endo*" geometry presumably being too hindered, as was discussed above.

From the evidence that the *endo* acetoxy conformation is sufficient for sigmatropic rearrangement toward C-1 to occur, it does not follow that *endo* acetoxy is the kinetically preferred mode of cycloreversion. It also does not follow that the sigmatropic rearrangement toward C-1 is particularly facile if the acetoxy group is in the *endo* position. Nevertheless, there are reasons for believing that both of the preferences referred to above may be real. First, a carbonyl ylide must have a considerable net dipole bisecting the ylide COC angle and having the negative end in the *endo* region. Stabilizing dipole–dipole and dipole – induced dipole interactions between a substituent and the ylide framework can therefore be expected to be largest if the substituent is close to the main dipole by lying in an *endo* position. An extreme representation of internal solvation is the imagined cyclization shown in eq. [7].

[7] 

Second, a sigmatropic rearrangement in an *endo* acetoxy carbonyl ylide *could* be unusually easy because an initial 1,7-antarafacial sigmatropic shift, from carbon to oxygen to form a new ylide with a strong O—H bond, is possible. The new ylide could then undergo a suprafacial 1,4-shift (eq. [8]).

[8] 

Although the two-step process is stereochemically different from a one-step rearrangement, there is no simple test available for distinguishing between the mechanisms. We mention the hypothesis of a 1,7-antarafacial initial step as an intriguing possibility. The fact that acetoxy carbonyl ylides such as **2b** afford products of 1,4-sigmatropic rearrangement in good yield whereas corresponding methoxy carbonyl ylides afford analogous products in low yield, except in the case of gas phase thermolysis (10), may be used to support the hypothesis.

In summary, many acyloxy-substituted carbonyl ylides undergo 1,4-sigmatropic H-migrations faster than ylide isomerization by rotations. The calculated rotational barrier[2] for the parent (unsubstituted) carbonyl ylide is 14 kcal mol^{-1} and experimental barriers of 8–13 kcal mol^{-1} have been reported for 1-cyano-1,3-diphenyl carbonyl ylide (11). It is very likely then that the free energy of activation for the observed sigmatropic rearrangement is less than 14 kcal mol^{-1}. Conformations of 1-acetoxy carbonyl ylides in which the acetoxy group is *endo* may actually rearrange by sequential 1,7-antarafacial and 1,4-suprafacial H-shifts, but the evidence for two steps is not compelling.

In those cases where sigmatropic rearrangement generated a trisubstituted double bond, the *E* isomer was formed, as predicted from a consideration of steric factors in the transition structure for the rearrangement. Sigmatropic migration of methine hydrogen from an isopropyl group was not observed. Fragmentation is the major fate of those ylides that would have to place an isopropyl group *endo* in order to be planar.

Experimental

General

Melting points were determined on a Thomas Hoover capillary melting point apparatus and are uncorrected. Proton NMR spectra were recorded on a Bruker AM-500 or an EM-390 spectrometer using TMS or residual ^1H signals from $CDCl_3$ or C_6D_6 as internal standards. ^{13}C NMR spectra were recorded with the Bruker AM-500 machine. Centrifugal chromatography was carried out on silica (Merck Kieselgel $60PF_{254}$) coated plates (coating 2 mm thick) spinning in a Chromatotron model 17924T apparatus. Plastic-backed, Merck Kieselgel $60F_{254}$, 0.2-mm silica plates were used for analytical thin-layer chromatography (TLC). Commercially available solvents and reagents were purified by standard procedures.

[2]Calculation by W. J. Hehre, quoted in ref. 11.

Acetylhydrazones of ketones (1)

Most of these were prepared by refluxing solutions of equimolar amounts of acetylhydrazine and of the appropriate ketone in benzene until all water was removed (Dean–Stark trap, 5–15 h). The solvent was removed under vacuum and the residue was recrystallized. The acetyl hydrazone of pinacolone (**1***e*) was obtained by refluxing a solution of acetylhydrazine in excess pinacolone for 20 h. Excess pinacolone was distilled off and the residue was recrystallized (12). New acetylhydrazones are reported below.

*1-Acetyl-2-(2,4-dimethyl-3-pentylidene)hydrazine (1*e*)*

The yield of **1***e* was 75%, mp 75–77°C (Et_2O/petroleum); ^{1}H NMR (90 MHz, $CDCl_3$) δ: 8.85 (br s, 1H, NH), 2.87 (sept, J = 6.9 Hz, 1H), 2.62 (sept, J = 6.9 Hz, 1H), 2.22 (s, 3H), 1.06 (d, J = 6.9 Hz, 6H), 1.04 (d, J = 6.9 Hz, 6H).

*1-(2-Methylpropanoyl)-2-(2-butylidene)hydrazine (1*g*)*

The general procedure afforded **1***g* in 70% yield, mp 60–68°C (Et_2O/EtOH); ^{1}H NMR (90 MHz, $CDCl_3$) δ: 8.62 (br s, 1H, NH), 3.42 (sept, J = 6.9 Hz, 1H), 2.37 (q, J = 7.5 Hz, 2H), 1.84 (s, 3H), 1.18 (d, J = 6.9 Hz, 6H), 1.12 (t, J = 7.5 Hz, 3H).

*1-(2-Methylpropanoyl)-2-(3-methyl-2-butylidene)hydrazine (1*h*)*

Yield 75%, mp 85–87°C (petroleum ether/benzene); ^{1}H NMR (90 MHz, $CDCl_3$) δ: 8.40 (br s, 1H, NH), 3.38 (sept, J = 6.9 Hz, 1H), 2.51 (sept, J = 6.9 Hz, 1H), 1.82 (s, 3H), 1.23 (d, J = 6.9 Hz, 6H), 1.17 (d, J = 6.9 Hz, 6H).

2-Acetoxy-2,5,5-trialkyl-Δ^3-1,3,4-oxadiazolines (2) by the route of eq. [1]

The lead tetraacetate oxidation of acylhydrazones of ketones was carried out as described previously (13). The products, purified by vacuum distillation, are described below. Some chemical shift assignments of methyl signals in ^{13}C NMR spectra are tentative.

*2-Acetoxy-5-ethyl-2,5-dimethyl-Δ^3-1,3,4-oxadiazoline (2*b*)*

The *trans*:*cis* ratio was 2.2:1; bp 44–45°C (0.5 Torr; 1 Torr = 133.3 Pa); ^{1}H NMR of *trans* isomer (500 MHz, C_6D_6) δ: 1.88 (s, 3H, Ac), 1.67–1.58 (m, 2H), 1.57 (s, 3H), 1.31 (s, 3H), 0.64 (t, J = 7.5 Hz, 3H); ^{1}H NMR of *cis* isomer (500 MHz, C_6D_6) δ: 1.82 (s, 3H, Ac), 1.76–1.67 (m, 2H), 1.58 (s, 3H), 1.19 (s, 3H), 0.77 (t, J = 7.5 Hz, 3H); ^{13}C NMR of *trans* isomer (125.76 MHz, C_6D_6) δ: 167.10 (CO), 130.19 (C-2), 126.27 (C-5), 30.90 (CH_2), 23.15 (Me at C-5), 22.24 (CH_3CO), 21.27 (Me), 7.62 (Me); ^{13}C NMR of *cis* isomer (125.76 MHz, C_6D_6) δ = 167.06 (CO), 130.49 (C-2), 126.66 (C-5), 30.39 (CH_2), 22.28 (CH_3CO), 22.21 (Me), 21.17 (Me), 8.08 (Me).

*2-Acetoxy-5,5-diethyl-1-methyl-Δ^3-1,3,4-oxadiazoline (2*c*)*

This compound was obtained in 75% yield, bp 53–54°C (0.4 Torr); ^{1}H NMR (90 MHz, $CDCl_3$) δ: 2.25–1.55 (m, 10H), 0.90 (t, J = 7.5 Hz, 3H), 0.77 (t, J = 7.5 Hz, 3H).

*2-Acetoxy-5-(1-methylethyl)-2,5-dimethyl-Δ^3-1,3,4-oxadiazoline (2*d*)*

The product, obtained in 75% yield, was a mixture, *trans*:*cis* ratio = 3:1; bp 53–55°C (0.5 Torr); ^{1}H NMR of *trans* isomer (500 MHz, C_6D_6) δ: 1.90–1.81 (m), 1.87 (s, 3H), 1.68 (s, 3H), 1.25 (s, 3H), 0.84 (d, J = 6.9 Hz, 3H), 0.73 (d, J = 6.9 Hz, 3H); ^{1}H NMR of *cis* isomer (500 MHz, C_6D_6) δ: 1.90–1.81 (m), 1.80 (s, 3H), 1.70 (s, 3H), 1.18 (s, 3H), 0.92 (d, J = 6.9 Hz, 3H), 0.76 (d, J = 6.9 Hz, 3H). The total integral for the overlapping signals in the region δ 1.90–1.81 was satisfactory. ^{13}C NMR of *trans* isomer (125.76 MHz, C_6D_6) δ: 167.11 (CO), 129.81 (C-2), 128.52 (C-5), 35.41 (CH), 21.81 (CH_3CO), 21.42 (2-CH_3), 20.04 (5-CH_3), 17.18 (CH_3), 16.93 (CH_3); ^{13}C NMR of *cis* isomer (125.26 MHz, C_6D_6) δ: 167.01 (CO), 130.37 (C-2), 129.21 (C-5), 35.27 (CH), 23.01 (CH_3CO), 21.29 (2-CH_3), 19.28 (5-CH_3), 17.77 (CH_3), 17.21 (CH_3).

*2-Acetoxy-5,5-di-(1-methylethyl)-2-methyl-Δ^3-1,3,4-oxadiazoline (2*e*)*

Oxadiazoline **2***e* was obtained in 72% yield; bp 58–60°C (0.1 Torr); ^{1}H NMR (90 MHz, C_6D_6) δ: 2.42–2.00 (m, 2H, CH), 1.98 (s, 3H, Ac), 1.62 (s, 3H), 0.97–0.59 (m, 12H).

*2-Acetoxy-5-(1,1-dimethylethyl)-2,5-dimethyl-Δ^3-1,3,4-oxadiazoline (2*f*)*

Mixture **2***f* was obtained in 70% yield; *trans*:*cis* ratio = 14.5:1; bp 53–55°C (0.3 Torr); mp 36–37°C (petroleum ether); ^{1}H NMR of *trans* isomer (500 MHz, C_6D_6) δ: 2.04 (s, 3H, Ac), 1.54 (s, 3H), 1.23 (s, 3H), 0.87 (s, 9H); ^{1}H NMR of *cis* isomer (500 MHz, C_6D_6) δ: 1.89 (s, 3H, Ac), 1.60 (s, 3H), 1.12 (s, 3H), 0.91 (s, 9H); ^{13}C NMR of *trans* isomer (125.76 MHz, C_6D_6) δ: 167.07 (CO), 130.68 (C-2), 129.89 (C-5), 37.27 (CMe_3), 25.45 (2-Me), 21.31 (CH_3CO or 5-Me), 21.06 ((CH_3)$_3$), 19.11 (5-Me or CH_3CO).

*2-Acetoxy-5-ethyl-2-(1-methylethyl)-5-methyl-Δ^3-1,3,4-oxadiazoline (2*g*)*

The yield was 60%, bp 65–66°C (0.3 Torr); *trans*:*cis* ratio 2.5:1; ^{1}H NMR of *trans* isomer (500 MHz, $CDCl_3$) δ: 2.84 (sept, J = 6.9 Hz, 1H), 2.05 (s, sum of two Ac integrals), 1.77–1.66 (m, 2H, CH_2), 1.52 (s, 3H), 1.12 (d, J = 6.9 Hz, 3H), 1.10 (t, J = 7.5 Hz, 3H), 1.02 (d, J = 6.9 Hz, 3H); ^{1}H NMR of *cis* isomer (500 MHz, $CDCl_3$) δ: 3.02 (sept, J = 6.9 Hz, 1H), 2.05 (s, sum of two Ac integrals), 2.00–1.90 (m, 2H, CH_2), 1.55 (s, 3H), 1.15 (d, J = 6.9 Hz, 3H), 1.00 (t, J = 7.5 Hz, 3H), 0.93 (d, J = 6.3 Hz, 3H); ^{13}C NMR of *trans* isomer (125.76 MHz, $CDCl_3$) δ: 167.39 (CO), 133.21 (C-2), 125.52 (C-5), 32.70 (CH), 30.48 (CH_2), 21.46 (5-Me), 20.70 (CH_3CO), 16.62 (CH_3), 16.32 (CH_3), 8.05 (CH_3); ^{13}C NMR of *cis* isomer (125.76 MHz, $CDCl_3$) δ: 167.39 (CO), 133.68 (C-2), 126.20 (C-5), 31.87 (CH), 30.55 (CH_2), 21.42 (5-Me), 20.83 (CH_3CO), 16.77 (CH_3), 16.08 (CH_3), 8.05 (CH_3). This last signal was assigned by analogy because one CH_3 signal of one isomer is superimposed on a CH_3 signal of the other isomer.

*2-Acetoxy-2,5-di-(1-methylethyl)-5-methyl-Δ^3-1,3,4-oxadiazoline (2*h*)*

Mixture **2***h* was formed in 65% yield; bp 66–68°C (0.3 Torr); *trans*:*cis* ratio = 2.4:1; ^{1}H NMR of *trans* isomer (500 MHz, $CDCl_3$) δ: 2.84 (sept, J = 6.9 Hz, 1H), 2.04 (s, 3H, Ac), 1.78 (sept, J = 6.9 Hz, 1H), 1.42 (s, 3H), 1.24 (d, J = 6.9 Hz, 3H), 1.10 (d, J = 6.9 Hz, 3H), 1.05 (d, J = 6.9 Hz, 3H), 1.04 (d, J = 6.9 Hz, 3H); ^{1}H NMR of *cis* isomer (500 MHz, $CDCl_3$) δ: 3.08 (sept, J = 6.9 Hz, 1H), 2.05 (s, 3H, Ac), 1.89 (sept, J = 6.9 Hz, 1H), 1.47 (s, 3H), 1.17 (d, J = 6.9 Hz, 3H), 1.16 (d, J = 6.9 Hz, 3H), 0.95 (d, J = 6.9 Hz, 3H), 0.90 (d, J = 6.9 Hz, 3H); ^{13}C NMR of *trans* isomer (125.76 MHz, $CDCl_3$) δ: 167.24 (CO), 133.04 (C-2), 127.86 (C-5), 35.44 (CH), 32.72 (CH), 18.10 (CH_3CO), 17.19 (CH_3), 16.90 (CH_3), 16.64 (CH_3), 16.39 (CH_3); ^{13}C NMR of *cis* isomer (125.76 MHz, $CDCl_3$) δ: 169.24 (CO), 133.50 (C-2), 128.76 (C-5), 35.66 (CH), 31.61 (CH), 21.39 (CH_3CO), 17.93 (CH_3), 17.10 (CH_3), 16.85 (CH_3), 16.02 (CH_3).

*2-Acetoxy-2,5,5-trialkyl-Δ^3-1,3,4-oxadiazolines, 2*b *and 2*d*, by the route of eq. [2]*

The reaction of **3***b* or **3***d* with methyllithium was carried out as described previously (14). Acetyl chloride in ethyl ether was used at the end of the reaction to trap the lithium alkoxide. The temperature during addition was kept at −40°C; then the cooling bath was removed and, while stirring, the reaction mixture was allowed to come to room temperature (2 h). Next it was quenched with water and extracted with ethyl ether (3 × 50 mL). The ether extracts were washed with 5% sodium bicarbonate solution (3 × 10 mL) and dried ($MgSO_4$). The drying agent was filtered off, and the filtrate was concentrated under vacuum and distilled. The oxadiazoline **2***b* obtained by this method was a 1.9:1 (*cis*:*trans*) mixture of isomers. The isomer ratio (*cis*:*trans*) of oxadiazoline **2***d* was 2.7:1.

*5-Ethyl-5-methyl-2-oxo-Δ^3-1,3,4-oxadiazoline (2*b*)*

This compound was prepared as described in the literature (14); ^{1}H NMR (90 MHz, $CDCl_3$) δ: 2.16 (q, J = 7.5 Hz, 2H), 1.72 (s, 3H), 0.80 (t, J = 7.5 Hz, 3H).

*5-(1-Methylethyl)-5-methyl-2-oxo-Δ^3-1,3,4-oxadiazoline (2*d*)*

This compound was prepared as described earlier (14); ^{1}H NMR (90 MHz, $CDCl_3$) δ: 2.27 (sept, J = 6.9 Hz, 1H), 1.69 (s, 3H), 1.10 (d, J = 6.9 Hz, 3H), 0.90 (d, J = 6.9 Hz, 3H).

5,5-Diethyl-2-(2-methylpropanoyloxy)-2-methyl-Δ^3-1,3,4-oxadiazoline (5)

To a stirred solution of 2-acetoxy-5,5-diethyl-2-methyl-Δ^3-1,3,4-oxadiazoline **2***c* (5 g, 0.025 mol) in THF (35.0 mL) under argon was added, dropwise at −50°C, methyllithium (0.055 mol, 37 mL of 1.5 M

solution). The reaction mixture was stirred at this temperature for 0.5 h and then for 1 h at −20°C before it was recooled to −60°C. At this temperature isobutyryl chloride (5.33 g, 0.05 mol) in THF (10 mL) was added dropwise. The cooling bath was removed and stirring was continued for another 3 h. After this time the solvent was removed under vacuum, the residue was dissolved in methylene chloride (50 mL), washed with saturated NaCl (2 × 10 mL), and dried ($MgSO_4$). The drying agent was filtered off, the solvent was evaporated under vacuum, and the residue was distilled to afford 3 g (53% yield) of **7**, bp 54–56°C (0.7 Torr); ^{1}H NMR (90 MHz, $CDCl_3$) δ: 2.57 (sept, J = 6.9 Hz, 1H), 2.17 (s, 3H), 2.18–1.68 (m, 4H), 1.21 (d, J = 6.9 Hz, 3H), 1.19 (d, J = 6.9 Hz, 3H), 0.95 (t, J = 7.5 Hz, 3H), 0.82 (t, J = 7.5 Hz, 3H).

Thermolysis of oxadiazolines

An oxadiazoline (40 mg) dissolved in benzene-d_6 (0.5 mL) was placed in a thick-walled NMR tube, which was put through three freeze–pump–thaw cycles (vacuum line pressure 10^{-2} Torr) prior to sealing. Thermolysis at 80.0 ± 0.2°C was monitored by taking the NMR spectrum, and was completed after 3 days. The tubes were opened after freezing in liquid nitrogen and the reaction mixture was analysed by gc, ms, and by nmr spectroscopy.

*Thermolysis of 2-acetoxy-5-ethyl-2,5-dimethyl-Δ^3-1,3,4-oxadiazoline (**2**b)*

The mixture of **2***b* (*trans*:*cis* ratio 2.2:1) gave in 90% yield a 2.2:1 mixture of 2-acetoxy-4-methylene-3-oxahexane (**7**) and *E*-2-acetoxy-4-methyl-3-oxahex-4-ene (**8**), respectively. A 1.9:1 (*cis*:*trans*) mixture of the isomers of **2***b* gave upon thermolysis, in 90% yield, a 1.6:1 mixture of **8** and **7**, respectively. ^{1}H NMR of **7** (500 MHz, C_6D_6) δ: 6.45 (q, J = 5.2 Hz, 1H, H-2), 4.13 (d, J = 2.5 Hz, 1H, *E*-methylene), 4.04–4.00 (m, 1H, *Z*-methylene), 2.03 (J = 7.5 Hz, 2H, H-5), 1.63 (s, 3H, Ac), 1.30 (d, J = 5.2 Hz, 3H, H-1), 0.96 (t, J = 7.5 Hz, 3H, H-6); ^{13}C NMR (125.76 MHz, C_6D_6) δ: 169.21 (CO), 162.21 (C-4), 91.79 (C-2), 83.62 (sp^2-methylene), 28.05 (C-5), 20.47 (C-1), 20.21 (CH_3CO), 11.38 (C-6); MS (ci, NH_3), *m*/*e*: 159; calcd. for $(C_8H_{14}O_3 + H)^+$: 159. ^{1}H NMR of **8** (500 MHz, C_6D_6) δ: 6.40 (q, J = 5.2 Hz, 1H, H-2), 4.76 (q, J = 6.8 Hz, 1H, H-5), 1.67–1.65 (m, 3H, 4-*Me*), 1.64 (s, 3H, Ac), 1.40 (d of q, J = 6.8 Hz and 0.9 Hz, 3H, H-6), 1.32 (d, J = 5.2 Hz, 3H, H-1); ^{13}C NMR (125.76 MHz, C_6D_6) δ: 169.22 (CO), 150.43 (C-4), 97.72 (C-5), 91.94 (C-2), 20.68 (CH_3CO), 20.58 (C-6), 15.29 (4-Me), 11.89 (C-1); MS (ci, NH_3), *m*/*e*: 159; calcd. for $(C_8H_{14}O_3 + H)^+$; 159.

*Thermolysis of 2-acetoxy-5,5-diethyl-2-methyl-Δ^3-1,3,4-oxadiazoline (**2**c)*

Thermolysis of **2***c* furnished, in 88% yield, *E*-2-acetoxy-4-ethyl-3-oxahex-4-ene (**20**). Diethyl ketone (**21**), butane-2,3-dione (**14**), and acetic anhydride (**22**) were detected as minor products.

E-*2-Acetoxy-4-ethyl-3-oxahex-4-ene (**20**)*: ^{1}H NMR (500 MHz, C_6D_6) δ: 6.26 (q, J = 5.2 Hz, 1H, H-2), 4.59 (q, J = 6.9 Hz, 1H, H-5), 2.14–2.08 (q, J = 7.5 Hz, 2H, CH_2), 1.91 (s, 3H, Ac), 1.51 (d, J = 6.9 Hz, 3H, H-6), 1.41 (d, J = 5.2 Hz, 2H, H-1), 1.02 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125.76 MHz, C_6D_6) δ: 170.01 (CO), 155.50 (C-4), 96.79 (C-2), 92.64 (C-5), 22.81 (CH_2), 21.13 (CH_3CO), 20.71 (C-6), 11.93 (C-1), 11.63 (Me); MS (ci, NH_3), *m*/*e*: 173; calcd. for $(C_9H_{16}O_3 + H)^+$: 173.

*Thermolysis of 2-acetoxy-5-(1-methylethyl)-2,5-dimethyl-Δ^3-1,3,4-oxadiazoline (**2**d)*

Thermolysis of a 3:1 mixture (*trans*:*cis*) of **2***d* furnished a 4:1 mixture of 2-acetoxy-5-methyl-4-methylene-3-oxahexane (**10**) and 3-methylbutan-2-one (**12**) in 86% yield. A 2.6:1 mixture (*cis*:*trans*) of **2***d* gave a 1.2:1 mixture of **12** and **10**, respectively, in 82% yield. 1,1-Diacetoxyethane (**23**), acetic anhydride (**22**), and biacetyl (**14**) were detected as minor products. ^{1}H NMR of **10** (500 MHz, C_6D_6) δ: 6.43 (q, J = 5.2 Hz, 1H, H-2), 4.04 (d, J = 2.6 Hz, 1H, vinyl), 4.00 (d, J = 2.6 Hz, 1H, vinyl), 2.24 (sept, J = 6.9 Hz, 1H, H-5), 1.65 (s, 3H, Ac), 1.29 (d, J = 5.2 Hz, 3H, H-1), 1.02 (d, J = 6.9 Hz, 3H, H-6), 1.00 (d, J = 6.9 Hz, 3H, H-6); ^{13}C NMR (125.76 MHz, C_6D_6) δ: 169.18 (CO), 165.84 (C-4), 91.88 (C-2), 82.28 (sp^2-methylene), 33.54 (C-5), 20.79 (C-6), 20.68 (CH_3CO), 20.43 (CH_3), 20.21 (C-1).

*Thermolysis of 2-acetoxy-5,5-di-(1-methylethyl)-2-methyl-Δ^3-1,3,4-oxadiazoline (**2**e)*

The crude pyrolysate showed, in the ^{1}H nmr spectrum (C_6D_6), a pair of doublets at δ 4.52 and 4.14 (J = 2.2 Hz) attributed to the terminal methylene group of **17**. The ^{13}C spin-sort spectrum gave a positive signal at δ 81.61 (H_2C=C of the enediol system). Analysis by gc/ms gave *m*/*e* 199.1332; calcd. for $C_{11}H_{19}O_3$: 199.1329 $(M - H)^+$.

*Thermolysis of 2-acetoxy-5-(1,1-dimethylethyl)-2,5-dimethyl-Δ^3-1,3,4-oxadiazoline (**2**f)*

Thermolysis of a 14.5:1 mixture (*trans*:*cis*) of **2***f* furnished almost exclusively 2-acetoxy-5,5-dimethyl-4-methylene-3-oxahexane **24**. Minor products were 1,1-diacetoxyethane (**23**) and pinacolone (**25**) in less than 5% yield. ^{1}H NMR of **24** (500 MHz, C_6D_6) δ: 6.43 (q, J = 5.2 Hz, 1H, H-2), 4.15 (d, J = 2.9 Hz, 1H, vinyl), 4.10 (d, J = 2.9 Hz, 1H, vinyl), 1.62 (s, 3H, Ac), 1.25 (d, J = 5.2 Hz, 3H, H-1), 1.10 (s, 9H); ^{13}C NMR (125.76 MHz, C_6D_6) δ: 169.17 (CO), 168.10 (C-4), 92.14 (C-2), 81.67 (CH_2), 35.79 (C-5), 28.30 (C-6), 20.40 (CH_3CO), 20.18 (C-1).

*Thermolysis of 2-acetoxy-5-ethyl-5-methyl-2-(1-methylethyl)-Δ^3-1,3,4-oxadiazoline (**2**g)*

A 2.5:1 mixture (*trans*:*cis*) of **2***g* furnished a 2:1 mixture of 3-acetoxy-2-methyl-5-methylene-4-oxaheptane (**18**) and *E*-3-acetoxy-2,5-dimethyl-4-oxahept-5-ene (**19**), respectively.

*3-Acetoxy-2-methyl-5-methylene-4-oxaheptane (**18**)*: ^{1}H NMR (500 MHz, C_6D_6) δ: 6.29 (d, J = 4.9 Hz, 1H, H-3), 4.30 (d, J = 2.3 Hz, 1H, vinyl), 4.01 (d, J = 2.3 Hz, 1H, vinyl), 2.02 (q, J = 7.5 Hz, 2H, C-6), 1.99–1.92 (m, H-2; superimposed on the same multiplet from **19**), 1.66 (s, 3H, Ac), 0.99–0.87 (m, ~9H, CH_3; superimposed on the Me signals of **19**); ^{13}C NMR (125.76 MHz, (C_6D_6) δ: 170.12 (CO), 162.89 (C-5), 97.10 (C-3), 84.35 (=CH_2), 33.51 (C-2), 28.68 (C-6), 20.92 (CH_3CO), 17.32 (CH_3), 17.10 (CH_3), 12.50 (C-7).

E-*3-Acetoxy-2,5-dimethyl-4-oxahept-5-ene (**19**)*: ^{1}H NMR (500 MHz, C_6D_6) δ: 6.20 (d, J = 4.9 Hz, 1H, H-3), 4.91 (q, J = 6.9 Hz, 1H, H-6), 1.95–1.92 (m, 1H, H-2), 1.68 (s, 3H, Ac), 1.62 (s, 3H, 5-Me), 1.41 (d, J = 6.9 Hz, 3H, H-7), 0.99–0.87 (m, 6H, CH_3); ^{13}C NMR (125.76 MHz, C_6D_6) δ: 170.19 (CO), 151.17 (C-5), 99.08 (C-3), 97.32 (C-6), 21.09 (C-2), 20.93 (CH_3-CO), 17.47 (C-7), 17.23 (CH_3), 16.93 (CH_3), 15.66 (CH_3).

*Thermolysis of 2-acetoxy-2,5-di-(1-methylethyl)-5-methyl-Δ^3-1,3,4-oxadiazoline (**2**h)*

A 2.4:1 mixture (*trans*:*cis*) of isomers of **2***h* furnished, after thermolysis, 3-acetoxy-2,6-dimethyl-5-methylene-4-oxaheptane (**26**) and methyl isopropyl ketone (**12**) in 2:1 ratio. The yield of these products was 90%. 4-Methylpentane-2,3-dione (**27**) as detected as a minor product.

*3-Acetoxy-2,6-dimethyl-5-methylene-4-oxaheptane (**26**)*: ^{1}H NMR (500 MHz, C_6D_6) δ: 6.23 (d, J = 4.9 Hz, 1H, H-3), 4.19 (d, J = 2.6 Hz, 1H, vinyl), 4.00 (d, J = 2.6 Hz, vinyl), 2.24 (sept, J = 6.9 Hz, 1H, methine), 1.95 (d of sept, J = 6.9 and 4.9 Hz, 1H, H-2), 1.69 (s, 3H, Ac), 1.02 (d, J = 6.9 Hz, 3H, Me), 1.01 (d, J = 6.9 Hz, 3H, Me), 0.90 (d, J = 6.9 Hz, 3H, Me), 0.89 (d, J = 6.9 Hz, 3H, Me); ^{13}C NMR (125.76 MHz, C_6D_6) δ: 169.48 (CO), 165.78 (C-5), 96.38 (C-3), 82.24 (=CH_2), 32.74 (C-6), 32.97 (C-2), 20.79 (CH_3CO), 20.75 (CH_3), 20.35 (CH_3), 16.79 (CH_3), 16.46 (CH_3).

*Thermolysis of 5,5-diethyl-2-(2-methylpropanoyloxy)-2-methyl-Δ^3-1,3,4-oxadiazoline (**5**)*

Thermolysis of this oxadiazoline gave the 2-(2-methylpropanoyloxy)-4-ethyl-3-oxahex-4-ene, presumably the *E* isomer (**28**), in 91% yield; ^{1}H NMR (500 MHz, C_6D_6) δ: 6.43 (q, J = 5.2 Hz, 1H, H-2), 4.66 (q, J = 6.8 Hz, 1H, H-5), 2.34 (sept, J = 6.9 Hz, 1H, CH-CO), 2.07 (q, J = 7.5 Hz, 2H, CH_2), 1.42 (d, J = 6.8 Hz, 3H, H-6), 1.33 (d, J = 5.2 Hz, 3H, H-1), 1.04–0.98 (m, 9H, CH_3); ^{13}C NMR (125.76 Hz, C_6D_6) δ: 175.88 (CO), 155.86 (C-4), 96.53 (C-2), 92.38 (C-5), 34.70 (*C*HCO), 23.31 (CH_2), 21.00 (CH_3), 19.36 (CH_3), 19.14 (CH_3), 12.36 (CH_3), 11.85 (CH_3).

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